GPC Tratamiento farmacológico del trastorno obsesivo compulsivo en adultos

Guía de práctica clínica
(basada en el método ADAPTE)

Tratamiento farmacológico del trastorno obsesivo compulsivo en adultos

AUTORES

José Manuel Menchón, Julio Bobes, Cecilio Álamo, María Pino Alonso, María Paz García Portilla, Ángela Ibáñez, Eva Real, Manuel Bousoño, María Dolores Saiz González y Jerónimo Saiz Ruiz

Sociedad Española de Psiquiatría SEP

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Conflicto de intereses

El Dr. Menchón ha recibido becas de investigación de la institución Medtronic, AB Biotics; becas de viaje de Servier y honorarios de Janssen como ponente. El Dr. Bobes ha recibido becas de investigación, ha sido consultor, asesor o ponente en los últimos cinco años de: AB-Biotics, Acadia Pharmaceuticals, Angelini, Casen Recordati, D&A Pharma, Exeltis, Gilead, GSK, Ferrer, Indivior, Janssen-Cilag, Lundbeck, Mundipharma, Otsuka, Pfizer, Reckitt-Benckiser, Roche, Servier, Shire y Schwabe Farma Ibérica; ha obtenido financiación para investigación por parte del Ministerio de Economía y Competitividad —Centro de Investigación Biomédica en Red de área de Salud Mental (CIBERSAM) del Instituto de Salud Carlos III—, Ministerio de Sanidad, Servicios Sociales e Igualdad español-Plan Nacional sobre Drogas y del 7.º Programa Marco de la Unión Europea. El Dr. Álamo ha sido ponente honorario de Adamed, Angelini, Casen-Recordati, Exeltis, Ferrer, Fuinsa, Grunenthal, Indivior, Janssen-Cilag, Juste SAQF, Kyowa Kiry, Lundbeck, Mudipharma, Normon, Novartis, Otsuka, Pfizer, Roche, Rovi, Rubió, Servier y Shire; consultor honorario para: Angelini, Casen-Recordati, Janssen-Cilag y Kyowa Kiry, Mudipharma, Normon. La Dra. García-Portilla es miembro del Consejo asesor de Angelini, European Medicines Agency, Janssen-Cilag; ha recibido becas de investigación del Instituto de Salud Carlos III, Janssen-Cilag y Lundbeck; ha participado en ponencias de: Janssen-Cilag, Lundbeck, Otsuka y Pfizer. La Dra. Ibáñez ha recibido becas y ha sido ponente o asesora para: Bristol-Myers Squibb, Lundbeck, Otsuka Pharmaceutical y Servier. El Dr. Bousoño ha sido ponente honorario para: Lundbeck, Servier, Exeltis, GlaxoSmithKline, Pfizer y Otsuka; ha recibido becas de viaje de: Lundbeck, Servier, Exeltis, GlaxoSmithKline, Pfizer y Otsuka. La Dra. Saiz-González ha participado como conferenciante o experto para: Otsuka, Janssen y Pfizer. El Dr. Saiz-Ruiz ha participado como conferenciante o experto para Adamed, Lundbeck, Servier, Neurofarmagen, Otsuka, Indivior, Schwabe y Janssen; ha recibido ayudas para investigación de Agencias Públicas (CIBERSAM, FIS, CAM, Universidad de Alcalá), Fundación Canis Majoris, Lundbeck, Janssen, Medtronic y Ferrer.

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PRÓLOGO

A pesar de la existencia de tratamientos efectivos basados en la evidencia para el tratamiento del trastorno obsesivo-compulsivo (TOC), el abordaje de esta enfermedad sigue siendo subóptimo. Disponer de una guía terapéutica farmacológica del TOC puede ayudar a mejorar el manejo de la enfermedad en nuestro entorno y contribuir a reducir la carga de la enfermedad para el paciente. Con el patrocinio de la Sociedad Española de Psiquiatría, un grupo de expertos ha desarrollado una guía para el tratamiento farmacológico del TOC a partir de algunas guías existentes siguiendo la metodología de la ADAPTE Collaboration.

En este libro se resume el proceso de elaboración de esta guía y las recomendaciones adoptadas por consenso por el grupo elaborador de las guías, que se han agrupado en cinco áreas de interés: tratamiento agudo, duración del tratamiento, predictores de respuesta y síntomas especiales, respuesta parcial a falta de reacción al tratamiento, y poblaciones especiales.

No queremos terminar este prólogo sin expresar nuestro agradecimiento a Fernando Rico-Villademoros (Cociente S. L., Madrid) por su asesoría metodológica durante todo el proyecto, así como su ayuda editorial en la preparación de esta guía; finalmente, nuestro más sincero reconocimiento a la Sociedad Española de Psiquiatría por su colaboración en la financiación del asesoramiento editorial.

INTRODUCCIÓN

El trastorno obsesivo compulsivo (TOC) es una enfermedad neuropsiquiátrica que afecta al 1,1-1,8% de la población a nivel internacional[1] y que se acompaña de un importante deterioro en la funcionalidad y en la calidad de vida del paciente[2]. Estudios recientes indican que el nivel educativo alcanzado se ve reducido de manera persistente y grave en los sujetos afectados por la enfermedad, especialmente cuando el trastorno se inicia en edades tempranas[3]. También se han descrito un elevado riesgo de suicidio[4,5] y una importante sobrecarga en los familiares y cuidadores que tienen que convivir con pacientes que a menudo presentan síntomas graves de manera continuada[6,7].

A pesar de la existencia de tratamientos efectivos basados en la evidencia, numerosos estudios indican que el abordaje del TOC sigue siendo subóptimo. Entre los pacientes que reciben asistencia, menos de un 40% siguen una terapia específica para el TOC, y menos de un 10% un tratamiento basado en la evidencia[8,9]. Existen otros factores adicionales que podrían estar influyendo de manera desfavorable sobre la respuesta al tratamiento y el curso de la enfermedad. Por un lado, el retraso entre el inicio de los síntomas obsesivos y la búsqueda de atención profesional es muy llamativo, alcanzando un rango de 8 a 17 años[10,11]. Este hecho es relevante porque en estudios naturalísticos el retraso en el tratamiento se ha asociado a una peor respuesta farmacológica[11] y la cronicidad basal de la patología como consecuencia de la ausencia de tratamiento es uno de los factores que más claramente se ha asociado a un peor pronóstico a largo plazo en los estudios evolutivos[12]. Por otro lado, el TOC presenta comorbilidad psiquiátrica con mucha frecuencia (depresión, otros trastornos de ansiedad, trastornos del control de los impulsos y trastornos por abuso de sustancias, entre otros)[9,13], lo cual dificulta, a su vez, el diagnóstico y la intervención terapéutica[14]. Finalmente, hay que considerar que la mayoría de los pacientes que se considerarán "respondedores" (porque han conseguido reducir la gravedad de los síntomas en más del 35% con el tratamiento) seguirán experimentando síntomas clínicos de manera continuada[15]. Estos factores parecen estar condicionando la impresión de muchos autores que describen el TOC como un trastorno crónico, debilitante y de mal pronóstico.

Disponer de una guía terapéutica farmacológica del TOC puede ayudar a mejorar el manejo de la enfermedad en nuestro entorno y contribuir a reducir la carga de la enfermedad para el paciente[16]. Con este objetivo y el patrocinio de la Sociedad Española de Psiquiatría, un grupo de expertos ha desarrollado una guía para el tratamiento farmacológico del TOC a partir de algunas guías existentes siguiendo la metodología propuesta por la ADAPTE Collaboration.

1 ELABORACIÓN DE LA GUÍA: MÉTODO ADAPTE

El desarrollo y actualización de guías de práctica clínica de calidad requiere una inversión de recursos muy importante. Por otra parte, numerosas organizaciones a nivel mundial realizan guías sobre el mismo problema de salud. Con objeto de aprovechar las guías existentes y disminuir la duplicación de esfuerzos se ha propuesto la adaptación como una alternativa eficiente al desarrollo *de novo* de guías terapéuticas[17].

La adaptación de guías es un proceso sistemático que busca respaldar o modificar las guías desarrolladas en un ámbito para su aplicación e implementación en otro distinto. El proceso de adaptación se lleva a cabo en tres fases[17]:

- Fase de puesta en marcha: se identifican las habilidades y recursos necesarios para llevar a cabo el proceso.
- Fase de adaptación: se seleccionan los temas o preguntas específicas a las que debe dar respuesta la guía, se realiza la búsqueda de guías, se valora su calidad y se seleccionan las guías que se utilizarán como fuente de la evidencia; se lleva a cabo posteriormente el proceso de recogida y, si procede, la adaptación de las recomendaciones recogidas
- Fase de finalización: se obtiene la opinión de decisores afectados por la guía para actualizar y crear el documento final.
- El manual completo de desarrollo de guías siguiendo el proceso ADAPTE puede consultarse en la página web de la Guidelines International Network[17].

1.1. Fase de puesta en marcha

El proyecto fue llevado a cabo por un grupo de expertos seleccionados por la Sociedad Española de Psiquiatría, compuesto por nueve psiquiatras con experiencia en el manejo de pacientes con trastorno obsesivo-compulsivo (TOC), un farmacólogo clínico y un experto en metodología de la investigación, que se constituyeron como grupo elaborador de la guía y establecieron en una primera reunión presencial el alcance y los aspectos clave que debería abordar la guía (Tabla 1).

Tabla 1. Aspectos clave abordados en la elaboración de la guía para el tratamiento farmacológico del trastorno obsesivo-compulsivo en adultos

1. Tratamiento agudo a) Tratamiento psicofarmacológico *versus* psicoterapia *versus* tratamiento combinado b) Eficacia, seguridad y tolerabilidad de los tratamientos psicofarmacológicos
2. Duración del tratamiento
3. Predictores de respuesta y síntomas especiales
4. Tratamiento farmacológico del trastorno obsesivo-compulsivo con respuesta parcial a falta de respuesta al tratamiento a) Optimización o sustitución del tratamiento b) Potenciación c) Otras opciones terapéuticas
5. Tratamiento farmacológico del trastorno obsesivo-compulsivo en poblaciones especiales a) Pacientes de edad avanzada b) Mujeres embarazadas y en período de lactancia c) Comorbilidad psiquiátrica

1.2. Fase de adaptación

Búsqueda, cribado y evaluación de las guías

Se realizó una búsqueda de guías relevantes para el tratamiento farmacológico del TOC en las siguientes fuentes: National Guidelines Clearinghouse, Guidelines International Network, Institute for Clinical Systems Improvement, Canadian Agency for Drugs and Technologies in Health, Canadian Medical Association, New Zealand Guidelines Group, Australian Clinical Practice Guidelines, Scottish Intercollegiate Guidelines Network, National Institute for Health and Care Excellence, Centre for Reviews and Dissemination University of York, American Psychiatric Association Practice Guidelines, World Health Organization, International College of Psychopharmacology, World Psychiatric Association, European College of Neuropsychopharmacology y World Federation of Biological Psychiatry.

Los criterios iniciales de selección de las guías fueron los siguientes: abarcar el tratamiento farmacológico del TOC y que la población objetivo de la guía incluyera los adultos. Con la búsqueda inicial se encontraron diez documentos[14,18-26], que se presentan en la Tabla 2. Dos de los documentos fueron excluidos de la evaluación, dado que no se trataba de guías de práctica clínica[24,25]. Los ocho documentos restantes seleccionados para la evaluación fueron agrupados en seis guías: la guía del National Institute for Health and Care Excellence del Reino Unido de 2005[21] y la actualización de 2013[20], la guía de la American Psychiatric Association de Estados Unidos de 2007[23] y la actualización de 2013[22], una guía canadiense de práctica clínica[18], la guía de la British Association for Psychopharmacology[19], la guía de la World Federation of Societies of Biological Psychiatry[26], y un consenso desarrollado por un grupo de expertos internacionales[14].

Tabla 2. Guías, consensos y otros documentos resultantes de la búsqueda de guías de práctica clínica del trastorno obsesivo-compulsivo

Guía	Fuente	Enlace/Referencia	Año
Canadian clinical practice guidelines for the management of anxiety, posttraumatic stress and obsessive-compulsive disorders	CMA, búsqueda bibliográfica	Katzman MA, Bleau P, Blier P, Chokka P, Kjernisted K, Van Ameringen M; Canadian Anxiety Guidelines Initiative Group on behalf of the Anxiety Disorders Association of Canada/Association Canadienne des troubles anxieux and McGill University, Antony MM, Bouchard S, Brunet A, Flament M, Grigoriadis S, Mendlowitz S, O'Connor K, Rabheru K, Richter PM, Robichaud M, Walker JR. Canadian clinical practice guidelines for the management of anxiety, posttraumatic stress and obsessive-compulsive disorders. BMC Psychiatry. 2014;14 Suppl 1:S1.	2014
Evidence-based pharmacological treatment of anxiety disorders, post-traumatic stress disorder and obsessive-compulsive disorder: A revision of the 2005 guidelines from the British Association for Psychopharmacology	Búsqueda bibliográfica	Baldwin DS, Anderson IM, Nutt DJ, Allgulander C, Bandelow B, den Boer JA, Christmas DM, Davies S, Fineberg N, Lidbetter N, Malizia A, McCrone P, Nabarro D, O'Neill C, Scott J, van der Wee N, Wittchen HU. Evidence-based pharmacological treatment of anxiety disorders, post-traumatic stress disorder and obsessive-compulsive disorder: a revision of the 2005 guidelines from the British Association for Psychopharmacology. J Psychopharmacol. 2014;28(5):403-39.	2014
Obsessive-compulsive disorder. Evidence Update September 2013	NICE	https://www.nice.org.uk/guidance/cg31/evidence/evidence-update-194847085	2013
Obsessive compulsive disorder (OCD) and body dysmorphic disorder (BDD) (CG31)	GIN, NICE	https://www.nice.org.uk/guidance/cg31/evidence/full-guideline-194883373	2005
Practice guideline for the Treatment of Patients With Obsessive-Compulsive Disorder	NGC, GIN, American Psychiatric Association Practice Guidelines, búsqueda bibliográfica	https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/ocd.pdf	2007
Guideline Watch (march 2013): Practice Guideline for the Treatment of Patients with Obsessive-Compulsive Disorder	American Psychiatric Association Practice Guidelines	http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/ocd-watch.pdf	2013
Obsessive-compulsive disorder. The role of the GP	Australian Clinical Practice Guidelines	http://www.racgp.org.au/download/Documents/AFP/2013/Sep/201309johnson.pdf	2013
A 2012 evidence-based algorithm for the pharmacotherapy for obsessive-compulsive disorder	Búsqueda bibliográfica	Stein DJ, Koen N, Fineberg N, Fontenelle LF, Matsunaga H, Osser D, Simpson HB. A 2012 evidence-based algorithm for the pharmacotherapy for obsessive-compulsive disorder. Curr Psychiatry Rep. 2012;14(3):211-9. DOI: 10.1007/s11920-012-0268-9	2012
Guidelines for the pharmacological treatment of anxiety disorders, obsessive-compulsive disorder and posttraumatic stress disorder in primary care	Búsqueda bibliográfica	Bandelow B, Sher L, Bunevicius R, Hollander E, Kasper S, Zohar J, Möller HJ; WFSBP Task Force on Mental Disorders in Primary Care; WFSBP Task Force on Anxiety Disorders, OCD and PTSD. Guidelines for the pharmacological treatment of anxiety disorders, obsessive-compulsive disorder and posttraumatic stress disorder in primary care. Int J Psychiatry Clin Pract. 2012;16(2):77-84. DOI: 10.3109/13651501.2012.667114. Epub 2012 Apr 30. Erratum in: Int J Psychiatry Clin Pract. 2012;16(3):242. Int J Psychiatry Clin Pract. 2013;17(1):76.	2012

Tabla 2. Guías, consensos y otros documentos resultantes de la búsqueda de guías de práctica clínica del trastorno obsesivo-compulsivo *(cont.)*

Guía	Fuente	Enlace/Referencia	Año
On the pharmacotherapy of obsessive-compulsive disorder: is a consensus possible?	Búsqueda bibliográfica	Todorov C, Freeston MH, Borgeat F. On the pharmacotherapy of obsessive-compulsive disorder: is a consensus possible? Can J Psychiatry. 2000;45(3): 257-62.	2000

CMA: Canadian Medical Association; GIN: Guidelines International Network; NGC: National Guidelines Clearinghouse; NICE: National Institute for Health and Care Excellence.

Las seis guías seleccionadas fueron evaluadas individualmente por diez miembros del grupo elaborador de la guía utilizando la herramienta de evaluación Appraisal of Guidelines for Research and Evaluation II (AGREE II)[27]. El AGREE II es un instrumento genérico que evalúa el proceso de desarrollo y comunicación de la guía. El instrumento tiene 23 ítems que se responden en una escala de acuerdo de 7 puntos; los 23 ítems se agrupan en seis dimensiones relacionadas con la calidad: alcance y objetivo, participación de los implicados, rigor en la elaboración, claridad en la presentación, aplicabilidad e independencia editorial. Además, el instrumento incluye una evaluación de la calidad global de las guías y una pregunta respecto a si el evaluador recomendaría la guía para su uso, con o sin modificaciones, o no la recomendaría. Todos los revisores utilizaron para su formación en la evaluación de las guías el tutorial propuesto por el AGREE II (disponible en: http://www.agreetrust.org/resource-centre/agree-ii-training-tools/). El cálculo de la puntuación se realizó de acuerdo con las recomendaciones incluidas en el AGREE II.

Los resultados de la evaluación de las seis guías se presentan en la Figura 1. En una reunión presencial del grupo elaborador de la guía se seleccionaron finalmente las cuatro guías que, a juicio de los evaluadores, presentaban una mayor calidad en función de la puntuación en rigor de elaboración y eran recomendables —con modificaciones— para su utilización. Estas guías fueron la guía del National Institute for Health and Care Excellence del Reino Unido de 2005[21] y la actualización de 2013[20] (denominadas a partir de ahora NICE), la guía de la American Psychiatric Association de Estados Unidos de 2007[23] y la actualización de 2013 (denominada a partir de ahora APA)[22], la guía canadiense de práctica clínica para el manejo de algunos trastornos de ansiedad (denominada a partir de ahora Canadiense)[18], y la guía de la British Association for Psychopharmacology (denominada a partir de ahora BAP)[19].

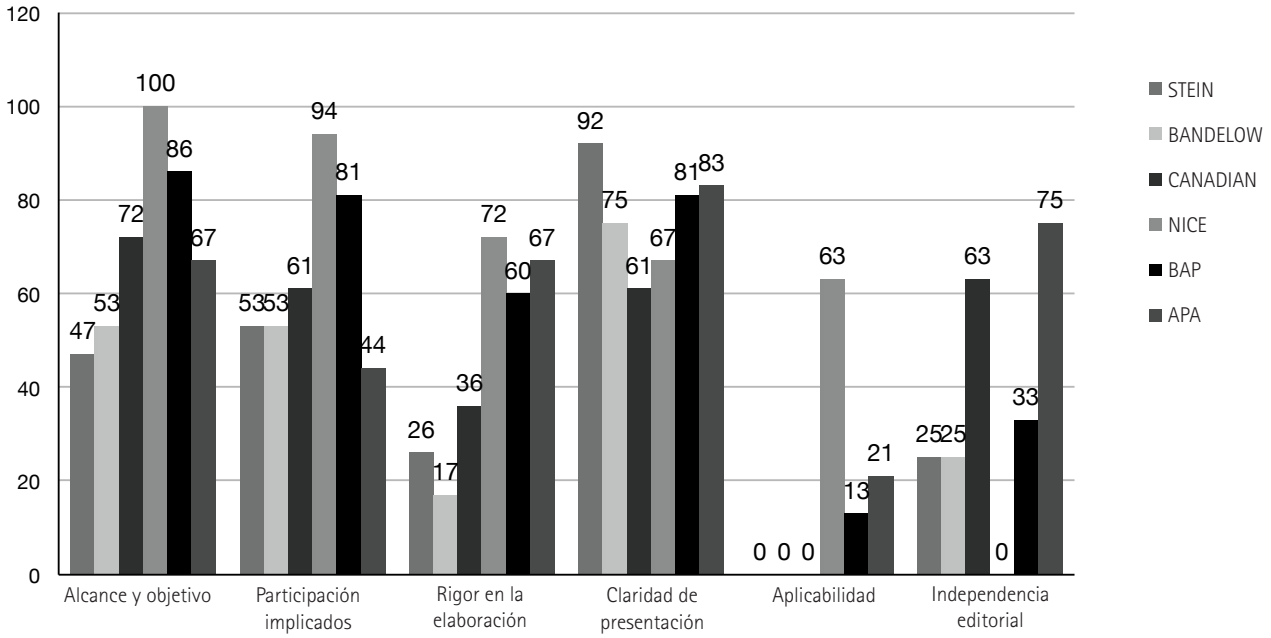

Figura 1. Evaluación de las guías de práctica clínica inicialmente seleccionadas mediante el instrumento AGREE II.

Selección y elaboración de las recomendaciones

Las recomendaciones de las cuatro guías fuente (NICE, APA, Canadiense y BAP) fueron recogidas por los diez evaluadores en una matriz de recomendaciones que incluía una por una las recomendaciones concretas incluidas en la guía, la fuente (esto es, la guía de procedencia de la recomendación) y posibles comentarios. Una vez recogidas todas las recomendaciones de las diferentes guías para cada uno de los temas abarcados por esta guía, el grupo elaborador se reunió mediante dos teleconferencias y una reunión presencial para discutir las recomendaciones y seleccionarlas en función de la consistencia de la recomendación con la situación de la evidencia actual y su aceptabilidad o aplicabilidad a nuestro contexto. Utilizando un sistema informal de consenso la recomendación fue finalmente adoptada, modificada o rechazada. Las recomendaciones seleccionadas en su versión original, su traducción o modificación y los motivos de la modificación u otros comentarios se pueden consultar en el Apéndice 1.

Para evaluar la consistencia de la recomendación con la evidencia actual se realizó inicialmente una búsqueda bibliográfica en PubMed, PsychInfo y Cochrane Library de ensayos clínicos aleatorizados o revisiones sistemáticas de intervenciones en TOC publicadas hasta febrero de 2016 y sin fecha límite de inicio. La estrategia de búsqueda se presenta en la Tabla 3. La búsqueda fue revisada por uno de los miembros del grupo elaborador de la guía experto en metodología de la investigación, que seleccionó y clasificó, de acuerdo con los temas abarcados por la guía, los artículos de interés; el documento resultante –que se muestra en el Apéndice 2— fue distribuido entre todos los miembros del grupo elaborador de la guía. Además, se realizó una búsqueda bibliográfica específica sobre TOC y embarazo o lactancia (Apéndice 3).

Tabla 3. Estrategia de búsqueda de ensayos clínicos aleatorizados o revisiones sistemáticas de estudios de intervenciones para el trastorno obsesivo-compulsivo

PUBMED (1.376 referencias)
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ENSAYOS CLÍNICOS (Estrategia Cochrane)
#3,"Search randomized controlled trial[pt]", 404220
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#5,"Search randomized[tiab]", 366746
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#8,"Search randomly[tiab]", 246514
#9,"Search trial[ti]",147449
#10,"Search #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9", 1009893
#11,"Search animals[mh] NOT humans[mh]", 4172885
#12,"Search #10 NOT #11", 931516
TOC + ENSAYOS CLÍNICOS
#13,"Search #2 AND #12", 1100
METAANÁLISIS/REVISIONES SISTEMÁTICAS (Estrategia utilizada)

Tabla 3. Estrategia de búsqueda de ensayos clínicos aleatorizados o revisiones sistemáticas de estudios de intervenciones para el trastorno obsesivo-compulsivo *(cont,)*
PUBMED (1.376 referencias)
#14,Search #2 Filters: Meta-Analysis; Systematic Reviews, 296
#15,"Search #2 AND meta-analysis[pt]", 111
#16,"Search #2 AND (metaanalysis[tiab] OR meta-analysis[tiab] OR ""systematic review""[tiab] OR cochrane[tiab] OR medline[tiab])", 229
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TOC (Ensayos clínicos y metaanálisis/Revisiones sistemáticas)
#13 OR #19, 1376
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MJSUB.EXACT("Obsessive Compulsive Disorder"), 9977
(words or phrases)
TI,AB("checking behavior") OR TI,AB("checking behaviors") OR TI,AB(compulsion) OR TI,AB(compulsions) OR TI,AB(compulsive) OR TI,AB(hoarding) OR TI,AB(obsession) OR TI,AB(obsessional) OR TI,AB(obsessions) OR TI,AB(obsessive) OR TI,AB(rituals), 36603
TOC (Mesh) + (words or phrases)
MJSUB.EXACT("Obsessive Compulsive Disorder") AND (TI,AB("checking behavior") OR TI,AB("checking behaviors") OR TI,AB(compulsion) OR TI,AB(compulsions) OR TI,AB(compulsive) OR TI,AB(hoarding) OR TI,AB(obsession) OR TI,AB(obsessional) OR TI,AB(obsessions) OR TI,AB(obsessive) OR TI,AB(rituals)), 9754
ENSAYOS CLÍNICOS
MJSUB.EXACT("Clinical trials"), 5586
DTYPE(randomized controlled trial) OR DTYPE(controlled clinical trial) OR TI,AB(randomized) OR TI,AB(placebo) OR TI,AB(randomly) OR TI(trial), 136658
MJSUB.EXACT("Clinical trials") AND DTYPE(randomized controlled trial) OR DTYPE(controlled clinical trial) OR TI,AB(randomized) OR TI,AB(placebo) OR TI,AB(randomly) OR TI(trial), 137729
TOC + ENSAYOS CLÍNICOS
TOC (9754 refs) AND Clinical trials (137729) = 765
METAANÁLISIS/REVISIONES SISTEMÁTICAS (Estrategia utilizada)
TI,AB(metaanalysis) OR TI,AB(meta-analysis) OR TI,AB(systematic review) OR TI,AB(cochrane) OR TI,AB(medline), 44556
TOC + METAANÁLISIS/REVISIONES SISTEMÁTICAS
MJSUB.EXACT("Obsessive Compulsive Disorder") AND (TI,AB("checking behavior") OR TI,AB("checking behaviors") OR TI,AB(compulsion) OR TI,AB(compulsions) OR TI,AB(compulsive) OR TI,AB(hoarding) OR TI,AB(obsession) OR TI,AB(obsessional) OR TI,AB(obsessions) OR TI,AB(obsessive) OR TI,AB(rituals)) AND (TI,AB(metaanalysis) OR TI,AB(meta-analysis) OR TI,AB(systematic review) OR TI,AB(cochrane) OR TI,AB(medline)), 241
MJSUB.EXACT("Obsessive Compulsive Disorder") AND (TI,AB("checking behavior") OR TI,AB("checking behaviors") OR TI,AB(compulsion) OR TI,AB(compulsions) OR TI,AB(compulsive) OR TI,AB(hoarding) OR TI,AB(obsession) OR TI,AB(obsessional) OR TI,AB(obsessions) OR TI,AB(obsessive) OR TI,AB(rituals)) AND Limits (meta-analysis y revisiones sistematicas), 153

Tabla 3. Estrategia de búsqueda de ensayos clínicos aleatorizados o revisiones sistemáticas de estudios de intervenciones para el trastorno obsesivo-compulsivo *(cont,)*
PUBMED (1.376 referencias)
Meta-análisis/RS (tw o límites), 241
TOC (Ensayos clínicos y metaanálisis/Revisiones sistemáticas)
TOC (9754 refs) AND Meta-análisis/Revisiones Sistemáticas (241) = 255
COCHRANE (686 referencias)
TOC (Mesh)
#1 MeSH descriptor: [Compulsive Behavior] explode all trees, 440
#2 MeSH descriptor: [Obsessive Behavior] explode all trees, 36
#3 MeSH descriptor: [Obsessive-Compulsive Disorder] explode all trees, 725
#4 (#1 or #2 or #3), 1175
(words or phrases)
#5 (checking behavior:ti,ab OR "checking behaviors":ti,ab OR compulsion:ti,ab OR compulsions:ti,ab OR compulsive:ti,ab OR hoarding:ti,ab OR obsession:ti,ab OR obsessional:ti,ab OR obsessions:ti,ab OR obsessive:ti,ab OR rituals:ti,ab), 1876
TOC (Mesh) + (words or phrases)
#6 (#4 and #5), 714
ENSAYOS CLÍNICOS
#7 randomized clinical trial:pt, 312647
#8 controlled clinical trial:pt, 394601
#9 randomized:ti,ab, 324787
#10 placebo:ti,ab, 163570
#11 randomly:ti,ab, 130571
#12 trial:ti, 162239
#13 MeSH descriptor: [Clinical Trials as Topic] this term only, 34554
#14 (#7 or #8 or #9 or #10 or #11 or #12 or #13), 664113
TOC + ENSAYOS CLÍNICOS
#15 (#6 and #14), 652
METAANÁLISIS/REVISIONES SISTEMÁTICAS (Estrategia utilizada)
#16 (metaanalysis or meta-analysis or systematic review*), 60853
#17 MeSH descriptor: [Meta-Analysis as Topic] explode all trees, 581
#18 MeSH descriptor: [Meta-Analysis] explode all trees, 166
#19 (#16 or #17 or #18), 60853
#20 (#6 and #19), 52
TOC (Ensayos clínicos y metaanálisis/Revisiones sistemáticas)
#15 or #20, 686

1.3. Fase de finalización

Tras la publicación de la guía el objetivo es recoger, a través de la página web de la Sociedad Española de Psiquiatría, las opiniones de los potenciales decisores a los que va dirigida para tenerlas en cuenta en futuras actualizaciones.

2 RESULTADOS DEL CONSENSO

1. Alcance del consenso

Este consenso es relevante para adultos (18 o más años de edad) diagnosticados de trastorno obsesivo-compulsivo (TOC) y sus familiares/cuidadores, así como para todos los profesionales sanitarios implicados en proporcionarles ayuda, tratamiento o cuidado a nivel de atención especializada de salud mental.

En cuanto al ámbito, este se refiere a la atención especializada de salud mental.

Finalmente, las acciones o intervenciones se refieren al tratamiento farmacológico, solo o en combinación con otras modalidades terapéuticas del TOC de distinta gravedad y respuesta al tratamiento previo.

2. Recomendaciones

Tras la búsqueda y análisis de los datos, se establecieron las recomendaciones que se muestran en los siguientes epígrafes.

2.1. Tratamiento agudo

a) Tratamiento psicofarmacológico *versus* psicoterapia *versus* tratamiento combinado (Tabla 4)

Tabla 4. Recomendaciones sobre tratamiento psicofarmacológico *versus* psicoterapia *versus* tratamiento combinado

Recomendación	Fuente
La TCC y los ISRS se recomiendan como tratamientos eficaces y seguros de primera línea en el TOC.	APA
El utilizar la TCC o un ISRS dependerá de la naturaleza y gravedad de los síntomas del paciente, la naturaleza de cualquier comorbilidad psiquiátrica o médica y su tratamiento, la disponibilidad de la TCC, y los antecedentes de tratamientos previos, medicación actual, capacidades y preferencias. La TCC sola, consistente en la EPR, se recomienda como tratamiento inicial para un paciente que no está muy deprimido, ansioso, o gravemente enfermo como para cooperar con esta modalidad de tratamiento, o para un paciente que prefiere no tomar medicación y esté dispuesto a esforzarse en lo que la TCC requiere.	APA
El tratamiento combinado debería tenerse en cuenta para pacientes con comorbilidad psiquiátrica para la cual el IRS es eficaz.	APA
El tratamiento combinado debería tenerse en cuenta para pacientes que desean limitar la duración del tratamiento con el IRS.	APA

Tabla 4. Recomendaciones sobre tratamiento psicofarmacológico *versus* psicoterapia *versus* tratamiento combinado *(cont.)*

Recomendación	Fuente
En el tratamiento inicial de adultos con TOC, los tratamientos psicológicos de baja intensidad (incluyendo EPR) (hasta 10 horas de terapia por paciente) se deberían ofrecer al enfermo si su grado de alteración funcional es leve y/o expresa su preferencia por esta estrategia.	NICE
En adultos con TOC con alteración funcional leve que no son capaces de implicarse en una TCC de baja intensidad (incluyendo EPR), o para los que el tratamiento de baja intensidad se ha demostrado que es inadecuado, debería ofrecérseles un intento terapéutico con un ISRS o una TCC más intensiva (incluyendo EPR) (más de 10 horas de terapia por paciente), dado que estos tratamientos parecen mostrar una eficacia similar.	NICE
En adultos con TOC con alteración funcional moderada debería ofrecérseles un intento terapéutico con un ISRS o una TCC más intensiva (incluyendo EPR) (más de 10 horas de terapia por paciente), dado que estos tratamientos parecen mostrar una eficacia similar.	NICE
En adultos con TOC con alteración funcional grave debería ofrecérseles tratamiento combinado con un ISRS y una TCC (incluyendo EPR).	NICE

APA: American Psychiatric Association; EPR: exposición y prevención de respuesta; IRS: inhibidor de la recaptación de serotonina (incluye clomipramina y los ISRS); ISRS: inhibidor selectivo de la recaptación de serotonina; NICE: National Institute for Health and Care Excellence; TCC: terapia cognitivo-conductual; TOC: trastorno obsesivo-compulsivo.

b) Eficacia, seguridad y tolerabilidad de los tratamientos psicofarmacológicos (Tabla 5)

Según señala la guía de la APA, aunque algunos metaanálisis de ensayos clínicos controlados con placebo sugieren una mayor eficacia de clomipramina respecto a fluvoxamina, fluoxetina y sertralina, los resultados de los ensayos clínicos que han comparado de forma directa la clomipramina y los inhibidores selectivos de la recaptación de serotonina (ISRS) no apoyan esta impresión[22.23]. Dado que los ISRS tienen un perfil de efectos secundarios menos problemático que la clomipramina, es preferible un ISRS como primer intento terapéutico[23].

Por otra parte, varios estudios han evaluado la relación dosis-respuesta con diferentes ISRS[28-32] y, de acuerdo con la guía BAP[19], existen algunas pruebas de una mayor eficacia de las dosis elevadas de ISRS, aunque con una menor tolerabilidad. En este mismo sentido, la guía de la APA señala también que se puede obtener una respuesta y alivio de los síntomas mayor con dosis que exceden las dosis máximas recomendadas por el fabricante[22].

Tabla 5. Recomendaciones sobre eficacia, seguridad y tolerabilidad de los tratamientos psicofarmacológicos

Recomendación	Fuente
Aunque todos los ISRS (incluyendo citalopram y escitalopram) parecen presentar la misma eficacia, el paciente individual puede responder a un tratamiento y no a otro. Para elegir el ISRS, el psiquiatra debería considerar la seguridad y aceptabilidad de determinados efectos adversos por el paciente, incluyendo cualquier precaución que aparezca en su ficha técnica, interacciones farmacológicas potenciales, respuesta al tratamiento previo y presencia de comorbilidades médicas generales.	APA
Para adultos con TOC, el tratamiento farmacológico inicial debería ser uno de los siguientes ISRS: citalopram, escitalopram, fluoxetina, fluvoxamina, paroxetina o sertralina (véanse las contraindicaciones en Tabla 6).	NICE
Los profesionales sanitarios deberían ser conscientes del aumento del riesgo de interacciones farmacológicas cuando prescriben un ISRS a un adulto con TOC que está en tratamiento con otras medicaciones.	NICE
En un adulto con TOC, si no ha habido respuesta a una pauta completa de tratamiento con un ISRS, se debería comprobar si el paciente está tomando la medicación de forma regular y a la dosis prescrita y que no existe interferencia por el alcohol o el abuso de sustancias.	NICE
La clomipramina debería considerarse en el tratamiento del adulto con TOC después de intentar al menos con un ISRS y este haya sido ineficaz o mal tolerado, si el paciente prefiere clomipramina, o ha habido previamente una buena respuesta a este fármaco.	NICE

Tabla 5. Recomendaciones sobre eficacia, seguridad y tolerabilidad de los tratamientos psicofarmacológicos *(cont.)*

Recomendación	Fuente
Antes de prescribir clomipramina a un adulto con TOC con un riesgo significativo de enfermedad cardiovascular se debería realizar un electrocardiograma y una medición de la presión arterial. Precauciones similares son aplicables a otros antidepresivos, por lo que en pacientes con este tipo de riesgo se deben tener en cuenta las recomendaciones de las correspondientes fichas técnicas.	NICE
En pacientes con factores de riesgo cardíacos conocidos, incluyendo hipopotasemia e hipomagnesemia, se deben evitar dosis elevadas de citalopram y los antidepresivos tricíclicos.	BAP
En adultos con TOC, si no ha habido respuesta adecuada a la dosis estándar de clomipramina, y no hay efectos secundarios relevantes, se debería considerar un aumento gradual de la dosis en consonancia con la pauta propuesta en su ficha técnica.	NICE
Los siguientes fármacos no deberían utilizarse como tratamiento inicial del TOC sin comorbilidad: - Antidepresivos tricíclicos distintos de clomipramina - Antidepresivos relacionados con los tricíclicos - Inhibidor de la recaptación de serotonina y noradrenalina - Inhibidor de la monoaminooxidasa - Ansiolíticos (excepto con precaución durante un período corto de tiempo para contrarrestar la activación inicial de los ISRS) - Antipsicóticos - Otros fármacos que no tengan la indicación de TOC	NICE

APA: American Psychiatric Association; BAP: British Association of Psychopharmacology; ISRS: inhibidor selectivo de la recaptación de serotonina; NICE: National Institute for Health and Care Excellence; TOC: trastorno obsesivo-compulsivo.

Tabla 6. Dosificación y contraindicaciones de los antidepresivos en el trastorno obsesivo-compulsivo

Principio activo	Indicación	Dosis inicial (FT) (mg/día)	Dosis recomendada (FT) (mg/día)*	Dosis objetivo (APA) (mg/día)	Dosis máxima (FT) (mg/día)	Contraindicaciones	Comentarios
Citalopram	Sí	20	20-40	40-60	40	Administración concomitante con IMAO a dosis > 10 mg o linezolid (IMAO no selectivo reversible) Antecedentes de intervalo QT largo o recibir medicamentos que puedan alargar el intervalo QT	
Clomipramina	Sí	25 mg/12 h (LI) 37,5 (LS)	100-150 (LI) 150 (LS) Una vez obtenida clara mejoría, reducir la dosis a: 50-100 (LI) 75 (LS)	100-250	250	En combinación con IMAO o 14 días antes o después de utilizarlos Infarto de miocardio reciente Síndrome del intervalo QT largo congénito	Una vez obtenida una clara mejoría, se irá reduciendo paulatinamente la dosis diaria hasta alcanzar un nivel medio de mantenimiento de 50-100 mg/día (LI) o 75 mg (LS). En tratamientos crónicos cada 6-12 meses se evaluará la necesidad de continuar con el mismo

Tabla 6. Dosificación y contraindicaciones de los antidepresivos en el trastorno obsesivo-compulsivo *(cont.)*

Principio activo	Indicación	Dosis inicial (FT) (mg/día)	Dosis recomendada (FT) (mg/día)*	Dosis objetivo (APA) (mg/día)	Dosis máxima (FT) (mg/día)	Contraindicaciones	Comentarios
Escitalopram	Sí	10	10-20	20	20	Administración concomitante con IMAO o linezolid (IMAO no selectivo reversible) Antecedentes de intervalo QT largo o recibir medicamentos que puedan alargar el intervalo QT	
Fluoxetina	Sí	NC	20	40-60	60	Con IMAO no selectivos irreversibles Con metoprolol cuando se utiliza en insuficiencia cardíaca	No se ha demostrado la eficacia a largo plazo (más de 24 semanas) en el TOC
Fluvoxamina	Sí	50	100-300	200	300	Con tizanidina o IMAO	No se ha demostrado la eficacia a largo plazo (más de 24 semanas) en el TOC Si la dosis diaria supera los 150 mg, es aconsejable que esta se divida en 2 o 3 tomas separadas
Paroxetina	Sí	20	40	40-60	60	Con IMAO Con tioridazina o con pimozida	Aumentar la dosis gradualmente, con incrementos de 10 mg hasta alcanzar la dosis recomendada
Sertralina	Sí, incluyendo pacientes de 6-17 años	50	50-200	200	200	Con IMAO irreversibles Con pimozida	Los cambios de dosis se deberán realizar en rangos de 50 mg, a intervalos de al menos una semana

APA: American Psychiatric Association; FT: ficha técnica; IMAO: inhibidor de la monoaminooxidasa; LI: liberación inmediata; LS: liberación sostenida; NC: no corresponde; TOC: trastorno obsesivo-compulsivo.
*Si la ficha técnica no especifica dosis recomendada, se incluye el rango de dosis especificado.

Tabla 7. Recomendaciones sobre la duración del tratamiento

Recomendación	Fuente
La duración óptima del tratamiento de continuación es desconocida.	BAP
Cuando el tratamiento farmacológico ha sido eficaz se debe mantener durante 1-2 años antes de considerar una retirada gradual.	APA
En los pacientes que han respondido al tratamiento agudo previo muestran una ventaja relevante si se mantienen con la medicación activa hasta 12 meses antes de considerar la retirada gradual.	BAP
Si el tratamiento se va a continuar durante un período superior a los 12 meses tras la remisión, se debe revisar periódicamente la necesidad de continuar con el tratamiento.	NICE

APA: American Psychiatric Association; BAP: British Association of Psychopharmacology; NICE: National Institute for Health and Care Excellence.

2.3. Predictores de respuesta y síntomas especiales

Aunque la búsqueda bibliográfica realizada localizó múltiples trabajos que han evaluado posibles predictores de la respuesta a los distintos tratamientos farmacológicos y no farmacológicos en distintas situaciones clínicas[11,33-75], e incluso se ha propuesto un modelo predictivo de respuesta al tratamiento farmacológico[70], la evidencia no es suficiente para realizar ninguna recomendación. Específicamente, la guía APA señala que "no existen variables clínicas o demográficas que constituyan predictores suficientemente precisos del resultado del tratamiento que permita su utilización en la selección del fármaco"[23].

Se ha comunicado que existe alguna evidencia de una disminución de la respuesta a algunos ISRS en pacientes con TOC que presentan tics y que la potenciación con antipsicóticos atípicos presenta una eficacia similar en pacientes con o sin tics[76].

Tanto la guía APA como la Canadiense señalan que la presencia de síntomas de acumulación puede asociarse con una menor respuesta al tratamiento psicofarmacológico[23,26]. Los pacientes con bajo *insight* presentan una mayor gravedad de los síntomas del TOC, incluyendo las conductas de acumulación, y una eficacia menor del tratamiento farmacológico y la terapia cognitivo-conductual, por lo que se ha propuesto que las técnicas conductuales dirigidas a mejorar el *insight* podrían ser beneficiosas en el TOC, en especial en los pacientes con conductas de acumulación[77]. No obstante, es importante señalar que el trastorno de acumulación es considerado actualmente una entidad nosológica distinta del TOC; por tanto, estos datos sobre el TOC y las conductas de acumulación deberían considerarse con precaución.

2.4. Tratamiento farmacológico del trastorno obsesivo-compulsivo con respuesta parcial o falta de respuesta al tratamiento

Las recomendaciones que se realizan a continuación se refieren al fracaso de un primer intento terapéutico. No existen recomendaciones específicas cuando el paciente no ha respondido a dos intentos terapéuticos.

a) Optimización o sustitución del tratamiento (Tabla 8)

Tabla 8. Recomendaciones sobre la optimización o sustitución del tratamiento

Recomendación	Fuente
Con respecto a los inhibidores de la recaptación de la serotonina, la opinión de los expertos apoya el cambio de estrategia terapéutica (sustitución del IRS o potenciación del IRS) tras un ensayo terapéutico de 8-12 semanas, con al menos 4-6 semanas a la dosis más elevada que sea tolerable.	APA
Con respecto a aquellos pacientes que no responden al primer ensayo con un IRS, la opinión de los expertos y los resultados de los ensayos apoyan la estrategia de cambiar a un IRS diferente.	APA
Cuando se requiere maximizar la eficacia se debe considerar combinar un ISRS o clomipramina con un tratamiento psicológico basado en la evidencia.	BAP
Se debe considerar el tratamiento con clomipramina después de un ensayo terapéutico a dosis (véase la Tabla 6) y duración adecuados con al menos un ISRS que ha sido ineficaz o mal tolerado, si el paciente prefiere clomipramina, o si existen antecedentes de buena respuesta a este fármaco.	NICE
Cuando el tratamiento inicial fracasa se debe considerar la combinación de tratamientos farmacológico y psicológico con evidencia demostrada.	BAP
Si no se ha conseguido una respuesta adecuada tras 12 semanas de tratamiento combinado con TCC (incluyendo EPR) y un ISRS, o no ha habido respuesta a un ISRS solo, o el paciente no se ha implicado en la TCC, debería ofrecerse un ISRS distinto o clomipramina.	NICE

APA: American Psychiatric Association; BAP: British Association of Psychopharmacology; EPR: exposición y prevención de respuesta; IRS: inhibidor de la recaptación de serotonina (incluye clomipramina y los ISRS); ISRS: inhibidor selectivo de la recaptación de serotonina; NICE: National Institute for Health and Care Excellence; TCC: terapia cognitivo conductual.

Además de las recomendaciones anteriores respecto a estrategias de optimización del tratamiento, se debe tener en cuenta que algunos pacientes que no responden al tratamiento inicial con un inhibidor de la recaptación de serotonina pueden responder simplemente tras un período más largo de tratamiento continuado con la misma medicación[22,23]. También señalan algunas guías que en determinados pacientes, como aquellos que han tenido una escasa respuesta a los tratamientos previos y toleran bien la medicación, puede ser beneficiosa la utilización de dosis más altas de las recomendadas en la ficha técnica (véase la Tabla 6), aunque esto debe hacerse tomando en consideración las circunstancias individuales[22,23].

b) Potenciación (Tabla 9)

Tabla 9. Recomendaciones sobre potenciación

Recomendación	Fuente
Si no se ha conseguido respuesta a un ensayo completo con al menos un ISRS en monoterapia, un tratamiento combinado de TCC (incluyendo EPR) y un ISRS, y un ensayo completo de clomipramina, se debería considerar la opción de añadir un antipsicótico al tratamiento con el ISRS o clomipramina. La evidencia de eficacia es superior para aripiprazol, risperidona y haloperidol.	NICE

EPR: exposición y prevención de respuesta; ISRS: inhibidor selectivo de la recaptación de serotonina; NICE: National Institute for Health and Care Excellence; TCC: terapia cognitivo-conductual.

c) Otras opciones terapéuticas

De acuerdo con las guías consultadas, se han evaluado otras opciones terapéuticas que no cuentan con evidencia suficiente para que pueda recomendarse su utilización de forma general; su uso debe considerarse cuando hayan fracasado las opciones terapéuticas recomendadas y después de haberse valorado las circunstancias individuales de cada caso.

Entre ellas se encuentran las siguientes:

- La combinación de clomipramina con un ISRS, con o sin terapia cognitivo-conductual (TCC).
- Anticonvulsivantes como carbamazepina, gabapentina, lamotrigina, pregabalina y topiramato.
- Antidepresivos IRSN (venlafaxina), inhibidores de la monoaminooxidasa (fenelzina, tranilcipromina) o mirtazapina.
- Moduladores glutamatérgicos como N-acetilcisteína, memantina, riluzole, glicina o ketamina intravenosa.
- La utilización de clomipramina intravenosa en pacientes que no hayan respondido a clomipramina por vía oral.
- Estimulantes como d-anfetamina
- Otros fármacos como ondansetrón, granisetrón, pindolol, celecoxib, morfina o tramadol.
- La estimulación cerebral profunda *(deep brain stimulation)* de ciertas dianas cerebrales (por ejemplo, núcleo *accumbens,* núcleo subtalámico, etc.) es un tratamiento físico que puede considerarse en aquellos pacientes con TOC resistente a múltiples ensayos farmacológicos y a la TCC. Los casos deben evaluarse siempre de manera individualizada y sopesando bien el riesgo-beneficio de la intervención.
- La neurocirugía (por ejemplo, cingulotomía) puede considerarse en aquellos pacientes con TOC resistente a múltiples ensayos farmacológicos y a la TCC. Los casos deben evaluarse siempre de manera individualizada y sopesando bien el riesgo-beneficio de la intervención, ya que los efectos adversos que pueden aparecer a menudo son de naturaleza irreversible.

2.5. Tratamiento farmacológico del trastorno obsesivo-compulsivo en poblaciones especiales

a) Pacientes de edad avanzada

No existe evidencia que permita realizar ninguna recomendación específica para el tratamiento del TOC en el paciente de edad avanzada. No obstante, la experiencia con el tratamiento psicofarmacológico en otras áreas de la psiquiatría permite sugerir el inicio de tratamiento a dosis más bajas e incrementar la dosis de manera más gradual que en adultos jóvenes[23,26]. Por otra parte, en el manejo del tratamiento psicofarmacológico de estos pacientes se debe tener presente la posible alteración de la función renal y sus implicaciones en la dosificación. Finalmente, en estos pacientes hay que considerar la frecuente utilización de otros fármacos para el tratamiento de enfermedades concomitantes y, por tanto, la posibilidad de interacciones farmacológicas[23,26].

b) Mujeres embarazadas y en período de lactancia

La guía de la APA señala que "tomar la decisión de iniciar o interrumpir un tratamiento psicofarmacológico durante el embarazo o la lactancia requiere hacer una evaluación de la relación del beneficio riesgo, pero sin disponer de información completa"[23]. En esa evaluación, como señala la guía Canadiense, se debe tener en cuenta el riesgo de no tratar[26]. Por tanto, no es posible realizar ninguna recomendación específica al respecto.

En la búsqueda bibliográfica realizada encontramos algunos trabajos de revisión sobre el impacto de eventos del ciclo reproductivo, incluyendo el embarazo o el parto, sobre el TOC[78-81], el impacto de la exposición a antidepresivos durante el embarazo o lactancia[82,83], la epidemiología, características y manejo del TOC durante el embarazo y postparto[81,82,84-92], que el lector interesado puede consultar. Existen, además, múltiples revisiones sistemáticas que han evaluado el impacto de los antidepresivos en el parto y el recién nacido[93-104] y que pueden orientar al lector sobre los riesgos asociados al tratamiento antidepresivo en el embarazo. Finalmente, la British Association for Psychopharmacology ha publicado recientemente una guía de consenso sobre el manejo de psicofármacos durante el embarazo y el postparto[105]; en la Tabla 10 se incluye un resumen de las recomendaciones de esta guía que hemos considerado más destacadas en relación con los trastornos de ansiedad y resaltando las referentes a antidepresivos, al tratarse de los fármacos de primera elección en el TOC.

Tabla 10. Recomendaciones de la British Association for Psychopharmacology para el tratamiento de los trastornos de ansiedad durante el embarazo y postparto

Área de interés	Recomendaciones
Manejo de los trastornos de ansiedad	El impacto de la ansiedad no tratada durante el embarazo es significativo. Existe incertidumbre respecto a si el tratamiento reduce los riesgos a largo plazo para el niño, pero esto no debe ser una razón para no tratar si los síntomas maternos están afectando al bienestar de la madre. Las decisiones respecto a cambiar o comenzar un tratamiento deben realizarse a nivel individual: Si la enfermedad está causando un sufrimiento o trastorno grave puede requerirse tratamiento farmacológico. Para elegir la medicación se deben tener en cuenta los antecedentes terapéuticos de la mujer y, especialmente si no ha recibido tratamientos previos, las recomendaciones terapéuticas para pacientes que no están embarazadas. Dado el importante volumen de datos respecto a su seguridad en el período perinatal, los ISRS son también el tratamiento de primera línea para los trastornos de ansiedad antes de la concepción y antenatalmente. Se debe revisar de forma regular la necesidad del tratamiento y este debe utilizarse durante el período más corto que se requiera.
Discusión de los riesgos y beneficios de los psicofármacos	Las mujeres deben ser conscientes de los riesgos conocidos o potenciales de la medicación, así como de las pruebas que existen de que dejar sin tratar su enfermedad puede asociarse con un aumento de los efectos adversos para la mujer, su embarazo o para el niño.
Beneficios y daños asociados a la utilización de antidepresivos	La mayoría de los datos sobre los efectos de los antidepresivos están influenciados por factores de confusión no controlados, incluyendo el impacto de la propia enfermedad. Cuando se estudian como grupo, los antidepresivos pueden tener un pequeño efecto sobre los resultados del embarazo (edad gestacional, puntuación Apgar), pero estos pueden deberse a confusión residual y, además, pueden carecer de relevancia clínica. Los antidepresivos que inhiben la recaptación de serotonina pueden asociarse a un aumento del riesgo de hemorragia postparto, aunque la magnitud y la relevancia clínica de este riesgo es incierta. Ha habido cierta preocupación respecto a la asociación de malformaciones cardíacas congénitas con la exposición intrauterina a los antidepresivos, principalmente ISRS y posiblemente en concreto con paroxetina. Sin embargo, este podría no ser el caso una vez se tienen en cuenta todos los confusores. Aunque existe un riesgo aumentado de hipertensión pulmonar persistente del recién nacido en niños que han sido expuestos intrauterinamente a ISRS, el riesgo absoluto es bajo.

ISRS: inhibidores selectivos de la recaptación de serotonina.

c) Comorbilidad psiquiátrica (Tabla 11)

Tabla 11. Recomendaciones sobre comorbilidad psiquiátrica

Recomendación	Fuente
Se debe realizar un seguimiento y control cuidadoso y frecuente por parte de los profesionales sanitarios de los adultos más jóvenes o de aquellos pacientes que se considera que tienen un riesgo aumentado de suicidio.	NICE
En pacientes con depresión mayor comórbida, los ISRS y los IRSN han demostrado ser eficaces en la mejoría de ambos trastornos.	Canadian

IRSN: inhibidor de la recaptación de serotonina y noradrenalina; ISRS: inhibidor selectivo de la recaptación de serotonina; NICE: National Institute for Health and Care Excellence.

3 CONCLUSIONES

De acuerdo con el Instituto de Medicina de los Estados Unidos, las guías de práctica clínica son declaraciones que incluyen recomendaciones que pretenden optimizar la atención a los pacientes[106]. Tienen el potencial de reducir variaciones inapropiadas de la práctica clínica, mejorar la traducción de la evidencia de la investigación en práctica clínica, y mejorar la calidad y seguridad de la atención sanitaria[106]. La guía de recomendaciones para el tratamiento farmacológico del TOC en adultos que hemos desarrollado constituye la primera guía elaborada en España con este objetivo. Sin embargo, esta guía tiene algunas limitaciones que se comentan a continuación.

Su desarrollo se ha basado en las recomendaciones provenientes de otras guías elaboradas en otros ámbitos, fundamentalmente en países anglosajones, cuya aplicabilidad, a excepción de la NICE, fue juzgada como baja durante el proceso de evaluación de las guías. A este respecto, hay que comentar que uno de los objetivos del grupo de expertos implicados en el desarrollo de estas guías fue incluir aquellas recomendaciones que eran aplicables a nuestro ámbito. El rigor de una de las guías seleccionadas –la Canadiense- fue juzgado como bajo por este grupo de expertos; no es de extrañar, por tanto, que tan solo se haya incluido una recomendación proveniente de esta guía.

Esta guía no abarca aspectos relevantes del manejo del TOC, en especial la psicoterapia, más que en lo que se refiere a la selección del tratamiento inicial; en nuestro medio se han realizado algunas iniciativas de guías psicoterapéuticas[107]. Otros aspectos del tratamiento, como la utilización de terapias físicas sobre las que se acumulan pruebas de su utilidad[108-110], aunque se mencionan en este documento, no han sido objeto de revisión, pero deben tenerse en cuenta por el especialista en el manejo de este trastorno.

A lo largo de la exposición de las recomendaciones también ha quedado claro que existen múltiples aspectos del manejo farmacológico del TOC sobre los que las evidencias son muy limitadas y no permiten hacer ninguna recomendación específica; estos incluyen la personalización del tratamiento a través de la utilización de factores predictivos, la utilización en poblaciones especiales como ancianos, o el manejo durante el embarazo.

Finalmente, hay que señalar que los beneficios potenciales de una guía de práctica clínica dependen de su calidad, difusión e implementación[111,112]. La difusión se pretende realizar a través de una publicación de acceso no restringido y por parte de la Sociedad Española de Psiquiatría entre sus miembros. Sin embargo, queda pendiente el desarrollo de actividades de implementación de la guía y evaluación de los resultados de esa implementación. A pesar de las limitaciones mencionadas, esperamos que esta guía pueda ser de utilidad para los psiquiatras que ejercen en España y, como era el objetivo inicial, pueda mejorar el manejo de la enfermedad en nuestro entorno y contribuir a reducir la carga de la enfermedad para el paciente.

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APÉNDICE 1

Recomendaciones seleccionadas: original (inglés), recomendación en la guía española y motivo de la modificación/comentarios

a) Tratamiento agudo con psicofármacos versus psicoterapia versus tratamiento combinado

Recomendación original (inglés)	Recomendación Guía Española	Comentario	Fuente
CBT and serotonin reuptake inhibitors (SRIs) are recommended as safe and effective first-line treatments for OCD.	La TCC y los ISRS se recomiendan como tratamientos eficaces y seguros de primera línea en el TOC.	La guía original hace referencia a los IRS. Este grupo de expertos considera que por seguridad deben limitarse a los ISRS.	APA
Whether to utilize CBT, an SRI, or combined treatment will depend on factors that include the nature and severity of the patient's symptoms, the nature of any co-occurring psychiatric and medical conditions and their treatments, the availability of CBT, and the patient's past treatment history, current medications, capacities, and preferences. CBT alone, consisting of exposure and response prevention, is recommended as initial treatment for a patient who is not too depressed, anxious, or severely ill to cooperate with this treatment modality, or who prefers not to take medications and is willing to do the work that CBT requires.	El utilizar la TCC o un ISRS dependerá de la naturaleza y gravedad de los síntomas del paciente, la naturaleza de cualquier comorbilidad psiquiátrica o médica y su tratamiento, la disponibilidad de la TCC, y los antecedentes de tratamientos previos, medicación actual, capacidades y preferencias. La TCC sola, consistente en la EPR, se recomienda como tratamiento inicial para un paciente que no está muy deprimido, ansioso o gravemente enfermo como para cooperar con esta modalidad de tratamiento, o para un paciente que prefiere no tomar medicación y esté dispuesto a esforzarse en lo que la TCC requiere.	La guía original hace referencia a los IRS. Este grupo de expertos considera que por seguridad deben limitarse a los ISRS. La guía original hace también referencia a la combinación de ambos tratamientos. Este grupo de expertos considera que el tratamiento combinado no ofrece ventajas respecto a la TCC sola.	APA
Combined treatment should be considered for patients with co-occurring psychiatric conditions for which SRIs are effective.	El tratamiento combinado debería tenerse en cuenta para pacientes con comorbilidad psiquiátrica para la cual el IRS es eficaz.		APA
Combined treatment should be considered for patients who wish to limit the duration of SRI treatment.	El tratamiento combinado debería tenerse en cuenta para pacientes que desean limitar la duración del tratamiento con el IRS.		APA

Recomendación original (inglés)	Recomendación Guía Española	Comentario	Fuente
In the initial treatment of adults with OCD, low intensity psychological treatments (including ERP) (up to 10 therapist hours per patient) should be offered if the patient's degree of functional impairment is mild and/or the patient expresses a preference for a low intensity approach.	En el tratamiento inicial de adultos con TOC, los tratamientos psicológicos de baja intensidad (incluyendo EPR) (hasta 10 horas de terapia por paciente) se deberían ofrecer al enfermo si su grado de alteración funcional es leve y/o expresa su preferencia por esta estrategia.		NICE
Adults with OCD with mild functional impairment who are unable to engage in low intensity CBT (including ERP), or for whom low intensity treatment has proved to be inadequate, should be offered the choice of either a course of an SSRI or more intensive CBT (including ERP) (more than 10 therapist hours per patient), because these treatments appear to be comparably efficacious.	En adultos con TOC con alteración funcional leve que no son capaces de implicarse en una TCC de baja intensidad (incluyendo EPR), o para los que el tratamiento de baja intensidad se ha demostrado que es inadecuado, debería ofrecérseles un intento terapéutico con un ISRS o una TCC más intensiva (incluyendo EPR) (más de 10 horas de terapia por paciente), dado que estos tratamientos parecen mostrar una eficacia similar.		NICE
Adults with OCD with moderate functional impairment should be offered the choice of either a course of an SSRI or more intensive CBT (including ERP) (more than 10 therapist hours per patient), because these treatments appear to be comparably efficacious.	En adultos con TOC con alteración funcional moderada debería ofrecérseles un intento terapéutico con un ISRS o una TCC más intensiva (incluyendo EPR) (más de 10 horas de terapia por paciente), dado que estos tratamientos parecen mostrar una eficacia similar.		NICE
Adults with OCD with severe functional impairment should be offered combined treatment with an SSRI and CBT (including ERP).	En adultos con TOC con alteración funcional grave debería ofrecérseles tratamiento combinado con un ISRS y una TCC (incluyendo EPR).		NICE

APA: American Psychiatric Association; EPR: exposición y prevención de respuesta; IRS: inhibidor de la recaptación de serotonina (incluye clomipramina y los ISRS); ISRS: inhibidor selectivo de la recaptación de serotonina; NICE: National Institute for Health and Care Excellence; TCC: terapia cognitivo-conductual; TOC: trastorno obsesivo-compulsivo.

b) Eficacia, tolerabilidad y seguridad de los tratamientos psicofarmacológicos

Recomendación original (inglés)	Recomendación Guía Española	Comentario	Fuente
All SSRIs appear to be equally effective in treating OCD, even though two —citalopram and escitalopram— are not approved by the U.S. Food and Drug Administration (FDA) for this indication. In choosing among the SSRIs, the psychiatrist should consider the safety and acceptability of side effects for the patient, including any applicable FDA warnings, potential drug interactions, past treatment response, and the presence of co-occurring general medical conditions.	Aunque todos los ISRS (incluyendo citalopram y escitalopram) parecen presentar la misma eficacia, el paciente individual puede responder a un tratamiento y no a otro. Para elegir el ISRS el psiquiatra debería considerar la seguridad y aceptabilidad de determinados efectos adversos por el paciente, incluyendo cualquier precaución que aparezca en su ficha técnica, interacciones farmacológicas potenciales, respuesta al tratamiento previo, y presencia de comorbilidades médicas generales.	La guía original hace referencia a las indicaciones y precauciones establecidas por la Food and Drug Administration y al hecho de que dos de ellos no estaban autorizados para la indicación.	APA
For adults with OCD, the initial pharmacological treatment should be one of the following SSRIs: fluoxetine, fluvoxamine, paroxetine, sertraline or citalopram.	Para adultos con TOC el tratamiento farmacológico inicial debería ser uno de los siguientes ISRS: citalopram, escitalopram fluoxetina, fluvoxamina, paroxetina o sertralina (ver contraindicaciones en Tabla 6).	La recomendación original no incluye escitalopram. Los ISRS se han ordenado alfabéticamente.	NICE
Healthcare professionals should be aware of the increased risk of drug interactions when prescribing an SSRI to adults with OCD who are taking other medications.	Los profesionales sanitarios deberían ser conscientes del aumento del riesgo de interacciones farmacológicas cuando prescriben un ISRS a un adulto con TOC que está en tratamiento con otras medicaciones.		NICE
For adults with OCD, if there has been no response to a full course of treatment with an SSRI, healthcare professionals should check that the patient has taken the drug regularly and in the prescribed dose and that there is no interference from alcohol or substance use.	En un adulto con TOC, si no ha habido respuesta a una pauta completa de tratamiento con un ISRS se debería comprobar si el paciente está tomando la medicación de forma regular y a la dosis prescrita y que no existe interferencia por el alcohol o el abuso de sustancias.		NICE

Recomendación original (inglés)	Recomendación Guía Española	Comentario	Fuente
Clomipramine should be considered in the treatment of adults with OCD after an adequate trial of at least one SSRI has been ineffective or poorly tolerated, if the patient prefers clomipramine or has had a previous good response to it.	La clomipramina debería considerarse en el tratamiento del adulto con TOC después de intentar al menos con un ISRS y este haya sido ineficaz o mal tolerado, si el paciente prefiere clomipramina, o ha habido previamente una buena respuesta a este fármaco.	Se aconseja incluir algún comentario sobre la posible mayor eficacia de clomipramina. Así, de acuerdo con la guía de la APA, "aunque algunos metaanálisis de ensayos clínicos controlados con placebo sugieren una mayor eficacia de clomipramina respecto a fluvoxamina, fluoxetina y sertralina, los resultados de los ensayos clínicos que han comparado de forma directa clomipramina y los ISRS no apoyan esta impresión. Dado que los ISRS tienen un perfil de efectos secundarios menos problemático que clomipramina, es preferible un ISRS como primer intento terapéutico".	NICE
An electrocardiogram (ECG) should be carried out and a blood pressure measurement taken before prescribing clomipramine for adults with OCD at significant risk of cardiovascular disease.	Antes de prescribir clomipramina a un adulto con TOC con un riesgo significativo de enfermedad cardiovascular se debería realizar un electrocardiograma y una medición de la presión arterial. Precauciones similares son aplicables a otros antidepresivos, por lo que en pacientes con este tipo de riesgo se deben tener en cuenta las recomendaciones de las correspondientes fichas técnicas.	Se ha incluido comentario sobre otros antidepresivos, ya que algunos incluyen recomendaciones similares en su ficha técnica.	NICE
Patients with known cardiac risk factors including hypokalemia and hypomagnesemia: avoid high doses of citalopram (more than 40 mg/day) and avoid tricyclic antidepressants.	En pacientes con factores de riesgo cardíacos conocidos, incluyendo hipopotasemia e hipomagnesemia, se deben evitar dosis elevadas de citalopram y los antidepresivos tricíclicos.		BAP
For adults with OCD, if there has not been an adequate response to the standard dose of clomipramine, and there are no significant side effects, a gradual increase in dose should be considered in line with the schedule suggested by the Summary of Product Characteristics.	En adultos con TOC, si no ha habido respuesta adecuada a la dosis estándar de clomipramina, y no hay efectos secundarios relevantes, se debería considerar un aumento gradual de la dosis en consonancia con la pauta propuesta en su ficha técnica.		NICE

Recomendación original (inglés)	Recomendación Guía Española	Comentario	Fuente
The following drugs should not normally be used to treat OCD without comorbidity: Tricyclic antidepressants other than clomipramine, Serotonin and noradrenaline re-uptake inhibitors (SNRIs), including venlafaxine. Be used to treat OCD or BDD without comorbidity, Tricyclic-related antidepressants. Monoamine oxidase inhibitors (MAOIs). Anxiolytics (except cautiously for short periods to counter the early activation of SSRIs).	Los siguientes fármacos no deberían utilizarse como tratamiento inicial del TOC sin comorbilidad: Antidepresivos tricíclicos distintos de clomipramina. Antidepresivos relacionados con los tricíclicos. Inhibidor de la recaptación de serotonina y noradrenalina. Inhibidor de la monoaminoxidasa. Ansiolíticos (excepto con precaución durante un período corto de tiempo para contrarrestar la activación inicial de los ISRS). Antipsicóticos. Otros fármacos que no tengan la indicación de TOC.	La guía original no especifica que se trate de tratamiento inicial y no especifica los antipsicóticos. Se han añadido otros fármacos que no tengan la indicación.	NICE

APA: American Psychiatric Association; BAP: British Association of Psychopharmacology; ISRS: inhibidor selectivo de la recaptación de serotonina; NICE: National Institute for Health and Care Excellence; TOC: trastorno obsesivo-compulsivo.

c) Duración del tratamiento

Recomendación original (inglés)	Recomendación Guía Española	Comentario	Fuente
The optimal long term therapy is uncertain.	La duración óptima del tratamiento de continuación es desconocida		BAP
Successful medication treatment be continued for 1-2 years before considering a gradual taper.	Cuando el tratamiento farmacológico ha sido eficaz se debe mantener durante 1-2 años antes de considerar una retirada gradual.		APA
Patients who have responded to previous acute treatment reveal a significant advantage for staying on active medication for up to 12 months before considering gradual taper.	En los pacientes que han respondido al tratamiento agudo previo muestran una ventaja relevante si se mantienen con la medicación activa hasta 12 meses antes de considerar la retirada gradual.		BAP
If it is continued for an extended period beyond 12 months after remission, the need for continuation should be reviewed at regular intervals.	Si el tratamiento se va a continuar por un periodo superior a los 12 meses tras la remisión, se debe revisar periódicamente la necesidad de continuar con el tratamiento		NICE

d) Tratamiento del trastorno obsesivo-compulsivo con respuesta parcial o falta de respuesta

Recomendación original (inglés)	Recomendación Guía Española	Comentario	Fuente
Optimización o sustitución del tratamiento			
About SRIs, expert opinion supports changing medication strategy (switching or augmenting) after a trial of 8-12 weeks, with at least 4-6 weeks at the highest comfortably tolerated dose.	Con respecto a los IRS, la opinión de los expertos apoya el cambio de estrategia terapéutica (sustitución del IRS o potenciación del IRS) tras un ensayo terapéutico de 8-12 semanas, con al menos 4-6 semanas a la dosis más elevada que sea tolerable.		APA
For patients who do not respond to their first SRI, expert opinion and clinical trial data support switching to a different SRI.	Con respecto a aquellos pacientes que no responden al primer ensayo con un IRS, la opinión de los expertos y los resultados de los ensayos apoyan la estrategia de cambiar a un IRS diferente.		APA
Consider combining an SSRI or clomipramine with an evidence-based psychological treatment when efficacy needs to be maximized.	Cuando se requiere maximizar la eficacia se debe considerar combinar un ISRS o clomipramina con un tratamiento psicológico basado en la evidencia.		BAP
Clomipramine should be considered after an adequate trial of at least one SSRI has been ineffective or poorly tolerated, if the patient prefers clomipramine or has had a previous good response to it.	Se debe considerar el tratamiento con clomipramina después de un ensayo terapéutico a dosis (véase Tabla 6) y duración adecuados con al menos un ISRS que ha sido ineficaz o mal tolerado, si el paciente prefiere clomipramina, o si existen antecedentes de buena respuesta a este fármaco.		NICE
When initial treatments fail consider combining evidence-based pharmacological and psychological treatments.	Cuando el tratamiento inicial fracasa se debe considerar la combinación de tratamientos farmacológico y psicológico con evidencia demostrada.		BAP
If there has not been an adequate response after 12 weeks of combined treatment with CBT (including ERP) and an SSRI, or there has been no response to an SSRI alone, or the patient has not engaged with CBT, a different SSRI or clomipramine should be offered.	Si no se ha conseguido una respuesta adecuada tras 12 semanas de tratamiento combinado con TCC (incluyendo EPR) y un ISRS, o no ha habido respuesta a un ISRS solo, o el paciente no se ha implicado en la TCC, debería ofrecerse un ISRS distinto o clomipramina.	Incluir un comentario de que no existe una recomendación específica cuando el paciente no ha respondido a dos intentos terapéuticos con ISRS.	NICE

Recomendación original (inglés)	Recomendación Guía Española	Comentario	Fuente
	Potenciación farmacológica del tratamiento		
If there has been no response to a full trial of at least one SSRI alone, a full trial of combined treatment with CBT (including ERP) and an SSRI, and a full trial of clomipramine alone, adding an antipsychotic to an SSRI or clomipramine should be considered.	Si no se ha conseguido respuesta a un ensayo completo con al menos un ISRS en monoterapia, un tratamiento combinado de TCC (incluyendo EPR) y un ISRS, y un ensayo completo de clomipramina, se debería considerar la opción de añadir un antipsicótico al tratamiento con el ISRS o clomipramina. La evidencia de eficacia es superior para aripiprazol, risperidona y haloperidol.		NICE

APA: American Psychiatric Association; BAP: British Association of Psychopharmacology; EPR: exposición y prevención de respuesta; IRS: inhibidor de la recaptación de serotonina (incluye clomipramina y los ISRS); ISRS: inhibidor selectivo de la recaptación de serotonina; NICE: National Institute for Health and Care Excellence; TCC: terapia cognitivo-conductual.

e) Comorbilidad psiquiátrica

Recomendación original (inglés)	Recomendación Guía Española	Comentario	Fuente
Younger adults or patients with comorbid depression or who are at an increased risk of suicide should be carefully and frequently monitored by healthcare professionals.	Se debe realizar un seguimiento y control cuidadoso y frecuente por parte de los profesionales sanitarios de los adultos más jóvenes o de aquellos pacientes que se considera que tienen un riesgo aumentado de suicidio.		NICE
Comorbid MDD: SSRIS and SNRIs have been shown to be effective in improving both disorders.	En pacientes con depresión mayor comórbida los ISRS y los IRSN han demostrado ser eficaces en la mejoría de ambos trastornos.		Canadiense

IRSN: inhibidor de la recaptación de serotonina y noradrenalina; ISRS: inhibidor selectivo de la recaptación de serotonina; NICE: National Institute for Health and Care Excellence.

APÉNDICE 2
Búsqueda bibliográfica tratamiento farmacológico del trastorno obsesivo-compulsivo

ENSAYOS CLÍNICOS

ÍNDICE

TRATAMIENTO FARMACOLÓGICO DEL TRASTORNO OBSESIVO-COMPULSIVO EN ADULTOS

Ámbito

Tratamiento farmacológico del trastorno obsesivo-compulsivo (TOC) como diagnóstico primario en pacientes adultos en el ámbito de la atención especializada.

Preguntas

1. TRATAMIENTO AGUDO

1.1. Psicofarmacológico versus *psicoterapia* versus *combinado (31 – 1977-2015)*

Amin MM, Ban TA, et al. Clomipramine (Anafranil) and behaviour therapy in obsessive-compulsive and phobic disorders. J Int Med Res. 1977; 5 Suppl 5: 33-7.

In a comparative study of three treatment regimens in patients with obsessive-compulsive or phobic manifestations, the most favourable therapeutic findings were seen in the clomipramine (Anafranil, Geigy Pharmaceuticals) plus behaviour therapy group and the least favourable therapeutic findings in the clomipramine plus simulated behaviour therapy group. The findings that a combination of behaviour therapy and clomipramine results in more favourable therapeutic changes than either of the two treatments alone is in line with reported studies in the literature.

Marks IM, Stern RS, et al. Clomipramine and exposure for obsessive-compulsive rituals: I. Br J Psychiatry. 1980;136:1-25.

Forty chronic obsessive-compulsive ritualizers were randomly assigned to treatment with oral clomipramine or placebo for 8 months. During weeks 4 to 7 these two groups were each randomly split into treatment by relaxation or by exposure in vivo, and during weeks 7 to 10 all patients had exposure in vivo. Double blind assessments were made at weeks 4, 7, 10, 18, 36, 62 and 114. Results are reported to one year. Clomipramine produced significant improvement in rituals, mood and social adjustment, but only in those patients who initially had depressed mood. The clomipramine effect was maximum from weeks 10 to 18 and diminished thereafter. On stopping clomipramine patients often relapsed and improved again on restarting the drug. Relaxation produced little change. Exposure produced significant lasting improvement in rituals, but less change in mood; improvement generalized to social adjustment at follow-up. Clomipramine plus exposure had a slight additive but not interactional effect. Clomipramine enhanced compliance both with exposure and with relaxation. Clomipramine is useful for compulsive ritualizers with depressed mood, but may need continuation for over a year and combination with exposure in vivo. Exposure in vivo remains the treatment of choice for rituals without depressed mood.

Stern RS, Marks IM, et al. Clomipramine and exposure for compulsive rituals: II. Plasma levels, side effects and outcome. Br J Psychiatry. 1980;136:161-6.

Forty obsessive-compulsive ritualizers received nightly placebo or clomipramine up to 225 mgs nocte for 8 months, and received behavioural treatment (exposure to vivo) from weeks 4 to 10. Plasma concentrations of clomipramine and its primary metabolite N-desmethylclomipramine steadily increased over the first 4 weeks of treatment after which they remained relatively steady. Plasma levels correlated significantly with dose and with outcome but not with side effects. Patients with plasma clomipramine levels in the range 100-250 ng/ml and N-desmethylclomipramine levels between 230-550 ng/ml were found to improve significantly more than patients outside these ranges, thus suggesting a therapeutic window for clomipramine and its primary metabolite.

Marks IM, Lelliott P, et al. Clomipramine, self-exposure and therapist-aided exposure for obsessive-compulsive rituals. Br J Psychiatry. 1988;152:522-34.

A randomised treatment design for 49 chronically obsessive-compulsive ritualising patients was devised and three controlled comparisons were made. 1. During 7 weeks of self-exposure instructions, clomipramine treatment improved some measures of rituals and depression significantly more than did placebo medication; this effect was transient and disappeared as drug treatment and exposure were continued for a further 15 weeks. 2. During 11-16 weeks of clomipramine treatment, self-exposure instructions yielded highly significantly more patient improvement than did anti-exposure instructions on nearly all measures of rituals and some of social adjustment. 3. Adding therapist-aided exposure (1.3 hours) to self-exposure instructions (3 hours) after 8 weeks had a barely significant transient effect of

dubious clinical value, which was lost by the end of exposure (at week 23) and during follow-up assessments to week 52. We conclude that of the three therapeutic factors tested, self-exposure was the most potent; clomipramine played a limited adjuvant role, and therapist-aided exposure a marginal one.

Cottraux J, Mollard E, et al. A controlled study of fluvoxamine and exposure in obsessive-compulsive disorder. Int Clin Psychopharmacol. 1990;5(1):17-30.

DSM-3 obsessive-compulsive out-patients were randomly assigned to fluvoxamine with antiexposure (F), fluvoxamine with exposure (Fe), or placebo with exposure (Pe) for 24 weeks. Of 65 patients offered treatment 60 entered the trial, 50 reached week 8, 44 completed treatment to week 24, and 37 reached follow up to week 48. On average the patient had depressed mood (mean Hamilton depression rating scale = 19). Drop-out numbers, clinical status and behavioural measures were comparable across groups. Most F patients did not do antiexposure, but Fe and Pe patients complied in doing exposure. All three groups improved in rituals and depression from week 0 to week 24 and 48, with a slight but non-significant superiority for combined treatment up to week 24. At week 8 there was a drug between-group effect on rituals, but not on depression. At week 24 there was a drug between-group effect on depression, but not on rituals. The drug superiority was short-lived. At week 48 there was no between-group difference in rituals or depression. Depression was related to ritual outcome at week 24 in F, and tended to be so in Fe.

Foa EB, Kozak MJ, et al. Treatment of depressive and obsessive-compulsive symptoms in OCD by imipramine and behaviour therapy. Br J Clin Psychol.1992;31(Pt 3):279-92.

The efficacy of behavioural treatment of obsessive-compulsive disorder (OCD) has been well documented. However, severely depressed OCD patients showed fewer short- and long-term benefits than less depressed patients. The present study tested the hypothesis that reduction of depression by imipramine prior to behaviour therapy would enhance the effects of behavioural therapy on depressed OC patients. Thirty-eight patients were divided into highly and mildly depressed groups according to their scores on the Beck Depression Inventory; half of each group received imipramine and half received placebo for six weeks. All patients then received three weeks of daily behavioural treatment (exposure and response prevention) followed by 12 weekly sessions of supportive psychotherapy. Results indicated that although imipramine improved depressive symptoms in depressed patients, it did not affect OC symptoms. Behaviour therapy markedly reduced OC symptoms but, contrary to our hypothesis, imipramine did not potentiate the effects of behaviour therapy. No differences between highly depressed and mildly depressed patients on OC symptoms were found in their responses to behavioural or supportive therapy.

Balkom AJ, Haan E, et al. Cognitive and behavioral therapies alone versus in combination with fluvoxamine in the treatment of obsessive compulsive disorder. The Journal of nervous and mental disease. 1998;186:492-9.

The purpose of this treatment package design study was to investigate the differential efficacy of cognitive therapy or exposure in vivo with response prevention for obsessive compulsive disorder (OCD) versus the sequential combination with fluvoxamine. Patients with OCD (N = 117) were randomized to one of the following five conditions: a) cognitive therapy for weeks 1 to 16, b) exposure in vivo with response prevention for weeks 1 to 16, c) fluvoxamine for weeks 1 to 16 plus cognitive therapy in weeks 9 to 16, d) fluvoxamine for weeks 1 to 16 plus exposure in vivo with response prevention in weeks 9 to 16, or e) waiting list control condition for weeks 1 to 8 only. Assessments took place before treatment (pretest) and after 8 (midtest), and 16 weeks (posttest). In the first 8 weeks, six treatment sessions were delivered. During weeks 9 to 16, another 10 sessions were given. Thirty-one patients dropped out. Outcome was assessed by patient-, therapist- and assessor-ratings of the Anxiety Discomfort Scale, the Yale-Brown Obsessive Compulsive Scale, and the Padua Inventory-Revised. In contrast with the four treatments, after 8 weeks the waiting list control condition did not result in a significant decrease of symptoms. After 16 weeks of treatment, all four treatment packages were effective on these OCD ratings, but they did not differ among each other in effectiveness. In OCD, the sequential combination of fluvoxamine with cognitive therapy or exposure in vivo with response prevention is not superior to either cognitive therapy or exposure in vivo alone.

Hohagen F, Winkelmann G, et al. Combination of behaviour therapy with fluvoxamine in comparison with behaviour therapy and placebo: Results of a multicentre study. The British Journal of Psychiatry. 1998;173(Suppl 35):71-8.

Investigated whether the combination of multi-modal behavior therapy (BT) with fluvoxamine (BTF) is superior to BT and placebo (BTP) in the acute treatment of severely ill in-patients (mean

age 35.5 yrs) with obsessive-compulsive disorder (OCD). In a randomized, double-blind design, 30 patients were treated for 9 wks with BTP and 30 patients with BTF (maximum dosage 300 mg, mean dose 288.1 mg). BT included exposure with response prevention, cognitive restructuring and development of alternative behaviors. Both groups showed a highly significant symptom reduction after treatment. There were no significant differences between the groups concerning compulsions. Obsessions were significantly more reduced in the BTF group than in the BTP group. Furthermore, the BTF group showed a significantly higher response rate (87.5 vs 60%) according to a previously defined response criterion. Severely depressed patients with OCD receiving BTP presented a significantly worse treatment outcome, according to the Yale Brown Obsessive-Compulsive Scale, than all other groups. The results suggest that BT should be combined with fluvoxamine when obsessions dominate the clinical picture and when a secondary depression is present. (PsycINFO Database Record (c) 2012 APA, all rights reserved).

Van Balkom AJ, de Haan E, et al. Cognitive and behavioral therapies alone versus in combination with fluvoxamine in the treatment of obsessive compulsive disorder. J Nerv Ment Dis.1998;186(8):492-9.

The purpose of this treatment package design study was to investigate the differential efficacy of cognitive therapy or exposure in vivo with response prevention for obsessive compulsive disorder (OCD) versus the sequential combination with fluvoxamine. Patients with OCD (N = 117) were randomized to one of the following five conditions: a) cognitive therapy for weeks 1 to 16, b) exposure in vivo with response prevention for weeks 1 to 16, c) fluvoxamine for weeks 1 to 16 plus cognitive therapy in weeks 9 to 16, d) fluvoxamine for weeks 1 to 16 plus exposure in vivo with response prevention in weeks 9 to 16, or e) waiting list control condition for weeks 1 to 8 only. Assessments took place before treatment (pretest) and after 8 (midtest), and 16 weeks (posttest). In the first 8 weeks, six treatment sessions were delivered. During weeks 9 to 16, another 10 sessions were given. Thirty-one patients dropped out. Outcome was assessed by patient-, therapist- and assessor-ratings of the Anxiety Discomfort Scale, the Yale-Brown Obsessive Compulsive Scale, and the Padua Inventory-Revised. In contrast with the four treatments, after 8 weeks the waiting list control condition did not result in a significant decrease of symptoms. After 16 weeks of treatment, all four treatment packages were effective on these OCD ratings, but they did not differ among each other in effectiveness. In OCD, the sequential combination of fluvoxamine with cognitive therapy or exposure in vivo with response prevention is not superior to either cognitive therapy or exposure in vivo alone.

O'Connor K, Todorov C, et al. Cognitive-behaviour therapy and medication in the treatment of obsessive-compulsive disorder: a controlled study. Can J Psychiatry. 1999;44(1):64-71.

OBJECTIVE: To evaluate the effect of combining cognitive-behaviour therapy (CBT) and medication in the treatment of obsessive-compulsive disorder (OCD). METHOD: Twenty-nine subjects diagnosed with OCD according to Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R) criteria were recruited through the Anxiety Clinic of Louis-H Lafontaine Hospital. They were evaluated at baseline and after treatment on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) by a psychiatrist who was blind to treatment modality. Subjects rated their degree of resistance to their rituals and the strength of their obsessional beliefs. Subjects then received 1 of 4 treatments: medication and CBT simultaneously (n = 9), CBT only (n = 6), medication while on a wait-list for CBT (n = 6), or no treatment while on a wait-list for CBT (n = 5). RESULTS: Multivariate analysis revealed that Y-BOCS scores and clinical ratings significantly improved posttreatment in all groups except the nontreatment wait-list control group. Subjects in the 2 active treatment groups receiving CBT showed reduced strength in their obsessional beliefs. The subsequent administration of CBT to those groups on the wait-list also decreased the strength of their primary obsessional beliefs and beliefs about the consequences of not performing the rituals. CONCLUSIONS: Our results suggest that either CBT or medication alone is more effective than no treatment. The combination of CBT and medication seems to potentiate treatment efficacy, and we found it more clinically beneficial to introduce CBT after a period of medication rather than to start both therapies simultaneously.

Kozak MJ, Liebowitz MR, et al. Cognitive behavior therapy and pharmacotherapy for obsessive-compulsive disorder: The NIMH-sponsored collaborative study. Obsessive-compulsive disorder: Contemporary issues in treatment, Lawrence Erlbaum Associates Publishers, Mahwah, NJ; 2000; p. 501-30.

Compared the efficacy and durability of the 2 most established treatments for obsessive-compulsive disorder (OCD), clomipramine and cognitive behavior therapy in this ongoing study. 61 participants were randomly assigned to the following 4 groups: clomipramine (CMI), pill placebo, cognitive-behavior therapy (CBT), and CMI plus CBT. Active treatment lasted 3 mo, followed by a 3-mo no-

treatment follow-up period. Ss were evaluated at pretreatment, 1 mo after CBT, 3 mo after CMI and CBT, and 3 mo after no treatment.CBT and CMI proved to be effective. At the end of 1 mo of treatment, both monotherapies and their combination were superior to placebo on various OCD measures. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (chapter).

Shaomei L. Combination of clomipramine with exposure therapy in treatment of obsessive-compulsive disorder. Chinese Mental Health Journal.2001;15(4):239-40.

Compared the effects of the combination of clomipramine with exposure therapy with clomipramine alone in treatment of obsessive-compulsive disorder (OCD). 28 patients with OCD according to the CCMD-2-R were randomly divided into two groups: clomipramine group and combination group. The duration of treatment was 8 wks for both groups. The Yale-Brown Obsessive–Compulsive Scale (Y-BOCS) to assess the effect of treatment. The combination group had much higher reduction rate in Y-BOCS than the clomipramine alone group, especially for those with compulsive behavior. It is concluded that the combination of clomipramine with exposure therapy is more effective than clomipramine alone, especially for compulsive behavior. (PsycINFO Database Record (c) 2012 APA, all rights reserved**)**

Hembree EA, Riggs DS, et al. Long-term efficacy of exposure and ritual prevention therapy and serotonergic medications for obsessive-compulsive disorder. CNS Spectr. 2003;8(5):363-71, 381.

What is the long-term outcome of patients with obsessive-compulsive disorder (OCD) who are treated with exposure and response (ritual) prevention (EX/RP) alone, serotonergic medications alone, or their combination? How is the long-term outcome of these patients affected by the discontinuation? Follow-up assessments were conducted with 62 patients treated for OCD an average of 17 months posttreatment (range: 6-43 months). Patients received one of three treatments: serotonergic medications (fluvoxamine or clomipramine), intensive behavior therapy involving EX/RP, or intensive EX/RP with concurrent antidepressant medication. At follow-up, no differences in OCD symptom severity were found among the three treatment groups. However, when current medication use was taken into consideration, differences among the three treatment groups emerged. Among patients who were medication-free at the time of follow-up assessment (n=37), those in the EX/RP-alone and EX/RP-with-medication groups had lower symptom severity ratings than those in the medication-only group on 4 out of 6 measures. There were no differences in OCD severity ratings among patients taking medications at follow-up (n=25). Although these findings are interpreted with caution due to the uncontrolled nature of the study, results suggested that long-term outcome may be superior following EX/RP than following serotonergic medications, after discontinuation. For patients who remain on medications, the treatment produced benefits equivalent to EX/RP.

Qing Y, Denghua T, et al. Comparative Study of Cognitive Therapy on Obsessional Compulsive Disorder. Chinese Mental Health Journal. 2004;18(6):421-2.

Objective: To explore the effect of cognitive therapy on obsessional compulsive disorder (OCD). Method: Forty-seven patients with OCD were randomly assigned to a cognitive therapy group and conventional treatment group, the latter with paroxetine treatment only as control. The results were assessed with Hamilton Anxiety Scale (HAMA), Yale-Brown Obsessional Compulsive Scale and Social Disability Screening Scale. Result: The cognitive therapy group had lower scores on HAMA and Y-BOCS than the control group after 8 weeks therapy; this difference remained in the follow-up after 6 months, when the cognitive group also had lower a score in social disability. Conclusion: Cognitive therapy can benefit patients with OCD more than medication only. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract).

Fang-Ru Y, Shuang-Luo Z, et al. Comparative Study of Solution-Focused Brief Therapy (SFBT) Combined with Paroxetine in the Treatment of Obsessive-Compulsive Disorder. Chinese Mental Health Journal. 2005;19(4):288-90.

Objectives: To evaluate the effect of Solution-Focused Brief Therapy (SFBT) combined with paroxetine in the treatment of Obsessive-Compulsive Disorder (OCD). Methods: 60 outpatients who met CCMD-3 criteria for OCD were randomly divided into experiment group (SFBT plus Paroxetine, n=30) and control group (paroxetine only, n =30) and treated for 10 weeks. The efficacy was assessed with Yale-Brown Obsessive- Compulsive Rating Scale (Y-BOCS) at the end of week 2, 4, 6, 8, and 10. Results: The Y-BOCS score in two groups were significantly decreased 2, 4, 6, 8, and 10 weeks after treatment ($P<0.05$ or $P<0.01$), and the Y-BOCS score in experiment group was significantly lower than that in control group ($P<0.05$ or $P<0.01$). Conclusions: SFBT combined with paroxetine and paroxetine have significant efficacy in the treatment of OCD, and SFBT combined with paroxetine has better effect than paroxetine alone. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract).

Foa EB, Liebowitz MR, et al. Randomized, placebo-controlled trial of exposure and ritual prevention, clomipramine, and their combination in the treatment of obsessive-compulsive disorder. Am J Psychiatry. 2005;162(1):151-61.

OBJECTIVE: The purpose of the study was to test the relative and combined efficacy of clomipramine and exposure and ritual prevention in the treatment of obsessive-compulsive disorder (OCD) in adults. Serotonin reuptake inhibitors (SRIs) and cognitive behavior therapy by exposure and ritual prevention are both established treatments for OCD, yet their relative and combined efficacy have not been demonstrated conclusively. METHOD: A double-blind, randomized, placebo-controlled trial comparing exposure and ritual prevention, clomipramine, their combination (exposure and ritual prevention plus clomipramine), and pill placebo was conducted at one center expert in pharmacotherapy, another with expertise in exposure and ritual prevention, and a third with expertise in both modalities. Participants were adult outpatients (N=122 entrants) with OCD. Interventions included intensive exposure and ritual prevention for 4 weeks, followed by eight weekly maintenance sessions, and/or clomipramine administered for 12 weeks, with a maximum dose of 250 mg/day. The main outcome measures were the Yale-Brown Obsessive Compulsive Scale total score and response rates determined by the Clinical Global Impression improvement scale. RESULTS: At week 12, the effects of all active treatments were superior to placebo. The effect of exposure and ritual prevention did not differ from that of exposure and ritual prevention plus clomipramine, and both were superior to clomipramine only. Treated and completer response rates were, respectively, 62% and 86% for exposure and ritual prevention, 42% and 48% for clomipramine, 70% and 79% for exposure and ritual prevention plus clomipramine, and 8% and 10% for placebo. CONCLUSIONS: Clomipramine, exposure and ritual prevention, and their combination are all efficacious treatments for OCD. Intensive exposure and ritual prevention may be superior to clomipramine and, by implication, to monotherapy with the other SRIs.

Nakatani E, Nakagawa A, et al. A randomized controlled trial of Japanese patients with obsessive-compulsive disorder--effectiveness of behavior therapy and fluvoxamine. Psychother Psychosom. 2005;74(5):269-76.

BACKGROUND: The aim of this study was to confirm and compare the efficacy of fluvoxamine (the only licensed SSRI for treatment for OCD in Japan) and behavior therapy in treating Japanese patients with OCD. In addition, we investigated predictors of these treatments. METHODS: Thirty-one outpatients meeting the DSM-III-R criteria for OCD without any axis I disorder were randomly assigned to one of three treatment conditions: BT (behavior therapy +/- pill placebo), FLV [autogenic training (a psychological placebo for OCD) +/- fluvoxamine] and control group [autogenic training (psychological placebo) +/- pill placebo] for 12 weeks of treatment. The Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) and the Clinical Global Impression-Improvement Scale (CGI-I) were administered blindly at baseline and week 4, 8 and 12. RESULTS: Twenty-eight patients completed this study. Patients in the BT and FLV groups showed significantly more improvement than those in the control group in the mean score of total Y-BOCS; moreover, the BT group showed significantly more reduction in total Y-BOCS score at the end of treatment than the FLV group (BT > FLV, $p < 0.01$). Patients with lower baseline total Y-BOCS, past history of a major depressive episode and absence of cleaning compulsion improved more with fluvoxamine. CONCLUSIONS: We confirmed the effectiveness of behavior therapy and fluvoxamine for Japanese patients with OCD. Behavior therapy improved the condition of OCD patients more than fluvoxamine.

Van Oppen P, van Balkom AJ, et al. Cognitive therapy and exposure in vivo alone and in combination with fluvoxamine in obsessive-compulsive disorder: a 5-year follow-up. J Clin Psychiatry. 2005;66(11):1415-22.

BACKGROUND: Information regarding the long-term effectiveness of the combination of pharmacotherapy and cognitive-behavioral therapy (CBT) in the treatment of obsessive-compulsive disorder (OCD) is limited. Our study is the first to examine the long-term effectiveness of cognitive therapy (CT) and to compare long-term effectiveness of CT alone, exposure in vivo with response prevention (ERP) alone, and CBT (either CT or ERP) in combination with fluvoxamine in the treatment of OCD. METHOD: Of 122 outpatients with primary DSM-III-R-defined OCD originally enrolled in 2 randomized controlled trials, 102 patients (45 male/57 female; mean +/- SD age = 36.2 +/- 10.7 years; range, 19-64 years) were available to be assessed for the presence and severity of OCD and comorbid psychopathology at follow-up. Follow-up data were collected from November 1996 to June 1999. RESULTS: After 5 years, 54% of the participants no longer met the DSM-III-R criteria for OCD. Long-term outcome did not differ between the 3 treatment groups. At follow-up, treatment dropouts appeared to have more severe OCD complaints compared with treatment completers. Compared with patients receiving CT alone, significantly ($p < .005$) more patients receiving CBT with fluvoxamine used antidepressants 5 years later. CONCLUSIONS: This study demon-

strates that at 5-year follow-up (1) prevalence of OCD had declined in all 3 treatment conditions, (2) the clinical benefits of all 3 treatment conditions were maintained, (3) OCD complaints were more severe for treatment dropouts than for treatment completers, and (4) about half of the patients initially treated with fluvoxamine continued antidepressant use.

O'Connor KP, Aardema F, et al. Cognitive behaviour therapy and medication in the treatment of obsessive-compulsive disorder. Acta Psychiatr Scand. 2006;113(5):408-19.

OBJECTIVE: To compare cognitive behaviour therapy (CBT) with CBT plus medication; medication alone; and placebo in the treatment of adult obsessive-compulsive disorder (OCD). METHOD: Forty-eight participants (43 completers) were recruited into two protocols. In the first protocol, 21 people with OCD were randomly allocated to either a standard medication (fluvoxamine) or standard placebo condition for a 5-month period. Both these groups subsequently received CBT for a further 5 months. In the second protocol, 22 people with OCD received CBT, one group was already stabilized on an antidepressant of choice; the second group was drug naive. RESULTS: All active treatments, but not the placebo, showed clinical improvement. There was no difference in treatment response to CBT regardless of whether participants had previously received medication or placebo. CONCLUSION: CBT has a more specific antiobsessional effect than medication but CBT plus medication shows greatest overall clinical improvement in mood.

Sousa MB, Isolan LR, et al. A randomized clinical trial of cognitive-behavioral group therapy and sertraline in the treatment of obsessive-compulsive disorder. J Clin Psychiatry. 2006;67(7):1133-9.

BACKGROUND: Cognitive-behavioral group therapy (CBGT) and serotonin reuptake inhibitors have proven efficacy in reducing symptoms of obsessive-compulsive disorder (OCD). There is no consensus about which of these forms of treatment is more effective. This study was conducted to evaluate the efficacy of CBGT as compared to that of sertraline in reducing OCD symptoms. METHOD: Fifty-six outpatients with an OCD diagnosis, according to DSM-IV criteria, participated in the randomized clinical trial: 28 took 100 mg/day of sertraline and 28 underwent CBGT for 12 weeks. Efficacy of treatments was rated according to the reduction in scores on the Yale-Brown Obsessive Compulsive Scale (YBOCS) and the Clinical Global Impressions-Severity of Illness scale. The trial was performed in 4 successive periods from March 2002 to December 2003. RESULTS: Both treatments were effective, although patients treated with CBGT obtained a mean YBOCS reduction of symptoms of 44%, while those treated with sertraline obtained only a 28% reduction ($p = .033$). Cognitive-behavioral group therapy was also significantly more effective in reducing the intensity of compulsions ($p = .030$). Further, 8 patients (32%) treated with CBGT presented a complete remission of OCD symptoms (YBOCS score < or = 8) as compared to only 1 patient (4%) among those who received sertraline ($p = .023$). CONCLUSION: Cognitive-behavioral group therapy and sertraline have shown to be effective in reducing OCD symptoms. Nevertheless, the rate of symptom reduction, intensity reduction of compulsions, and percentage of patients who obtained full remission were significantly higher in patients treated with CBGT.

Wilhelm S, Buhlmann U, et al. Augmentation of behavior therapy with D-cycloserine for obsessive-compulsive disorder. Am J Psychiatry. 2008;165(3):335-41; quiz 409.

OBJECTIVE: This study examined whether d-cycloserine, a partial agonist at the N-methyl-D-aspartate (NMDA) glutamatergic receptor, enhances the efficacy of behavior therapy for obsessive-compulsive disorder (OCD). METHOD: A randomized, double-blind, placebo-controlled trial investigating D-cycloserine versus placebo augmentation of behavior therapy was conducted in 23 OCD patients. Patients first underwent a diagnostic interview and pretreatment evaluation, followed by a psychoeducational/treatment planning session. Then they received 10 behavior therapy sessions. Treatment sessions were conducted twice per week. One hour before each of the behavior therapy sessions, the participants received either D-cycloserine, 100 mg, or a placebo. RESULTS: Relative to the placebo group, the D-cycloserine group's OCD symptoms were significantly more improved at mid-treatment, and the D-cycloserine group's depressive symptoms were significantly more improved at posttreatment. CONCLUSIONS: These data provide support for the use of D-cycloserine as an augmentation of behavior therapy for OCD and extend findings in animals and other human disorders suggesting that behavior therapy acts by way of long-term potentiation of glutamatergic pathways and that the effects of behavior therapy are potentiated by an NMDA agonist.

Maina G, Rosso G, et al. No effect of adding brief dynamic therapy to pharmacotherapy in the treatment of obsessive-compulsive disorder with concurrent major depression. Psychother Psychosom. 2010;79(5):295-302.

BACKGROUND: Until now no studies have investigated the benefits of adding brief dynamic therapy (BDT) to medication in obsessive-compulsive disorder (OCD), while a number of recent investi-

gations have demonstrated the efficacy of supplemental BDT among patients with major depressive disorders (MDD). The objective of the present study was to explore the efficacy of BDT combined with pharmacotherapy in comparison with pharmacotherapy alone in the treatment of OCD with concurrent MDD. METHODS: A 12-month randomized clinical trial compared a standard selective serotonin reuptake inhibitor treatment with (n = 27) or without (n = 30) supplemental BDT in patients with OCD and concurrent MDD. Supplemental BDT was added during the first 16-week trial; all patients continued to be treated with only pharmacotherapy in the following continuation phase. The primary efficacy assessments were the Yale-Brown Obsessive Compulsive Scale and the 17-item Hamilton Rating Scale for Depression; the secondary efficacy measures included the Clinical Global Impression scale and the Global Assessment of Functioning. The data analysis was conducted on the 'intent-to-treat (ITT) efficacy patient sample'. RESULTS: Fifty patients completed the study. No difference between the 2 treatment groups was found at any point by any assessment method in the ITT study sample. CONCLUSIONS: Supplemental BDT in the treatment of patients with OCD with concurrent MDD who are receiving effective medication has no significant clinical effect on both obsessive and depressive symptoms.

Nazari H, Momeni N, et al. Comparison of eye movement desensitization and reprocessing with citalopram in treatment of obsessive-compulsive disorder. Int J Psychiatry Clin Pract. 2011;15(4):270-4.

OBJECTIVE: Obsessive-compulsive disorder (OCD) is one of the chronic anxiety disorders that interfere with routine individual life, occupational and social functions. There is controversy about the first choice of treatment for OCD between medication and psychotherapy. AIM: the aim was to investigate the efficacy of eye movement desensitization and reprocessing (EMDR) compared with medication by citalopram in treatment of OCD. METHODS: This randomized controlled trial was carried out on 90 OCD patients that randomly were assigned into two groups. They either received therapeutic sessions of EMDR or citalopram during 12 weeks. Both groups blindly were evaluated by the Yale-Brown scale before and after the trial period. RESULTS: Pretreatment average Yale-Brown score of citalopram group was about 25.26 as well as 24.83 in EMDR group. The after treatment scores were 19.06 and 13.6, respectively. There was significant difference between the mean Yale-Brown scores of the two groups after treatment and EMDR was more effective than citalopram in improvement of OCD signs. CONCLUSION: It is concluded that although both therapeutic methods (EMDR and Citalopram) had significant effect in improving obsessive signs but it seems that in short term EMRD has better effect in improvement of final outcome of OCD.

Sharreh H, Gharaie B, et al. Comparison of metacognitive therapy, fluvoxamine and combined treatment in Improving metacognitive beliefs and subjective distress of patients with obsessive-compulsive disorder. Advances in Cognitive Science. 2011;12(4[48]):1-15.

Objective: The aim of this study was to investigate the efficacy of metacognitive therapy (MCT) compare to fluvoxamine and the combination of MCT with fluvoxamine in improving metacognitive beliefs and subjective distress in treating patients with obsessive-compulsive disorder (OCD). Methods: In an experimental study, 21 OCD outpatients were randomly assigned to one of three treatment conditions: MCT, fluvoxamine and combined treatment group. All the patients received 10 weeks of treatment. Two questionnaires were administered at pre-treatment and post-treatment: Subjective Units of Distress (SUD) and Metacognitions Questionnaire-Short Form (MCQ-30). Results: Results showed that unlike the fluvoxamine the MCT and combined treatment lead to significant improvements in positive beliefs about worry, negative beliefs about worry, need for thought control, cognitive confidence and subjective distress ($P < .01$). There were no significant differences between MCT and combined therapy (all $Ps > 0.05$). Conclusion: MCT and the combination of MCT with fluvoxamine are more effective than fluvoxamine in improving metacognitive beliefs and subjective distress in treating OCD. (PsycINFO Database Record (c) 2013 APA, all rights reserved) (journal abstract).

Aderka IM, Anholt GE, et al. Sudden gains in the treatment of obsessive-compulsive disorder. Psychother Psychosom. 2012;81(1):44-51.

BACKGROUND: The present study examined sudden gains during treatment for obsessive-compulsive disorder (OCD) and their relationship to short- and long-term outcome. METHODS: Ninety-one individuals (age 19-64) completed either cognitive treatment, exposure treatment, or their combination with fluvoxamine for OCD. Participants' obsessive-compulsive symptoms were assessed before each weekly treatment session. In addition, obsessive-compulsive and depressive symptoms were assessed pre treatment and post treatment as well as 12 months following treatment termination. RESULTS: Sudden gains were found among 34.1% of participants and constituted 65.5% of the total reduction in obsessive-compulsive symptoms. Compared to

individuals who did not experience sudden gains, individuals who experienced sudden gains reported lower levels of OCD symptoms post treatment, and this was maintained during follow-up. CONCLUSIONS: Sudden gains are common in treatments for OCD and are predictive of treatment outcome and follow-up. Sudden gains mark a distinct trajectory of response to treatment for OCD. Individuals with sudden gains greatly improve during treatment and maintain their gains during follow-up, whereas individuals without sudden gains improve to a significantly lesser extent. Thus, treatment planning and development can benefit from considering sudden gains and the intra-individual course of improvement.

Balkom AJ, Emmelkamp PM, et al. Cognitive therapy versus fluvoxamine as a second-step treatment in obsessive-compulsive disorder nonresponsive to first-step behavior therapy. Psychotherapy and psychosomatics. 2012;81:366-74. DOI: 10.1159/000339369.

BACKGROUND: To compare the effectiveness of second-step treatment with cognitive therapy (CT) versus fluvoxamine in patients with obsessive-compulsive disorder (OCD) who are nonresponsive to exposure in vivo with response prevention (ERP). METHODS: A 12-week randomized controlled trial at an outpatient clinic in the Netherlands comparing CT with fluvoxamine in OCD. Of 118 subjects with OCD treated with 12 weeks of ERP, 48 appeared to be nonresponders (Y-BOCS improvement score of less than one third). These nonresponders were randomized to CT (n = 22) or fluvoxamine (n = 26). The main outcome measure was the Y-BOCS severity scale. Statistical analyses were conducted in the intention-to-treat sample (n = 45) on an 'as randomized basis' and in the per-protocol sample (n = 30). Due to selective dropout in the fluvoxamine group, two additional sensitivity analyses were performed. RESULTS: Complete data could be obtained from 45 subjects (94%) after 12 weeks. Fifty percent of the patients refused fluvoxamine after randomization compared to 13% who refused CT [?(2)(1) = 7.10; p = 0.01]. CT as a second-step treatment did not appear to be effective in this sample of nonresponders. Fluvoxamine was significantly superior to CT in the intention-to-treat sample, in the per-protocol sample and in the two separately defined samples in which the sensitivity analyses were performed. CONCLUSIONS: OCD patients who are nonresponsive to ERP may benefit more from a switch to treatment with an antidepressant instead of switching to CT. In clinical practice, it may be important to motivate this subgroup of patients to undergo psychopharmacological treatment, as this may improve their outcome considerably.

Belotto-Silva C, Diniz JB, et al. Group cognitive-behavioral therapy versus selective serotonin reuptake inhibitors for obsessive-compulsive disorder: a practical clinical trial. J Anxiety Disord. 2012;26(1):25-31.

Clinical effectiveness of group cognitive-behavioral therapy (GCBT) versus fluoxetine in obsessive-compulsive disorder outpatients that could present additional psychiatric comorbidities was assessed. Patients (18-65 years; baseline Yale-Brown Obsessive-Compulsive-Scale [Y-BOCS] scores >/= 16; potentially presenting additional psychiatric comorbidities) were sequentially allocated for treatment with GCBT (n=70) or fluoxetine (n=88). Mean Y-BOCS scores decreased by 23.13% in the GCBT and 21.54% in the SSRI groups (p=0.875). Patients presented a mean of 2.7 psychiatric comorbidities, and 81.4% showed at least one additional disorder. A reduction of at least 35% in baseline Y-BOCS scores and CGI ratings of 1 (much better) or 2 (better) was achieved by 33.3% of GCBT patients and 27.7% in the SSRI group (p=0.463). The Y-BOCS reduction was significantly lower in patients with one or more psychiatric comorbidities (21.15%, and 18.73%, respectively) than in those with pure OCD (34.62%; p=0.034). Being male, having comorbidity of Major Depression, Social Phobia, or Dysthymia predicted a worse response to both treatments. Response rates to both treatments were similar and lower than reported in the literature, probably due to the broad inclusion criteria and the resulting sample more similar to the real world population.

Giasuddin NA, Nahar JS, et al. Efficacy of combination of fluoxetine and cognitive behavioral therapy and fluoxetine alone for the treatment of obsessive compulsive disorder. Pak J Pharm Sci. 2013;26(1):95-8.

A number of pharmacological approaches as well as psychological interventions are effective in the treatment of obsessive-compulsive disorder (OCD). The present study was conducted to see the relative efficacy of treatment approaches. 30 diagnosed cases of OCD were taken and divided into two groups. Each group consisted of 15 patients. Group A (N=15) received capsule fluoxetine and Group B (N=15) received capsule fluoxetine and CBT (13 weekly sessions). Twenty six participants completed the study (13 in each group). Dhaka University Obsessive-compulsive Scale (DUOCS) was used to measure the symptom severity. Symptom scores were measured at weeks 1, 5, 9 and 13. After 13 weeks, analysis of the data was done and the means of initial DUOCS score and 13th week

score were compared. In both the groups the mean score changes were highly significant (p=0.000). Intra group analysis revealed that both the treatment approaches were highly efficacious. Inter-group analysis revealed that the response in combination group was significantly higher starting from 9th week, continuing up to 13th week. Mean symptom reduction and mean percentage reduction of symptoms were also higher in the case of combination group.

Ma JD, Wang CH, et al. Cognitive-coping therapy for obsessive-compulsive disorder: a randomized controlled trial. J Psychiatr Res. 2013;47(11):1785-90.

Pharmacotherapy and cognitive-behavioral therapy (CBT) are widely used to treat obsessive-compulsive disorder (OCD). These treatments have helped many patients with OCD, but there still is room for improvement. Recently, a promising psychotherapy for OCD, cognitive-coping therapy (CCT), has been developed. Pharmacotherapy plus CCT (PCCT) demonstrates higher efficacy in a shorter period of time and lower relapses than pharmacotherapy or pharmacotherapy plus CBT. In this randomized controlled trial, we investigated the efficacy of CCT for OCD treatment. One hundred and forty-five OCD patients were randomly assigned into two groups: pharmacotherapy (N = 72) and PCCT (N = 73). In each group, drug-resistant (DR) and non-drug-resistant (NDR) OCD were further analyzed to examine the efficacy of CCT. Some clinical features and the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) were blindly assessed pre-treatment and post-treatment at week 1, 2, 3, 4, and 12. The Y-BOCS scores were significantly lower in PCCT than in the pharmacotherapy group at any post-treatment time-point ($P < 0.001$). Compared with pre-treatment, the Y-BOCS scores were significantly reduced at any time-point ($P < 0.001$) in PCCT group, but only at week 12 ($P < 0.001$) in the pharmacotherapy group. In the PCCT group, there were no differences between DR and NDR groups' Y-BOCS scores at any post-treatment time-point. The response rates and remission rates were higher in PCCT than in the pharmacotherapy group. Three variables, the number of weeks of treatment, insight, and disregarding of obsessions, were significantly correlated with the Y-BOCS score. Therefore, CCT might be a potential treatment for OCD.

Hu XZ, Ma JD, et al. Highly efficacious cognitive-coping therapy for overt or covert compulsions. Psychiatry Research. 2015;229(3):732-8.

Pharmacotherapy and cognitive-behavioral therapy (CBT) present limitations when they are used to treat obsessive–compulsive disorder (OCD), a severe and debilitating psychiatric disorder. To search for more efficacious treatment, we investigated the effects of pharmacotherapy plus cognitive-coping therapy (pCCT) on adult OCD patients with overt or covert compulsions. Two hundred and fifteen OCD patients were randomized into pharmacotherapy plus psychological support (PPS, n = 107) and pCCT (n = 108). The Yale–Brown Obsessive Compulsive Scale (Y–BOCS) was used to measure severity of symptoms in the OCD patients. The Y–BOCS scores were significantly lower in pCCT than in PPS in both acute term (< 3 months) and long-term follow-up. In pCCT, severity of symptoms was not different between those with covert compulsions and those with overt compulsions, but was significantly reduced at any post-treatment time-point. Y–BOCS scores in the two subtype compulsions were significantly lower in pCCT than in PPS at any post-treatpost-treatment time-point. Compared with PPS, effect size, response rate and remission rate were significantly higher in pCCT. Our findings corroborated with the hypothesis that pCCT could efficaciously treat OCD with overt compulsions or covert compulsion, suggesting that pCCT might be a potential option for adult OCD. (PsycINFO Database Record (c) 2015 APA, all rights reserved) (journal abstract).

Landsheer JA, Smit JH, et al. Assignment refusal and its relation to outcome in a randomized controlled trial comparing Cognitive Therapy and Fluvoxamine in treatment-resistant patients with obsessive compulsive disorder. Psychiatry research. 2015;226:198-203. DOI: 10.1016/j.psychres.2014.12.050.

The effectiveness of Fluvoxamine was compared to that of Cognitive Therapy (CT) in a 12-week randomized controlled trial (RCT) in 48 patients with obsessive-compulsive disorder (OCD), who were treatment-resistant to a previous behavior therapy (BT). A considerable amount of patients did not comply with the assigned treatment and switched treatments. The aim of this study was to identify patient characteristics predictive of assignment compliance and to study whether these characteristics were related to outcome. A logistic model, based on psychological and social patient characteristics, in addition to or in interaction with the assignment, was used for the explanation of compliance with treatment assignment. Especially patients who have a higher score on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) tend to comply with the effective Fluvoxamine treatment. The same set of variables was related to both compliance and outcome of therapy received. Therefore, the logistic model of compliance could be used to reduce the positive bias of As-Treated analysis (AT). The difference between the results of Fluvoxamine and Cognitive Therapy remained

statistically significant after correcting for the positive bias as the result of assignment refusal and after applying the assumption that two drop-out patients needed imputation of lesser results.

1.2. Eficacia, tolerabilidad y seguridad de los tratamientos psicofarmacológicos en monoterapia (estudios versus *placebo)*

1.2.1. ISRS (20 – 1985-2010)

Turner SM, Jacob RG, et al. Fluoxetine treatment of obsessive-compulsive disorder. J Clin Psychopharmacol. 1985;5(4):207-12.

Fluoxetine hydrochloride, a new antidepressant, was administered to 10 obsessive-compulsive patients, and the effects of treatment were examined in a single-blind placebo design. The effects of fluoxetine were examined with respect to depressive symptomatology and obsessions and compulsions per se. The results suggest that fluoxetine affected depressive symptoms but also had an effect on self-reported measures of obsessions and ritualistic behavior. Results are discussed in terms of improvement in obsessive-compulsive disorder, the relation of improvement to initial levels of depression, and patients' ability to tolerate the drug.

Perse TL, Greist JH, et al. Fluvoxamine treatment of obsessive-compulsive disorder. Am J Psychiatry. 1987;144(12):1543-8.

Sixteen outpatients who met DSM-III criteria for obsessive-compulsive disorder completed a 20-week double-blind, crossover trial with fluvoxamine and placebo. Thirteen (81%) improved with fluvoxamine, while three (19%) improved with placebo. Fluvoxamine treatment was associated with significant improvement on measures of obsessive-compulsive symptoms, anxiety, and depression. Depressed subjects' improvement on obsessive-compulsive measures correlated with improvement in symptoms of depression. Nondepressed subjects also showed improvement on measures of obsessive-compulsive symptoms. In this trial, fluvoxamine was an effective and safe treatment for obsessive-compulsive disorder.

Price LH, Goodman WK, et al. Treatment of severe obsessive-compulsive disorder with fluvoxamine. Am J Psychiatry. 1987;144(8):1059-61.

Ten obsessive-compulsive patients received single-blind treatment with fluvoxamine, a selective serotonin reuptake inhibitor, for several weeks following at least 2 weeks of placebo. The group showed significant improvement, as measured by several clinical scales and self-ratings; six patients were judged responders. Fluvoxamine appears effective in treating severe obsessive-compulsive disorder.

Goodman WK, Price lh, et al. Efficacy of fluvoxamine in obsessive-compulsive disorder. A double-blind comparison with placebo. Arch Gen Psychiatry. 1989;46(1):36-44.

A six- to eight-week double-blind placebo-controlled trial of the potent and selective serotonin reuptake inhibitor fluvoxamine was conducted in 42 patients with primary obsessive-compulsive disorder (OCD). Approximately one half of the patients also had symptoms of major depression. Fluvoxamine was significantly better than placebo on all measures of obsessive-compulsive symptoms. Nine of 21 patients were responders ("much improved") with fluvoxamine compared with no responders with placebo, and fluvoxamine was effective in patients with OCD both with and without secondary depression. Response of OCD was not correlated with severity of baseline depression. These data lend partial support to the serotonin hypothesis of OCD. However, since a number of patients failed to respond to fluvoxamine, the role of other neurochemical systems in this disorder needs to be explored.

Chouinard G, Goodman W, et al. Results of a double-blind placebo controlled trial of a new serotonin uptake inhibitor, sertraline, in the treatment of obsessive-compulsive disorder. Psychopharmacol Bull. 1990;26(3):279-84.

Eighty-seven patients with a DSM-III diagnosis of obsessive-compulsive disorder (OCD) without depression were entered into a double-blind, placebo-controlled study of the efficacy of sertraline, a new serotonin uptake inhibitor. After a 1-week washout period, patients were randomly assigned to receive either placebo or sertraline. After a 2-week titration period in which the once-daily sertraline dose was increased from 50 mg/day to a maximum of 200 mg/day, dosage was maintained until the end of the eighth week, then patients were titrated off medication over the next 2 weeks. Efficacy was measured by the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), NIMH General Obsessive-Compulsive Scale, Maudsley Obsessive Compulsive (MOC) Inventory, and Clinical Global

Impressions (CGI) Severity and Improvement scales. Results on the MOC Inventory showed trends in favor of active drug that were not statistically significant compared with placebo. Results of the Y-BOCS total score, the NIMH score, and the global severity and improvement scores demonstrated a statistically significant superiority of sertraline compared with placebo.

Jenike MA, Baer L, et al. Sertraline in obsessive-compulsive disorder: a double-blind comparison with placebo. Am J Psychiatry. 1990;147(7):923-8.

Many agents that affect the brain's serotonergic system appear to be at least partially effective in the treatment of patients with obsessive-compulsive disorder. However, in this 10-week double-blind trial in which 10 patients received sertraline and nine received placebo, sertraline was ineffective according to four measures of obsessive-compulsive symptoms. The authors discuss the implications of these preliminary findings for the serotonergic theory of obsessive-compulsive disorder and the need to explore the role of other neurochemical systems in this disorder.

Jenike MA, Hyman S, et al. A controlled trial of fluvoxamine in obsessive-compulsive disorder: implications for a serotonergic theory. Am J Psychiatry. 1990;147(9):1209-15.

Thirty-eight patients with primary obsessive-compulsive disorder participated in a 10-week, double-blind, placebo-controlled trial of the potent, selective serotonin reuptake inhibitor fluvoxamine. Fluvoxamine was significantly better than placebo on two of three measures of improvement in obsessive-compulsive symptoms. The authors also compared studies of the serotonergic agents fluvoxamine, sertraline, fluoxetine, and clomipramine and found that a greater effect size was associated with less serotonergic specificity and that some ability to affect other neurotransmitter systems may be a necessary but not sufficient requirement for antiobsessional activity. These data lend only partial support to a serotonin hypothesis of obsessive-compulsive disorder.

Chouinard G. Sertraline in the treatment of obsessive compulsive disorder: two double-blind, placebo-controlled studies. Int Clin Psychopharmacol. 1992;7 Suppl 2:37-41.

Sertraline is a non-tricyclic, potent and selective serotonin reuptake inhibitor (SSRI) which is currently approved for the treatment of depression in several countries, including the UK and the USA. The role of serotonin in the aetiology of obsessive compulsive disorder (OCD) has been established through considerable indirect evidence. The strongest evidence comes from the fact that drugs known to be SSRIs have been found to be useful in the pharmacotherapy of OCD. Two double-blind, placebo-controlled studies, including a total of 412 patients, were undertaken to evaluate the efficacy and safety of sertraline in OCD. The first of these studies of a flexible dosing design showed that sertraline, given for eight weeks in daily dosages of 50-200 mg, was a safe and effective treatment for OCD, and superior to placebo. The second study of a fixed dose design and 12 weeks duration confirmed the efficacy and safety of sertraline in OCD at fixed dosages of 50, 100, or 200 mg/day and demonstrated that further improvement in OCD symptoms can be achieved through continued treatment with sertraline. A comparison between the results of these two studies and similar studies with clomipramine shows that, while both drugs have significant therapeutic efficacy, their side-effect profiles may be markedly distinct.

Mallya GK, White K, et al. Short- and long-term treatment of obsessive-compulsive disorder with fluvoxamine. Annals of Clinical Psychiatry. 1992;4(2):77-80.

28 patients with Diagnostic and Statistical Manual of Mental Disorders-III-Revised (DSM-III-R) diagnosis of obsessive-compulsive disorders (OCDs) completed a 10-wk double-blind placebo controlled trial of a serotonergic uptake blocker, fluvoxamine (FVX). Six Ss (43%) improved more than 35% in the FVX group, whereas only 1 S (7%) improved in the placebo group. Analysis of the change scores on the Yale-Brown Scale for OCD showed significantly greater improvement with FVX than with placebo. 21 of the Ss then participated in an open trial with FVX for a period of 2–22 mo. 12 Ss (57%) showed improvement. Seven of 9 relapsed within a few days to weeks of discontinuation of FVX.

George MS, Trimble MR, et al. Fluvoxamine and sulpiride in comorbid obsessive-compulsive disorder and Gilles de la Tourette Syndrome. Human Psychopharmacology: Clinical and Experimental. 1993;8(5):327-34.

Explores the relationship between 5-hydroxytryptamine (5-HT) and dopamine in Tourette's Syndrome (TS) and obsessive-compulsive disorder (OCD) with a 14-wk, double-blind, placebo-controlled crossover trial of fluvoxamine (a specific 5-HT reuptake inhibitor) vs sulpiride (a dopamine antagonist) followed by single-blind combined therapy (4 wks) in 11 Ss with comorbid OCD and TS.

Sulpiride monotherapy significantly reduced tics and non-significantly improved OCD symptoms. Fluvoxamine, either alone or combined with sulpiride, non-significantly ameliorated tics and reduced OCD symptoms. Additionally, tics and OCD symptoms covaried. These results are consistent with a possible coupling of dopaminergic and 5-HT systems in comorbid OCD/TS Ss. (PsycINFO Database Record (c) 2012 APA, all rights reserved).

Montgomery SA, McIntyre A, et al. A double-blind, placebo-controlled study of fluoxetine in patients with DSM-III—R obsessive-compulsive disorder. European Neuropsychopharmacology. 1993;3(2):143-52.

Studied the effect of fixed doses of fluoxetine and placebo in the treatment of 207 adult patients with obsessive–compulsive disorder (OCD). The study was conducted in Europe and was of a design complementary to D. Wheadon's (191) study in the US. Ss received double-blind treatment with 20 mg, 40 mg, or 60 mg daily doses of fluoxetine or with placebo for 8 wks. The symptoms were monitored weekly for the 1st half of this period and biweekly for the 2nd half. Those Ss who had improved significantly continued another 16 wks of placebo-controlled, double-blind therapy with progress monitored monthly. The results support the therapeutic value of fluoxetine in patients with OCD, and suggest that response to all forms of pharmacotherapy may be relatively slow and incremental with best response being seen after months rather than weeks of treatment. (PsycINFO Database Record (c) 2013 APA, all rights reserved).

Tollefson GD, Rampey AH Jr., et al. A multicenter investigation of fixed-dose fluoxetine in the treatment of obsessive-compulsive disorder. Arch Gen Psychiatry. 1994;51(7):559-67.

OBJECTIVES: To determine the effectiveness of fluoxetine hydrochloride at fixed doses of 20 mg/d, 40 mg/d, and 60 mg/d in patients with obsessive-compulsive disorder (OCD) and to evaluate its safety. METHODS: Fixed-dose fluoxetine hydrochloride (20 mg/d, 40 mg/d, 60 mg/d) was compared with placebo in two randomized, double-blind, parallel, 13-week trials of identical design in 355 outpatients with OCD aged 15 to 70 years (DSM-III-R criteria; 1 year's duration or longer; depression secondary if present). RESULTS: Fluoxetine (all doses) was significantly (P < or = .001) superior to placebo on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) total score (mean baseline-to-end-point decrease, 4.6, 5.5, and 6.5 vs 0.9, respectively, studies pooled) and other efficacy measures (P < or = .01). A trend suggesting greater efficacy at 60 mg/d was observed. Most patients (79.2%) completed the study. Eight adverse events were statistically significantly more frequent with fluoxetine and one, with placebo. For some events, incidence tended to increase with increasing dosage; however, few patients discontinued treatment for any single event. CONCLUSION: Fluoxetine was associated with a statistically significant reduction in OCD severity, including time engaged in obsessional and/or compulsive behaviors. Adverse events infrequently led to study discontinuation.

Goodman WK, Kozak MJ, et al. Treatment of obsessive-compulsive disorder with fluvoxamine: a multicentre, double-blind, placebo-controlled trial. Int Clin Psychopharmacol. 1996;11(1):21-9.

One hundred and sixty patients with a primary diagnosis of obsessive-compulsive disorder were enrolled in a multicentre, randomized, double-blind, placebo-controlled study of fluvoxamine. After a placebo washout phase, patients were randomized to treatment with placebo or fluvoxamine (100-300 mg/day) for 10 weeks. Seventy-eight patients in each group were evaluable for efficacy. Fluvoxamine was significantly more effective than placebo as assessed by the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), the National Institute of Mental Health Obsessive-Compulsive (NIMH-OC) scale and the Global Improvement item of the Clinical Global Impression (CGI) scale. The percentage of patients classified as "responders" (much or very much improved according to the Global Improvement item) was also significantly higher in the fluvoxamine group from Week 6 onwards, with 33.3% of fluvoxamine-treated patients and 9.0% of those given placebo classified as "responders" at endpoint. The "responders" to fluvoxamine experienced a substantial clinical benefit as reflected in decreases in their Y-BOCS and NIMH-OC scores. Fluvoxamine was well tolerated with the majority of adverse events considered mild or moderate.

Kronig MH, Apter J, et al. Placebo-controlled, multicenter study of sertraline treatment for obsessive-compulsive disorder. J Clin Psychopharmacol. 1999;19(2):172-6.

The safety and efficacy of sertraline versus placebo were examined in a group of nondepressed outpatients with obsessive-compulsive disorder (OCD). Patients with moderate-to-severe OCD were recruited at 10 sites. After a 1-week placebo lead-in, patients were treated in a double-blind fashion for 12 weeks with sertraline or placebo. Sertraline was administered at a starting dose of 50 mg/day, with flexible titration up to 200 mg/day. The efficacy measures were the Yale-Brown Obsessive Compulsive Scale (Y-BOCS), the National Institute of Mental Health Global Obsessive Compulsive Scale (NIMH),

and the Clinical Global Impression Scale (CGI) Severity of Illness and Improvement subscales. One hundred sixty-seven patients were randomly assigned and received at least one dose of double-blind medication: 86 received sertraline and 81 received placebo. All efficacy measures showed significantly greater improvement in the sertraline group from the end of week 8 until the end of week 12. Significantly greater improvement ($p < 0.05$) in the sertraline group first became apparent by the end of week 3 on the Y-BOCS and the CGI Improvement scale, and by the end of weeks 6 and 8, respectively, on the NIMH and CGI Severity scale. Sertraline was well tolerated, without serious adverse effects. In conclusion, sertraline was safe and effective in the treatment of patients with OCD.

Zitterl W, Meszaros K, et al. Efficacy of fluoxetine in Austrian patients with obsessive-compulsive disorder. Wien Klin Wochenschr. 1999;111(11):439-42.

In an 8-week double-blind placebo-controlled trial we studied the efficacy of fluoxetine (FLX) in 53 Austrian patients with obsessive compulsive disorder (OCD) diagnosed according to DSM-III-R. The dosage of FLX was fixed at either 20, 40, or 60 mg per day. Response was prospectively defined as an at least 25% reduction on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) and an improvement on Clinical Global Impression (CGI) rating to at least "much improved" at the endpoint. Patients treated with at least 40 mg FLX per day showed significantly higher response rates than did those receiving either placebo or FLX 20 mg/day. Compulsions were more reduced than obsessions and we also observed a strong placebo effect which is largely attributable to an improvement in the Y-BOCS compulsion subscore.

Black DW, Gabel J, et al. A double-blind comparison of fluvoxamine versus placebo in the treatment of compulsive buying disorder. Ann Clin Psychiatry. 2000;12(4):205-11.

Nondepressed outpatients with a compulsive buying disorder were recruited by advertisement and word of mouth for inclusion in a controlled treatment trial. Following a 1-week single-blind placebo washout, subjects were randomly assigned to fluvoxamine (n = 12) or placebo (n = 11). Subjects received fluvoxamine (up to 300 mg daily) or placebo for 9 weeks. There were few dropouts. Outcome measures included the Yale-Brown Obsessive-Compulsive Scale--Shopping Version (YBOCS-SV), three Clinical Global Impressions (CGI) ratings, the Hamilton Rating Scale for Depression (HRSD), and the Maudsley Obsessive-compulsive Inventory (MOI). At the conclusion of the trial, 50% of fluvoxamine recipients and 63.6% of placebo recipients achieved CGI ratings of "much" or "very much" improvement, while 33% of fluvoxamine recipients were "very much" improved compared with 18% of placebo recipients (by endpoint analysis). Subjects in both treatment cells showed improvement as early as the second week of the trial, and for most, improvement continued during the 9-week study. There were no significant differences between fluvoxamine- and placebo-treated subjects on any of the outcome measures, with the exception that fluvoxamine recipients achieved greater improvement than placebo recipients on the MOI ($p = .02$). Adverse experiences were more frequent in the group receiving fluvoxamine, particularly nausea, insomnia, decreased motivation, and sedation. We conclude that in a short-term treatment trial of compulsive buying, subjects receiving fluvoxamine or placebo respond similarly.

Hollander E, Koran LM, et al. A double-blind, placebo-controlled study of the efficacy and safety of controlled-release fluvoxamine in patients with obsessive-compulsive disorder. J Clin Psychiatry. 2003;64(6):640-7.

OBJECTIVE: The aim of this 12-week, double-blind, flexible-dose, placebo-controlled, parallel-arm, multicenter trial was to determine the safety and efficacy of fluvoxamine in a controlled-release (CR) formulation in adult outpatients with obsessive-compulsive disorder (OCD). METHOD: 253 adult outpatients with DSM-IV OCD were randomly assigned to receive 100 to 300 mg of fluvoxamine CR (N = 127) or placebo (N = 126) once daily for 12 weeks. Intent-to-treat analyses of efficacy assessments with the Yale-Brown Obsessive Compulsive Scale (YBOCS), Clinical Global Impressions-Severity of Illness scale (CGI-S), and Clinical Global Impressions-Improvement scale (CGI-I) were conducted. RESULTS: Fluvoxamine CR was significantly ($p <.05$) superior to placebo in decreasing YBOCS total score beginning at week 2. This early response was sustained at all subsequent visits. At endpoint, there was a mean decrease of 8.5 +/- 0.7 (31.7%) in the YBOCS total score compared with baseline in the fluvoxamine CR treatment group versus a mean decrease of 5.6 +/- 0.7 (21.2%) in the placebo group ($p =.001$). Fluvoxamine CR was also significantly superior to placebo in lowering the severity of illness (CGI-S, $p =.002$) and in producing clinical improvement (CGI-I, $p <.01$). At endpoint, significantly greater percentages of the fluvoxamine CR treatment group were responders ($p =.002$) and remitters ($p =.019$) compared with the placebo group. CONCLUSION: Over 12 weeks, fluvoxamine CR treatment was associated with a statistically significant and clinically relevant reduction in OCD severity and was found to be safe and well tolerated. The early onset of therapeutic effect, starting from week 2, was of particular interest.

Kamijima K, Murasaki M, et al. Paroxetine in the treatment of obsessive-compulsive disorder: randomized, double-blind, placebo-controlled study in Japanese patients. Psychiatry Clin Neurosci. 2004;58(4):427-33.

The efficacy of paroxetine in the treatment of obsessive-compulsive disorder in Western populations is well established. The present study compares the efficacy and safety of paroxetine with placebo in the treatment of obsessive-compulsive disorder in Japanese patients. Patients aged 16 years or older who met Diagnostic and Statistical Manual of Mental Disorders (4th edn; DSM-IV) criteria for obsessive-compulsive disorder and had a Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) score of >/=16 were randomized to receive 12 weeks' therapy in a double-blind manner. Paroxetine 20-50 mg/day or placebo was administered following a 1 week, placebo run-in phase. One hundred and ninety-one patients were randomized to either paroxetine or placebo, 188 patients were assessed as the full analysis set (FAS) and 144 patients completed the 12 week study. After adjustment for the Y-BOCS total score at baseline, reductions in obsessive-compulsive total score at week 6 and at the end of therapy were significantly greater in the paroxetine group than the placebo group. Most of the adverse events that occurred during the study were of mild to moderate intensity. Paroxetine is effective and well tolerated in Japanese adult patients with obsessive-compulsive disorder.

Khan MN, Hotiana UA, et al. Escitalopram in the treatment of obsessive-compulsive disorder: a double blind placebo control trial. J Ayub Med Coll Abbottabad. 2007;19(4):58-63.

BACKGROUND: The tolerability and efficacy for patients with obsessive-compulsive disorder (OCD) in a large, sample on Escitalopram was studied. METHODS: A total of 100 adults with a confirmed diagnosis of OCD were included. The percentage of patients with an adequate drug trial, defined as 42 days of continuous treatment with a serotonin- reuptake inhibitor or placebo at dosages at or above established minimal effective dosages. RESULTS: Ninety-six percent of the adults who were newly diagnosed with OCD in the index year had an adequate trial of medication after their first visit for OCD. By the second half of 42 days the patient who were responding to the treatment were randomly allocated to two groups. One group received the same drug and other group was given placebo. The results were complied at the end of three months of each patient treatment. No additional psychotherapy was offered to these patients during this time period. CONCLUSIONS: Despite the typically chronic course of OCD, many patients with OCD responded to the Esciatolpram at the dosage of twenty milligram per day.

Koran LM, Bromberg D, et al. Extended-release fluvoxamine and improvements in quality of life in patients with obsessive-compulsive disorder. Compr Psychiatry. 2010;51(4):373-9.

OBJECTIVE: We hypothesized that subjects with obsessive-compulsive disorder (OCD) who received extended-release fluvoxamine (fluvoxamine ER) in a 12-week placebo-controlled trial would exhibit improvements in psychosocial domains of health-related quality of life (HRQOL) and that additional improvements would occur after a 40-week open-label extension trial. We also hypothesized that greater OCD symptom improvement in the first 12 weeks of treatment would be associated with greater HRQOL improvement after 52 weeks of treatment. METHODS: In the 12-week placebo-controlled trial, subjects were randomized to receive placebo or 100 mg/d of fluvoxamine ER and then titrated in weekly 50 mg increments to a final dose of 100 to 300 mg/d. All subjects enrolled in the 40-week extension trial followed a similar titration, during which they were maintained on their highest well-tolerated dose. RESULTS: After 12 weeks of treatment, fluvoxamine ER subjects experienced significantly greater decreases than placebo subjects in Yale-Brown Obsessive-Compulsive Scale scores (P = .001). Both the active drug and placebo groups exhibited significant improvements in psychosocial domains of HRQOL; further improvement occurred after 40 weeks of open-label treatment with active drug. The greater the improvement in OCD severity at 12 weeks, the greater the improvement at 52 weeks in the psychosocial domains (Social Functioning r = -0.39, P = .027; Emotional Problems r = -0.37, P = .037; Mental Health r = -0.49, P = .004). CONCLUSION: Improvement in Yale-Brown Obsessive-Compulsive Scale severity scores during treatment with fluvoxamine ER was associated with improvements in psychosocial aspects of HRQOL that increased over an extended period of treatment.

1.2.2. Tricíclicos (19 – 1975-1995)

Ananth J, Solyom L, et al. Doxepin in the treatment of obsessive compulsive neurosis. Psychosomatics. 1975;16(4):185-7.

Wyndowe J, Solyom L, et al. Anafranil in obsessive compulsive neurosis. Curr Ther Res Clin Exp. 1975;18(5):611-7.

Stern RS, Marks IM, et al. Clomipramine and exposure for compulsive rituals: II. Plasma levels, side effects and outcome. Br J Psychiatry. 1980;136:161-6.

Forty obsessive-compulsive ritualizers received nightly placebo or clomipramine up to 225 mgs nocte for 8 months, and received behavioural treatment (exposure to vivo) from weeks 4 to 10. Plasma concentrations of clomipramine and its primary metabolite N-desmethylclomipramine steadily increased over the first 4 weeks of treatment after which they remained relatively steady. Plasma levels correlated significantly with dose and with outcome but not with side effects. Patients with plasma clomipramine levels in the range 100-250 ng/ml and N-desmethylclomipramine levels between 230-550 ng/ml were found to improve significantly more than patients outside these ranges, thus suggesting a therapeutic window for clomipramine and its primary metabolite.

Mavissakalian M, Turner SM, et al. Tricyclic antidepressants in obsessive-compulsive disorder: antiobsessional or antidepressant agents? II. Am J Psychiatry. 1985;142(5):572-6.

The authors explored the relationship between the antiobsessional and antidepressant effects of tricyclic drugs in primary obsessive-compulsive disorders. Study 1 consisted of a controlled 12-week trial with clomipramine (N = 7) and placebo (N = 5); study 2 analyzed the pooled data from 15 patients uniformly selected and treated with either clomipramine or imipramine. Although the antiobsessional and antidepressant effects of the drugs covaried, their antidepressant action was not a prerequisite for their antiobsessional effect. The findings suggest that clomipramine and probably imipramine possess specific antiobsessive effects that are at least partially independent of their antidepressant effects.

Foa EB, Steketee G, et al. Effects of imipramine on depression and obsessive-compulsive symptoms. Psychiatry Research. 1987;21(2):123-36.

Most of the controlled studies on the efficacy of medical treatments of obsessive-compulsive disorder (OCD) have involved clomipramine. To test the possibility that clomipramine's antidepressant action mediates the reduction of obsessive-compulsive symptoms, the present authors treated 37 OCD adults with imipramine or placebo for 6 wks and assessed improvement on both obsessive-compulsive and depressive symptoms. Imipramine reduced depression in highly depressed OCD Ss but did not affect obsessive-compulsive symptoms in these or in less depressed Ss. (PsycINFO Database Record (c) 2012 APA, all rights reserved).

Foa EB, Steketee G, et al. Imipramine and placebo in the treatment of obsessive-compulsives: their effect on depression and on obsessional symptoms. Psychopharmacol Bull. 1987;23(1):8-11.

Monteiro WO, Noshirvani HF, et al. Anorgasmia from clomipramine in obsessive-compulsive disorder. A controlled trial. Br J Psychiatry. 1987;151:107-12.

Forty-six patients with obsessive-compulsive disorder undergoing a double-blind controlled study of clomipramine and placebo were interviewed to assess changes in sexual function. Of 33 patients with previously normal organism, nearly all of the 24 on clomipramine developed total or partial anorgasmia; none of the 9 on placebo did so. Anorgasmia persisted with minimal tolerance over the five months that clomipramine was taken. Men and women were equally affected. Sexual side-effects are easily missed without a structured interview, and can detract from the value of drug treatment.

Kasvikis Y, Marks IM. Clomipramine in obsessive-compulsive ritualisers treated with exposure therapy: relations between dose, plasma levels, outcome and side effects. Psychopharmacology (Berl). 1988;95(1):113-8.

Forty-nine obsessive-compulsive ritualisers completed a double-blind controlled study of clomipramine and exposure therapy. More severely ill patients allowed higher doses of medication to be prescribed and had higher plasma levels of both clomipramine and desmethylclomipramine. Exposure instructions had a strong effect, whereas the clomipramine effect was small and short-lived. Plasma levels of desmethylclomipramine but not of clomipramine correlated with outcome at weeks 8 and 17. There was no evidence of a therapeutic window for either clomipramine or its metabolite. Patients' physical complaints before treatment correlated positively with depression and anxiety, especially sexual difficulties. Dry mouth, as a side effect, was most evidently related to clomipramine and its usefulness in monitoring drug compliance for patients on clomipramine is reaffirmed.

DeVeaugh-Geiss J, Landau P, et al. Preliminary results from a multicenter trial of clomipramine in obsessive-compulsive disorder. Psychopharmacol Bull. 1989;25(1):36-40.

Two multicenter, double-blind, placebo-controlled clinical trials were conducted to evaluate the effectiveness of 10 weeks of treatment with up to 300 mg daily of clomipramine in nondepressed pa-

tients with OCD. There were 575 patients enrolled in these clinical trials, and preliminary analyses of data from 384 of these patients demonstrate a virtual absence of placebo response, a very low rate of premature discontinuation, and for patients receiving clomipramine, a statistically and clinically significant improvement in OCD symptoms (40%-45% mean improvement with clomipramine vs. 4%-5% mean improvement with placebo). In general, clomipramine was well tolerated in doses of up to 300 mg daily.

DeVeaugh-Geiss J, Landau P, et al. Treatment of Obsessive Compulsive Disorder with clomipramine. Psychiatric Annals. 1989;19(2):97-101.

Conducted 2 double-blind, placebo-controlled clinical trials to evaluate the effectiveness of clomipramine (CIM) for treating nondepressed patients with obsessive-compulsive disorder (OCD). 384 OCD Ss were administered 25–300 mg of CIM or placebo and assessed on measures including an obsessive compulsive scale and a patient self-rating scale. Results indicate that CIM significantly improved OCD symptoms (40–45% mean improvement with CIM vs 4–5% mean improvement with placebo). CIM was well tolerated up to 300 mg. (PsycINFO Database Record (c) 2012 APA, all rights reserved).

Jenike MA, Baer L, et al. Obsessive-compulsive disorder: a double-blind, placebo-controlled trial of clomipramine in 27 patients. Am J Psychiatry. 1989;146(10):1328-30.

Clomipramine was significantly superior to placebo in a 10-week double-blind, placebo-controlled trial in 27 outpatients who met DSM-III-R criteria for obsessive-compulsive disorder.

Greist JH, Jefferson JW, et al. Clomipramine and obsessive compulsive disorder: a placebo-controlled double-blind study of 32 patients. J Clin Psychiatry. 1990;51(7):292-7.

Thirty-two nondepressed patients with obsessive compulsive disorder were randomly assigned to treatment with clomipramine (N = 16) or placebo (N = 16) in a 10-week double-blind study. Of the 15 patients who received at least 3 weeks of clomipramine treatment, 11 (73%) improved, 5 (33%) improved by more than 50%, and none worsened. Only 2 (12.5%) of the 16 placebo-treated patients improved, 1 (6%) by more than 50%; two (13%) worsened. Clomipramine treatment was associated with statistically significant improvement on several measures of obsessive compulsive symptoms. Side effects were more frequent and severe with clomipramine than with placebo. Although most patients tolerated clomipramine well, 3 discontinued treatment because of side effects.

Katz RJ, DeVeaugh-Geiss J. The antiobsessional effects of clomipramine do not require concomitant affective disorder. Psychiatry Res. 1990;31(2):121-9.

Two multicenter double-blind trials of clomipramine (CMI) vs. placebo were carried out in patients with DSM-III defined obsessive-compulsive disorder (OCD). Study entry criteria were similar, but the trials differed in their permitted initial degree of affective disturbance. Subgroups of patients with primary OCD and no mood disturbance were identified in both trials. Analyses of findings from both trials were essentially equivalent and were consistent with significant antiobsessional effects of CMI but not placebo in nondepressed patients with primary OCD. Further comparisons with subgroups with concomitant affective disturbance did not demonstrate marked differences in outcome.

Katz RJ, DeVeaugh-Geiss J, et al. Clomipramine in obsessive-compulsive disorder. Biol Psychiatry. 1990;28(5):401-14.

The effects of clomipramine hydrochloride (CMI) versus placebo upon DSM-III-defined obsessive-compulsive disorder (OCD) were assessed in a 10-week double-blind multicenter trial and in a corresponding 1-year double-blind extension study. The NIMH global O-C scale, a 15-point ordinal severity scale, incorporating categorical features specific to OCD, was used to evaluate the severity of obsessive compulsive symptoms over the course of treatment, and a physician's rating of global therapeutic effect was used to assess overall change from baseline. In the core study, patients receiving placebo demonstrated minor and nonsystematic changes, whereas patients who received CMI had clinically and statistically significant reductions in the global severity of their disorder. Findings from the extension study were consistent with continuing efficacy for CMI, whereas corresponding data for patients receiving long-term placebo were difficult to interpret. Based upon shifts in categorical severity, symptoms for over half those patients who received CMI were rendered subclinical or within a range of normal functioning. In contast, less than 5% of patients receiving placebo had their symptoms reduced to a subclinical level. Generally, both treatments were well tolerated. Previous studies have indicated therapeutic potential for CMI in obsessive compulsive disorder. These findings confirm and extend previous observations.

Mavissakalian MR, Jones B, et al. Clomipramine in obsessive-compulsive disorder: clinical response and plasma levels. J Clin Psychopharmacol. 1990;10(4):261-8.

Two related data sets are presented that point to a specific pharmacological effect and support a predominantly serotonergic mediation of clomipramine's antiobsessional effect. A significant placebo versus clomipramine contrast from both the between- and within-group perspectives was found in 25 patients with moderate to severe obsessive-compulsive disorder of at least 2 years' duration and no evidence of depression who completed a double-blind, placebo-controlled, 10-week study. There was no significant improvement in the placebo group, six of whom subsequently improved with clomipramine. Analysis of the clinical significance of pharmacotherapy and the relationship between outcome and plasma drug concentrations in 33 obsessive-compulsive disorder patients treated with clomipramine (239.4 +/- 57.0 mg/day) revealed that 47% of the patients were rated in the subclinical range with one third of the sample being virtually symptom-free. Plasma levels of clomipramine, but not N-desmethylclomipramine, correlated significantly with posttreatment outcome measures, with responders having significantly higher clomipramine levels and a trend toward lower desmethylclomipramine ratios.

Montgomery SA, Montgomery DB, et al. Early response with clomipramine in obsessive compulsive disorder: A placebo controlled study. Progress in Neuro-Psychopharmacology & Biological Psychiatry. 1990;14(5):719-27.

14 patients (aged 27–54 yrs) with obsessive-compulsive disorder participated in a 4-wk crossover design study with placebo and the 5-hydroxytryptamine (5-HT) uptake inhibitor clomipramine. Outcome was determined by weekly ratings of psychopathology using a 6-item obsessional scale derived from the Comprehensive Psychopathological Rating Scale and a depression rating scale. Results show a virtual absence of response to placebo and a significant early response to clomipramine. The obsessional scale is appended. (PsycINFO Database Record (c) 2012 APA, all rights reserved).

Clomipramine in the treatment of patients with obsessive-compulsive disorder. The Clomipramine Collaborative Study Group. Arch Gen Psychiatry. 1991;48(8):730-8.

Two double-blind studies at 21 centers evaluated the therapeutic efficacy, safety, and tolerability of up to 300 mg/d of clomipramine hydrochloride or an equivalent number of placebo capsules in the treatment of 520 patients with obsessive-compulsive disorder, of whom 239 had had the disorder for at least 2 years (study 1) and 281 had been ill for at least 1 year (study 2). On the two principal measures of the severity of the disorder, ie, the Yale-Brown Obsessive Compulsive Scale and the National Institute of Mental Health Global Obsessive Compulsive Scale, clomipramine was significantly more effective than placebo in both studies. The mean reduction in the Yale-Brown Obsessive Compulsive Scale score at the end of 10 weeks of treatment was 38% and 44% in studies 1 and 2, respectively, for the clomipramine-treated patients and 3% and 5% for the placebo-treated patients. The drug was also found to be superior on the basis of the physicians' and patients' evaluations of global therapeutic change. The most frequently observed adverse effects during clomipramine therapy were those typically associated with tricyclic antidepressant drugs. Although uncommon, the occurrence of seizures and elevated aminotransferase values are potentially serious side effects of clomipramine. Clomipramine was generally well tolerated and was effective in reducing obsessive and compulsive symptoms.

Hoehn-Saric R, McLeod DR, et al. Symptoms and physiologic manifestations in obsessive compulsive patients before and after treatment with clomipramine. J Clin Psychiatry. 1993;54(7):272-6.

BACKGROUND: Anxiety and hyperarousal constitute important aspects of obsessive compulsive disorder (OCD). This study examined the effects of clomipramine on symptoms, arousal-related physiologic states, and stress reactions in OCD patients. METHOD: Twenty-five OCD patients were randomly assigned to a clomipramine or placebo group and were assessed for 10 weeks using a double-blind parallel design. They were assessed clinically with the Yale-Brown Obsessive Compulsive Scale, the National Institute of Mental Health Global Obsessive-Compulsive Scale, the patient- and investigator-rated Global Improvement Scales, and the Hamilton Rating Scale for Depression. Prior to treatment, and again during the last day of medication, physiologic states (heart rate, respiration, skin conductance, blood pressure, and EMG) were measured at rest and during both nonspecific (psychomotor tasks) and pathology-specific (visualization) stressors. RESULTS: Patients taking clomipramine, but not those taking placebo, improved significantly on all clinical measures. With the exception of heart rate, treatment did not affect resting physiologic states. Heart rate increased in patients taking clomipramine and decreased in patients taking placebo. Autonomic reactivity to nonspecific and to pathology-specific stressors was attenuated by clomipramine, but not by placebo. CONCLUSION: Clinical improvement on clomipramine treatment was independent of the physi-

ologic state of the patients and was not associated with autonomic down-regulation. The attenuation of autonomic reactivity to stressors appears not to be pathology-specific but may reflect either a direct pharmacologic effect of clomipramine on the autonomic nervous system or a heightened indifference to psychological stressors in general.

Mundo E, Bellodi L, et al. Effects of acute intravenous clomipramine on obsessive-compulsive symptoms and response to chronic treatment. Biol Psychiatry. 1995;38(8):525-31.

The aim of this study was to test the hypothesis that obsessive-compulsive symptoms are temporarily worsened by acute intravenous clomipramine, suggesting that there is a basal hypersensitivity of serotonin (5-HT) receptors in obsessive-compulsive (OC) patients. We also investigated the relationship of the effects of acute (intravenous) and chronic (oral) administration of clomipramine. Twenty-eight OC patients were recruited. The first part of the study included placebo and clomipramine infusions and monitoring of OC symptoms by 100 mm Visual Analogue self-rated scales (VAS). There was significant worsening of obsessions in the whole sample during clomipramine infusion. The second part included standardized 10-week oral treatments with clomipramine and evaluation of clinical efficacy. Among the 18 patients who completed the second part of the study, oral clomipramine significantly reduced OC symptoms, but OC patients who had become worse after clomipramine infusion showed higher Y-BOCS scores.

1.2.3. IRSN (venlafaxina)

Los estudios realizados con venlafaxina son frente a comparador activo (ver secciones 1.3.1 y 1.3.2).

1.2.4. Otros (17 – 1964-2013)

Venkobarao A. A controlled trial with 'Valium' in obsessive compulsive state. J Indian Med Assoc. 1964;42:564-7.

Lin HN, Chen CC. A double-blind test on the effect of bromazepam in obsessive-compulsive neurosis. Taiwan Yi Xue Hui Za Zhi. 1979;78(3):267-75.

Insel TR, Hamilton JA, et al. D-amphetamine in obsessive-compulsive disorder. Psychopharmacology (Berl). 1983;80(3):231-5.

In a double-blind crossover study, single doses of d-amphetamine and placebo were administered to 12 patients with severe chronic obsessive-compulsive disorder (OCD). Improvement of obsessional symptoms was significant on clinical ratings and was correlated with improved performance on an attention task. Changes were also significant for self-rated measures of activation and altered reality. The behavior response to amphetamine was not statistically correlated with subsequent improvement during a 6-week clomipramine trial, although the direction of change was the same during both treatments for every patient studied.

Den Boer JA, Westenberg HG. Oxytocin in obsessive compulsive disorder. Peptides. 1992;13(6):1083-5.

A double-blind, placebo-controlled study with syntocinon (oxytocin) was carried out in 12 patients, nine females and three males with obsessive compulsive disorder (OCD). Patients were treated by intranasal administration of oxytocin spray (18 IU per day) or placebo. No reductions in the number of obsessions or compulsive behaviors were observed in either treatment group. To evaluate whether a higher dosage would exert more beneficial effects, two additional patients were treated with a threefold higher dosage of oxytocin using an open design. In one patient a slight reduction in the number of checking rituals was observed, whereas in the other patient virtually no effect was observed. The results of this study do not support the hypothesis that oxytocin might be a potential anticompulsive agent.

Maruno CA, Hart LL:. Buspirone in obsessive-compulsive disorder. Ann Pharmacother. 1992;26(10):1248-51.

Pigott TA, L'Heureux F, et al. A double-blind, placebo controlled study of trazodone in patients with obsessive-compulsive disorder. J Clin Psychopharmacol. 1992;12(3):156-62.

Patients with obsessive-compulsive disorder (OCD) have been shown to be preferentially responsive to serotonin (5-HT) uptake-inhibiting antidepressants including clomipramine, fluoxetine, fluvoxamine,

and sertraline. The nontricyclic antidepressant, trazodone, also possesses serotonin reuptake inhibiting properties and has been reported to be efficacious in OCD in several case reports and open trials. In order to investigate trazodone's potential antiobsessive efficacy in a controlled fashion, 21 patients with OCD were entered into a double-blind, parallel design comparison of trazodone and placebo. There were no significant differences in baseline rating scores of OCD or depressive symptoms between those who entered the trazodone phase (N = 13) versus those who entered the placebo phase (N = 8). As measured by standardized OCD and depression rating scales, there was no significant difference in OCD or depressive symptoms in the 17 patients who completed 10 weeks of trazodone (N = 11, mean daily dose, 235 +/- 10 mg) versus 10 weeks of placebo (N = 6) administration. In comparison to clomipramine and fluoxetine treatment which we have found to be associated with greater than 95% reduction in platelet 5-HT concentration, there was only a 26% mean reduction in platelet 5-HT concentration after 10 weeks of trazodone administration. These results indicate that trazodone lacks substantial antiobsessive effects and is associated with only modest reductions in platelet 5-HT concentrations.

Smeraldi E, Mundo E, et al. 5HT-3 receptor and antiobsessional effect. Human Psychopharmacology: Clinical and Experimental. 1992;7(4):291-2.

Administered placebo or ondansetron, a selective 5-hydroxytryptamine-3 (5-HT-3) antagonist, to 10 patients (mean age 26 yrs) with obsessive-compulsive disorder. No significant differences were found between groups, implying that the 5-HT-3 receptor is not involved in the antiobsessional effect of 5-HT reuptake inhibitors. (PsycINFO Database Record (c) 2012 APA, all rights reserved).

Stein DJ, Hollander E, et al. Comparison of clomipramine, alprazolam and placebo in the treatment of obsessive-compulsive disorder. Human Psychopharmacology: Clinical and Experimental. 1992;7(6):389-95.

Compared the efficacy of clomipramine (CMI), alprazolam, and placebo in the treatment of obsessive-compulsive disorder (OCD). 44 patients (aged 18–65 yrs) with OCD were entered into a double-blind randomly assigned treatment protocol with CMI or placebo. Alprazolam was administered to 14 OCD patients in a separate open-treatment study. The response rate of patients completing treatment was 50% with CMI, 19% with placebo, and 18% with alprazolam. Self-ratings of OCD symptoms in both assigned patients and treatment completers demonstrated a significantly greater benefit with CMI than with alprazolam. Ratings of depression and clinician ratings of obsessionality did not, however, indicate differences between the treatment groups. (PsycINFO Database Record (c) 2013 APA, all rights reserved).

Epperson CN, McDougle CJ, et al. Intranasal oxytocin in obsessive-compulsive disorder. Biol Psychiatry. 1996;40(6):547-9.

Fux M, Levine J, et al. Inositol treatment of obsessive-compulsive disorder. Am J Psychiatry. 1996;153(9):1219-21.

OBJECTIVE: Earlier studies reported that inositol, a simple polyol second messenger precursor, was effective in controlled trials for patients with depression and panic. In this study its effectiveness in obsessive-compulsive disorder was investigated. METHOD: Thirteen patients with obsessive-compulsive disorder completed a double-blind, controlled crossover trial of 18 g/day of inositol or placebo for 6 weeks each. RESULTS: The subjects had significantly lower scores on the Yale-Brown Obsessive Compulsive Scale when taking inositol than when taking placebo. CONCLUSIONS: The authors conclude that inositol is effective in depression, panic, and obsessive-compulsive disorder, a spectrum of disorders responsive to selective serotonin reuptake inhibitors.

Keuler DJ, Altemus M, et al. Behavioral effects of naloxone infusion in obsessive-compulsive disorder. Biol Psychiatry. 1996;40(2):154-6.

Hollander E, Kaplan A, et al. A double-blind, placebo-controlled trial of clonazepam in obsessive-compulsive disorder. World J Biol Psychiatry. 2003;4(1):30-4.

Selective serotonin reuptake inhibitors (SSRIs) are currently the first-line pharmacological agents in treating obsessive-compulsive disorder (OCD). Appropriate treatment for OCD also involves cognitive behavioural therapy (CBT), including exposure and response prevention. As there is a time delay in seeing full therapeutic response, and not all patients tolerate SSRIs, there remains an unmet need for additional treatment approaches in OCD. In addition, most responders report only a partial reduction in symptoms. Clonazepam has demonstrated effectiveness in several preliminary reports in treating OCD. Twenty-seven patients with OCD were entered into a 10 week, double-blind, parallel design trial of clonazepam vs. placebo. Overall, only 3 out of 25 patients who had >/= 1 rating on

clonazepam/placebo were judged to be treatment responders, by scoring a 1 (very much improved) or 2 (much improved) on the CGI improvement scale. Responders included 2 of 9 in the placebo group and 1 of 16 in the clonazepam group. No significant difference was found between clonazepam and placebo groups on responder/non responder status (Chi(2)=1.39, df =1,24, p=0.238), nor on change in YBOCS, Ham-A, Ham-D or NIMH scales from beginning to last evaluation carried forward. These findings suggest that clonazepam is not effective as monotherapy in treating OCD. Its effectiveness in specific subgroups of OCD patients with co-morbid anxiety disorders or as an augmentation strategy added to SSRIs remains to be determined.

Kobak KA, Taylor LV, et al. St John's wort versus placebo in obsessive-compulsive disorder: results from a double-blind study. Int Clin Psychopharmacol. 2005;20(6):299-304.

Although St John's wort (Hypericum perforatum) is one of the most widely used and studied herbal medicines for depression, less is known about its efficacy in anxiety disorders, in spite of the fact that patients with anxiety disorders are among the most likely to self-medicate using alternative treatments. Pharmacokinetic evidence for the serotonergic, domaminergic and GABAminergic activity of hypericum, and a recent successful open-label study, suggests that it may be effective for obsessive-compulsive disorder (OCD). Sixty subjects were randomized to 12 weeks of treatment with St John's wort (LI 160) or matching placebo. Subjects with Hamilton Depression Scale scores of 16 or above were excluded. A flexible-dose schedule was utilized (600-1800 mg/day). The mean change on the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) with St John's wort (3.43) was not significantly different than the mean change found with placebo (3.60) (P=899). No significant differences were found on any of the Y-BOCS subscales. The percentage of patients rated as 'much' or 'very much' improved at endpoint was not significantly different between St John's wort (17.9%) and placebo (16.7%) (P=0.905). Only one patient from each group discontinued due to adverse events [sinus infection (St John's wort); confusion (placebo)]. The results fail to support the efficacy of St John's wort for OCD.

Sayyah M, Boostani H, et al. Efficacy of aqueous extract of Echium amoenum in treatment of obsessive-compulsive disorder. Prog Neuropsychopharmacol Biol Psychiatry. 2009;33(8):1513-6.

Traditionally, the dried flower of Echium amoenum (Boraginaceae) has been used in Iran as an anxiolytic and mood enhancer. This study investigated the efficacy and safety of an aqueous extract of E. amoenum in treatment of obsessive-compulsive disorder. Forty-four patients were randomly assigned to receive either E. amoenum aqueous extract (500 mg/day) or placebo in a 6-week, double blind, parallel-group trial. Patients were assessed before the study and during weeks 1, 2, 4, and 6 by the Yale-Brown Obsessive Compulsive (Y-BOCS), the Hamilton Rating Scale for Anxiety (HAM-A), and a score sheet on adverse effects. In weeks 4 and 6, the extract showed a significant superiority over placebo in reducing obsessive and compulsive and anxiety symptoms. There was no significant difference between the two groups in terms of adverse effects. The results suggest that E. amoenum aqueous extract has some anti obsessive and compulsive effects. However, further studies are needed to confirm these findings.

Pakseresht S, Boostani H, et al. Extract of valerian root (Valeriana officinalis L.) vs. placebo in treatment of obsessive-compulsive disorder: a randomized double-blind study. J Complement Integr Med. 2011;8.

OBJECTIVE: Obsessive-Compulsive Disorder (OCD) is a common neuropsychiatric condition. Many herbs with psychotropic effects exist which can have fewer side effects compared to more conventional medications. Valeriana Officinalis L. is a well-known medicinal plant with a long history of usage in the world with an effect on GABA. This plant is reported to be safe on humans. Our objective in this study was to compare the efficacy of the extract of Valeriana Officinalis L. with placebo in the treatment of OCD. METHODS: The study was an 8-week pilot double-blind randomized trial. Thirty-one adult outpatients who met the DSM-IV-TR criteria for OCD based on the structured clinical interview participated in the trial. In this double-blind and randomized trial, patients were randomly assigned to receive either capsule of the extract (765 mg/day) or placebo (30 mg/day) for 8 weeks. RESULTS: The results showed significant difference between the extract and placebo in the end of treatment (P=0.000). Somnolence was the only significant difference between the two groups in terms of observed side effects (P=0.02). CONCLUSION: The results suggest that Valeriana Officinalis L. has some antiobsessive and compulsive effects. However, further studies are needed to confirm these findings. Psychiatrists often find that many patients cannot tolerate the side effects of psychiatry medicine Valeriana Officinalis L. is a well-known medicinal plant with a long history of usage in world with effect on GABA.The results showed significant difference between the extract and placebo in the treatment of OCD. There was also no significant difference between the two groups in terms of observed side effects.

Rodriguez CI, Kegeles LS, et al. Randomized controlled crossover trial of ketamine in obsessive-compulsive disorder: proof-of-concept. Neuropsychopharmacology. 2013;38(12):2475-83.

Serotonin reuptake inhibitors (SRIs), the first-line pharmacological treatment for obsessive-compulsive disorder (OCD), have two limitations: incomplete symptom relief and 2-3 months lag time before clinically meaningful improvement. New medications with faster onset are needed. As converging evidence suggests a role for the glutamate system in the pathophysiology of OCD, we tested whether a single dose of ketamine, a non-competitive N-methyl-D-aspartate (NMDA) glutamate receptor antagonist, could achieve rapid anti-obsessional effects. In a randomized, double-blind, placebo-controlled, crossover design, drug-free OCD adults (n=15) with near-constant obsessions received two 40-min intravenous infusions, one of saline and one of ketamine (0.5 mg/kg), spaced at least 1-week apart. The OCD visual analog scale (OCD-VAS) and the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) were used to assess OCD symptoms. Unexpectedly, ketamine's effects within the crossover design showed significant (p<0.005) carryover effects (ie, lasting longer than 1 week). As a result, only the first-phase data were used in additional analyses. Specifically, those receiving ketamine (n=8) reported significant improvement in obsessions (measured by OCD-VAS) during the infusion compared with subjects receiving placebo (n=7). One-week post-infusion, 50% of those receiving ketamine (n=8) met criteria for treatment response (>/=35% Y-BOCS reduction) vs 0% of those receiving placebo (n=7). Rapid anti-OCD effects from a single intravenous dose of ketamine can persist for at least 1 week in some OCD patients with constant intrusive thoughts. This is the first randomized, controlled trial to demonstrate that a drug affecting glutamate neurotransmission can reduce OCD symptoms without the presence of an SRI and is consistent with a glutamatergic hypothesis of OCD.

1.3. Eficacia, tolerabilidad y seguridad comparativa de los tratamientos psicofarmacológicos en monoterapia

1.3.1. ISRS *versus* ISRS (3 – 1997-2007)

Mundo E, Bianchi L, et al. Efficacy of fluvoxamine, paroxetine, and citalopram in the treatment of obsessive-compulsive disorder: a single-blind study. J Clin Psychopharmacol. 1997;17(4):267-71.

Obsessive-compulsive disorder (OCD) has been successfully treated with proserotonergic agents for some years. Clomipramine was the first drug used, but several clinical trials have been conducted more recently to assess the antiobsessional efficacy of selective serotonin reuptake inhibitors (SSRIs). The aim of this study was to compare the antiobsessional efficacy of three SSRIs, fluvoxamine, paroxetine, and citalopram. Thirty obsessive-compulsive patients without comorbid axis I diagnoses except for tic disorder as assessed by DSM-III-R criteria gave informed consent and were recruited consecutively; they underwent a 10-week randomized treatment with fluvoxamine, paroxetine, or citalopram. Ratings were performed under blind conditions every 2 weeks from baseline to the end of the study and by the Yale-Brown Obsessive-Compulsive Scale, the National Institute of Mental Health-Obsessive-Compulsive Scale, the Clinical Global Impressions Scale, and the Hamilton Rating Scale for Depression. Quantitative and qualitative analyses of the antiobsessional efficacy of the three drugs were completed with analysis of variance with repeated measures and survival analysis. The results showed no significant differences between the three treatments. The preliminary conclusions drawn from this study concern the interchangeable antiobsessional effects of different SSRIs, although further studies of "cross-response" to these drugs are needed.

Bergeron R, Ravindran AV, et al. (2002) Sertraline and fluoxetine treatment of obsessive-compulsive disorder: results of a double-blind, 6-month treatment study. Journal of clinical psychopharmacology. 2002;22:148-54.

The purpose of this study was to evaluate the comparative efficacy and tolerability of sertraline and fluoxetine in the treatment of obsessive-compulsive disorder (OCD). Outpatients meeting DSM-IV criteria for OCD, with a Yale-Brown Obsessive-Compulsive (Y-BOCS) total score >or= 17, an NIMH Global Obsessive-Compulsive (NIMH-OC) scale score >or= 7, and a CGI-Severity score >or= 4 were randomized to 24 weeks of double-blind treatment with sertraline (N = 77) or fluoxetine (N = 73). Primary efficacy measures consisted of the Y-BOCS, the NIMH-OC scale, and the CGI-Severity (CGI-S) and Improvement (CGI-I) scales. Equivalent and significant ($p < 0.001$) improvement was found at week 24 in Y-BOCS and NIMH-OC scale scores for sertraline and fluoxetine. After 12 weeks, 49.2% of patients on sertraline were rated on the CGI-S scale as being mildly ill or not ill compared to 24.6% on fluoxetine ($p < 0.01$). A Cox analysis found patients on sertraline to have a statistically nonsignificant 42% greater likelihood of achieving a response by week 12 (CGI-I, much or very much improved; 95% CI, 0.85, 2.38; $p = 0.18$). Sertraline treatment also resulted in a higher propor-

tion of remissions than fluoxetine (defined as a CGI-I <or= 2 and a Y-BOCS score <or= 11), both at week 12 (20% vs. 8%; chi2, 3.95; df 1; p = 0.047) and week 24 (36% vs. 22%; chi2, 3.18; df, 1; p = 0.075). Both medications were well-tolerated and demonstrated significant efficacy in the treatment of outpatients with moderate to severe OCD with the subjects treated with sertraline showing a greater likelihood of remission as well as an earlier improvement on some but not all efficacy measures.

Stein DJ, Andersen EW, et al. Escitalopram in obsessive-compulsive disorder: a randomized, placebo-controlled, paroxetine-referenced, fixed-dose, 24-week study. Curr Med Res Opin. 2007;23(4):701-11.

OBJECTIVE: A randomized, placebo controlled fixed-dose trial was undertaken to determine the efficacy and tolerability of escitalopram in obsessive-compulsive disorder (OCD), using paroxetine as the active reference. RESEARCH DESIGN AND METHODS: A total of 466 adults with OCD from specialized clinical centres, psychiatric hospital departments, psychiatric practices, or general practice were randomized to one of four treatment groups: escitalopram 10 mg/day (n = 116), escitalopram 20 mg/day (n = 116), paroxetine 40 mg/day (n = 119), or placebo (n = 115) for 24 weeks. The primary efficacy endpoint was the mean change in the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) total score from baseline to week 12. Secondary efficacy endpoints included remission (defined as Y-BOCS total score < or =10), NIMH-OCS, and CGI-S and CGI-I scores at weeks 12 and 24. Tolerability was based on the incidence of adverse events, and on changes in vital signs (blood pressure and pulse). Main outcome measures; RESULTS: Escitalopram 20 mg/day was superior to placebo on the primary and all secondary outcome endpoints, including remission. Escitalopram 10 mg/day and paroxetine 40 mg/day were also effective on the primary scale as well as some other outcome measures. In the escitalopram 20 mg/day group, the improvement in Y-BOCS total score was significantly better than in the placebo group as early as week 6. The most common AEs in the active treatment groups were nausea (19-27%), headache (17-22%), and fatigue (12-19%). More paroxetine-treated patients withdrew due to adverse events than escitalopram- or placebo-treated patients. CONCLUSION: Given that escitalopram 20 mg/day was associated with an earlier onset, higher response and remission rates, improved functioning, and better tolerability than the reference drug, escitalopram deserves to be considered as one of the first-line agents in the pharmacotherapy of OCD for longer-term treatment periods.

1.3.2. ISRS *versus* TCA (13 – 1990-2001)

Pigott TA, Pato MT, et al. Controlled comparisons of clomipramine and fluoxetine in the treatment of obsessive-compulsive disorder. Behavioral and biological results. Arch Gen Psychiatry. 1990;47(10):926-32.

Treatment with fluoxetine hydrochloride was compared with treatment with clomipramine hydrochloride in two groups of patients with obsessive-compulsive disorder using two different experimental designs. In the first group of 11 patients with obsessive-compulsive disorder studied using a randomized, double-blind, crossover design, treatment with fluoxetine for 10 weeks was found to produce therapeutic effects similar to treatment with clomipramine for 10 weeks. There were significantly fewer total side effects reported during fluoxetine than clomipramine treatment. Drug tapering and placebo substitution in the 4-week crossover interval phase led to substantial relapses in obsessive-compulsive disorder symptoms and depression. Furthermore, responses to the second drug took as long to occur as responses to the first drug, although both drugs are thought to act by a common mechanism, serotonin uptake inhibition. A second group of 21 patients with obsessive-compulsive disorder that had been previously stabilized on clomipramine treatment with at least partial benefit were crossed over to fluoxetine treatment in a double-blind fashion. After 10 weeks of fluoxetine administration, most patients manifested behavioral rating scores of obsessive-compulsive disorder and depressive symptoms that were comparable with precrossover ratings completed during clomipramine treatment. A significant exacerbation in obsessive-compulsive disorder and depression ratings as well as a similar lag in therapeutic efficacy were also noted in this second cohort of patients with obsessive-compulsive disorder. Platelet 5-HT concentrations were reduced 95% during both clomipramine and fluoxetine treatment periods. These results suggest that fluoxetine may represent a viable alternative to clomipramine in the treatment of obsessive-compulsive disorder, although further studies with larger sample sizes are needed.

Smeraldi E, Erzegovesi S, et al. Fluvoxamine vs clomipramine treatment in obsessive-compulsive disorder: A preliminary study. New Trends in Experimental & Clinical Psychiatry. 1992;8(2):63-5.

12 patients (aged 18–50 yrs) with obsessive-compulsive disorder randomly received either fluvoxamine or clomipramine for 12 wks, with dosage increasing from 50 mg at Day 1 to 200 mg from Day 10 onward. 10 Ss completed treatment. Both drugs were effective in improving obsessive, compulsive, and depressive symptoms. Both S groups rated the side effects of both drugs as mild. (PsycINFO Database Record (c) 2012 APA, all rights reserved).

Freeman CP, Trimble MR, et al. Fluvoxamine versus clomipramine in the treatment of obsessive compulsive disorder: a multicenter, randomized, double-blind, parallel group comparison. J Clin Psychiatry. 1994;55(7):301-5.

BACKGROUND: To examine the efficacy of fluvoxamine and clomipramine in obsessive compulsive disorder and to compare their tolerabilities. METHOD: In this multicenter, randomized, double-blind trial, fluvoxamine (100-250 mg/day) was compared with clomipramine (100-250 mg/day) for 10 weeks in the treatment of 66 psychiatric outpatients, aged 18 to 65 years, with a diagnosis of obsessive compulsive disorder. The main efficacy variable was the Yale-Brown Obsessive Compulsive Scale; secondary variables were the National Institute of Mental Health Global Obsessive Compulsive Scale and the Clinical Global Impressions-Improvement scale. RESULTS: Seventeen patients withdrew prematurely, 6 in the fluvoxamine group and 11 in the clomipramine group. In the intent-to-treat population (34 fluvoxamine patients and 30 clomipramine patients), there were no significant differences with respect to the mean reduction in total Yale-Brown Obsessive Compulsive Scale score (last observation carried forward) at any time-point; a mean reduction of 8.6 (33%) was seen in the fluvoxamine group and 7.8 (31%) in the clomipramine group. Similar results were obtained in virtually all secondary variables. The only exception was the obsession-free interval for the Yale-Brown Obsessive Compulsive Scale, which was significantly longer in the fluvoxamine group, especially in a population of patients with disease of > 12 months' duration ($F = 5.298$, $df = 1$, $p = .026$). Adverse events were mostly tolerable; 9 patients (5 receiving fluvoxamine, 4 receiving clomipramine) withdrew due to adverse events related to treatment. CONCLUSION: Fluvoxamine and clomipramine were equally effective in the treatment of obsessive compulsive disorder. Both agents were well tolerated; fluvoxamine produced fewer anticholinergic side effects and caused less sexual dysfunction than clomipramine, but more reports of headache and insomnia.

Koran LM, McElroy SL, et al. Fluvoxamine versus clomipramine for obsessive-compulsive disorder: a double-blind comparison. J Clin Psychopharmacol. 1996;16(2):121-9.

The efficacy and tolerability of fluvoxamine (100-300 mg/day) and clomipramine (100-250 mg/day) were compared in a randomized, double-blind, parallel-group study of 79 patients with obsessive-compulsive disorder (OCD) without coexisting major depression. After a 2-week placebo lead-in period, patients were randomized to fluvoxamine (37 patients) or clomipramine (42 patients) for 10 weeks. Efficacy was evaluated with the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), the National Institute of Mental Health Obsessive-Compulsive scale, and Patient and Clinical Global Improvement scales. Hamilton Rating Scale for Depression scores and somatic symptoms were also assessed. Seventy-eight percent of fluvoxamine patients and 64% of clomipramine patients completed the study. At the end of treatment, 56% of fluvoxamine patients were classified as responders (> or = 25% decrease in Y-BOCS score), compared with 54% of clomipramine patients. Both groups showed steady improvement throughout the study; no statistically significant differences were observed between the groups for any efficacy variable at any time. A similar percentage of patients in both groups withdrew because of adverse events. No serious adverse events related to drug occurred with either drug. Insomnia, nervousness, and dyspepsia were more statistically frequent with fluvoxamine; dry mouth and postural hypotension were more frequent with clomipramine. In this study, fluvoxamine and clomipramine were equally effective in reducing OCD symptoms over a 10-week treatment period but displayed different side effect profiles.

López-Ibor JJ, Jr., Saiz J, et al. Double-blind comparison of fluoxetine versus clomipramine in the treatment of obsessive compulsive disorder. Eur Neuropsychopharmacol. 1996;6(2):111-8.

There is evidence of the clinical efficacy and safety of clomipramine and the newer selective serotonin reuptake inhibitors (SSRIs) for the treatment of obsessive-compulsive disorder (OCD). In the present study, we have compared the efficacy and safety of 40 mg/day of fluoxetine and 150 mg/day of clomipramine in patients with OCD, diagnosed according to DSM-IIIR. A total of 55 patients entered this 8-week, double-blind controlled study. Efficacy for both drugs was comparable. The primary efficacy criterion, the Y-BOCS Total score, did not show any significant differences between treatment arms.

Response rate was higher with clomipramine, using a 25% decrease in Y-BOCS Total score as response threshold, but there were no significant differences between treatment arms using a 35% threshold. Overall safety and tolerability were good for both drugs, being slightly better for fluoxetine.

Zohar J, Judge R. Paroxetine versus clomipramine in the treatment of obsessive-compulsive disorder. The British Journal of Psychiatry. 1996;169(4):468-74.

Assessed the effect of a flexible dose of paroxetine, compared with clomipramine and placebo, in a multinational randomized study of 406 patients (aged 16–70 yrs) with obsessive-compulsive disorder (OCD) of at least 6 mo duration. Ss received double-blind medication for up to 12 wks. Doses were adjusted according to therapeutic effect and side-effects. Primary efficacy measures were the Yale-Brown Obsessive Compulsive Scale and the NIMH Obsessive-Compulsive Scale. Paroxetine was significantly more effective than placebo and was of comparable efficacy to clomipramine. Paroxetine had significantly superior tolerability to clomipramine on 3 measures: Clinical Global Impression efficacy index, anticholinergic adverse events, and adverse events leading to withdrawal. (PsycINFO Database Record (c) 2012 APA, all rights reserved).

Bisserbe JC, Lane RM, et al. A double-blind comparison of sertraline and clomipramine in outpatients with obsessive-compulsive disorder. European Psychiatry. 1997;12(2):82-93.

Compared the efficacy, safety, and tolerability of sertraline and clomipramine in the treatment of obsessive-compulsive disorder. 168 19–73 yr old male and female outpatients met the Diagnostic and Statistical Manual of Mental Disorders-III-Revised (DSM-III-R) criteria for obsessive-compulsive disorder for 1 yr were randomized to double-blind treatment with sertraline or clomipramine. Ss were assessed at screening, baseline, and after 1, 2, 4, 6, 8, 12, and 16 wks of therapy. Sertraline showed greater efficacy than clomipramine in the intent-to-treat patient group. Adverse events were reported more commonly in the clomipramine group and were more severe. The difference in efficacy between treatments is almost wholly accounted for by a greater number of clomipramine withdrawals due to the poor patient acceptance of clomipramine. Thus, results clearly show a therapeutic advantage for sertraline over clomipramine in terms of the proportion of obsessive-compulsive disorder patients who can be maintained successfully on antiobsessional treatment. (PsycINFO Database Record (c) 2012 APA, all rights reserved).

Milanfranchi A, Ravagli S, et al. A double-blind study of fluvoxamine and clomipramine in the treatment of obsessive-compulsive disorder. Int Clin Psychopharmacol. 1997;12(3):131-6.

A double-blind trial was carried out to assess the efficacy and safety of fluvoxamine, a selective serotonin reuptake inhibitor, in comparison with clomipramine, a classical tricyclic antidepressant, in the treatment of obsessive-compulsive disorder. A total of 26 individuals with obsessive-compulsive disorder and with no comorbid disorders at baseline were included in the study. The obsessive-compulsive disorder symptom severity was rated using the Yale-Brown Obsessive-Compulsive Scale and the Clinical Global Impression Scale. The primary efficacy measures indicated an equal improvement in the two groups (38% in the patients taking fluvoxamine and 40% in those taking clomipramine, as compared with baseline values), but onset was faster in the clomipramine group. Side effects, in particular anticholinergic side effects, were more prominent in the clomipramine group. The present double-blind trial confirms an equal efficacy of clomipramine and fluvoxamine in obsessive-compulsive patients. Although clomipramine had a faster onset, fluvoxamine was better tolerated, so that it seems more suitable for long-term treatment of obsessive-compulsive patients.

Pidrman V. Fenfluramine challenge test in obsessive-compulsive disorder--first results. Acta medica (Hradec Králové) / Universitas Carolina, Facultas Medica Hradec Králové. 1997;40:99-102

Obsessive-compulsive disorder is a chronic psychiatric illness, affecting up to 3% of the general population, to the middle of 60-th it was supposed to be untreatable. Antidepressant pharmacotherapy is one of the treatment alternatives today. We compared efficacy and safety of citalopram versus clomipramine (serotoninergic antidepressants) in 6 weeks in double blind therapy of obsessive-compulsive disorder. The second objective was to compare prolactin response to a fenfluramine challenge test before the treatment of patients and after 6 weeks of the treatment. In a sample of 14 patients we confirmed significant therapeutic response after 3 weeks of pharmacotherapy, better in obsession than in compulsion. We found low level of adverse effects in the first week of therapy--dry mouth, anxiety, nausea, somnolence, tremor, and sexual adverse events. There were no changes in the laboratory, test EEG, and ECG examinations. Fenfluramine challenge test showed statistically significant decrease of prolactin levels 1 hour after administration of fenfluramine. It was not observed after six weeks of the therapy. Statistically significant negative correlation between prolactin plasma levels at the 6th hour

after administration of fenfluramine and obsession item of YBOC Scale was showed after the 3rd and 6th week of the therapy. The correlation was not observed for compulsion item YBOC Scale. Side effects observed during and after the challenge test were anxiety and nervousness and gastrointestinal problems, lasted from 1 hour to 10 hours. These preliminary result could support the idea, that obsessions and compulsions have not necessary the same biological background. The challenge paradigm appears to be a possible way to clarify the pathogenesis of OCD. Our study will continue.

Mundo E, Bareggi SR, et al. Effect of acute intravenous clomipramine and antiobsessional response to proserotonergic drugs: is gender a predictive variable? Biol Psychiatry. 1999;45(3):290-4.

BACKGROUND: Previous studies on serotonergic responsivity in obsessive-compulsive disorder (OCD) showed about 50% of patients experiencing an acute worsening of OC symptoms when administered meta-chlorophenylpiperazine or i.v. clomipramine. The aim of this study was to determine what variables influence the response to acute i.v. clomipramine. Could this response be predictive of the response to chronic treatment with two serotonergic drugs with differing selectivity profiles: clomipramine and fluvoxamine? METHODS: Fifty OC patients were consecutively recruited. All underwent a challenge with 25 mg i.v. clomipramine and placebo and were administered 10-week oral clomipramine or fluvoxamine according to a double-blind design. The efficacy of the antiobsessional treatment was evaluated by Yale-Brown Obsessive-Compulsive Scale and Clinical Global Impression scale scores. RESULTS: Obsessions worsened in 42% patients as rated by change values in 100-mm visual analogue scale scores for the clomipramine vs. placebo infusion. There was a significant difference in gender distribution between "worsened" and "unchanged" patients, since female subjects were more frequently "unchanged." Thirty-one patients completed the 10-week treatment. According to both qualitative and quantitative evaluations, female subjects showed a better antiobsessional response, and this difference was enhanced in the clomipramine-treated group. CONCLUSIONS: Results suggest a role for reproductive hormones in the pathophysiology or treatment of OC patients.

Hoehn-Saric R, Ninan P, et al. Multicenter double-blind comparison of sertraline and desipramine for concurrent obsessive-compulsive and major depressive disorders. Arch Gen Psychiatry. 2000;57(1):76-82.

BACKGROUND: Serotonin reuptake inhibitors (SRIs) have demonstrated consistent efficacy in the treatment of obsessive-compulsive disorder (OCD), while agents that are primarily norepinephrine reuptake inhibitors have not. Comparable efficacy has been demonstrated for SRI and non-SRI antidepressants in uncomplicated major depressive disorder (MDD). This multicenter trial is the first comparison of an SRI (sertraline) and a non-SRI antidepressant (desipramine) in the treatment of OCD with concurrent MDD. METHODS: One hundred sixty-six patients diagnosed using structured clinical interviews and recruited from 16 treatment sites were randomly assigned to double-blind treatment with either sertraline (up to 200 mg/d) or desipramine (up to 300 mg/d) over 12 weeks. Measures of severity of OCD and MDD symptoms, as well as adverse effects of the medications, were monitored over the course of the treatment period. RESULTS: Patients assigned to sertraline responded significantly better at end point on measures of OCD and MDD symptoms compared with patients assigned to desipramine. Sertraline was also associated with a significantly greater number of patients who achieved a "robust" improvement in OCD symptoms (> or =40% reduction) compared with desipramine. More patients receiving desipramine than sertraline discontinued treatment because of adverse events. CONCLUSIONS: The SRI sertraline was more effective in reducing MDD and OCD symptoms than the primarily norepinephrine reuptake inhibitor desipramine for patients with concurrent OCD and MDD.

Mundo E, Maina G, et al. Multicentre, double-blind, comparison of fluvoxamine and clomipramine in the treatment of obsessive-compulsive disorder. Int Clin Psychopharmacol. 2000;15(2):69-76.

The aim of this prospectively randomized, double-blind, parallel group, multicentre study was to compare the efficacy and tolerability of fluvoxamine and clomipramine in patients suffering from obsessive-compulsive disorder (OCD) (DSM-III-R). Fourteen centres participated in this trial. Sixty-eight patients were randomized to receive fluvoxamine and 65 to receive clomipramine. The duration of the study was 10 weeks. The two treatment groups showed a marked improvement of obsessive-compulsive symptomatology, as determined by the Yale-Brown Obsessive-Compulsive Scale, the National Institute of Mental Health Obsessive-Compulsive Global Scale and Clinical Global Impression. No statistically significant differences were found between fluvoxamine and clomipramine in terms of efficacy during the study. A similar number of patients in each group withdrew from the study prematurely, but there were more dropouts due to adverse events in the clomipramine group. Concerning tolerability, there were significantly more reports of constipation and dry mouth in the clomipramine group. The results show that fluvoxamine and clomipramine have similar efficacy

in the treatment of patients suffering from OCD, but fluvoxamine is better tolerated. In view of the superior safety profile of fluvoxamine compared to clomipramine in terms of a risk-benefit assessment, the use of fluvoxamine would appear to be advantageous for this patient population.

Mundo E, Rouillon F, et al. Fluvoxamine in obsessive-compulsive disorder: Similar efficacy but superior tolerability in comparison with clomipramine. Human Psychopharmacology: Clinical and Experimental. 2001;16(6):461-8.

The aim of this double-blind, randomized, multicenter study was to directly compare the efficacy and safety of fluvoxamine and clomipramine in patients with OCD. A total of 227 adult patients were randomized to flexible doses of fluvoxamine or clomipramine (both 150–300 mg/day) for 10 wks. Fluvoxamine and clomipramine were both clinically effective and there were no statistically significant differences between the 2 treatment groups, at any visit, on the National Institute of Mental Health Obsessive-Compulsive global rating scale, the Yale-Brown Obsessive-Compulsive scale (total score and obsession and compulsion subscores), the Clinical Global Impression severity of illness and global improvement subscales, the Clinical Anxiety Scale and the 17-item Hamilton Depression Rating Scale. However, there were differences in safety between the two treatments. Compared with fluvoxamine-treated patients, those treated with clomipramine had more anticholinergic side effects (dry mouth, constipation and tremor) and premature withdrawals due to adverse events (18 vs 9). The results from this controlled study indicate that fluvoxamine is as effective as clomipramine in the treatment of OCD but has a better tolerability profile. (PsycINFO Database Record (c) 2012 APA, all rights reserved).

1.3.3. TCA *versus* TCA (4 – 1980-1988)

Thoren P, Asberg M, et al. Clomipramine treatment of obsessive-compulsive disorder. I. A controlled clinical trial. Arch Gen Psychiatry. 1980;37(11):1281-5.

The effect of clomipramine hydrochloride in severe obsessive-compulsive disorder (OCD) was compared with that of nortriptyline hydrochloride and placebo in a five-week randomized, double-blind trial. Clomipramine, but not nortriptyline, was superior to placebo in interview-based ratings of severity of OCD. The effect was not clear-cut until after five weeks of treatment. When clomipramine was given openly to 22 patients after the end of the controlled trial, half of the patients responded to the drug. The response could not be predicted from severity or duration of illness, sex or age of the patient, or presence or absence of secondary depressive symptoms. The amelioration with clomipramine was not sustained if the drug was withdrawn.

Ananth J, Pecknold JC, et al. Double-blind comparative study of clomipramine and amitriptyline in obsessive neurosis. Prog Neuropsychopharmacol. 1981;5(3):257-62.

Volavka J, Neziroglu F, et al. Clomipramine and imipramine in obsessive-compulsive disorder. Psychiatry Res. 1985;14(1):85-93.

Twenty-three outpatients with primary obsessive-compulsive disorder (OCD) were started in a 12-week double-blind clinical trial of clomipramine (CLI) (n = 11) and imipramine (IMI) (n = 12). There was no placebo and no crossover. After 6 weeks of treatment, data on 19 subjects (9 CLI, 10 IMI) were available. After week 12, the sample was reduced to 16 patients (8 CLI, 8 IMI). At both time points, OCD symptoms showed modest reductions (in comparison with the pretreatment baseline) in both CLI and IMI groups. Both drugs showed a major antidepressant effect. Analyses accounting for the differences in the baseline levels indicated a somewhat superior effect of CLI over IMI on OCD as well as depression. The effect of CLI and IMI on OCD was independent of the initial severity of depression. There were no clear differences in the safety of the treatments.

Leonard H, Swedo S, et al. Treatment of childhood obsessive compulsive disorder with clomipramine and desmethylimipramine: a double-blind crossover comparison. Psychopharmacol Bull. 1988;24(1):93-5.

1.3.4. ISRS *versus* IRSN (2 – 2003-2004)

Denys D, van der Wee N, et al. A double blind comparison of venlafaxine and paroxetine in obsessive-compulsive disorder. J Clin Psychopharmacol. 2003;23(6):568-75.

SUMMARY: While the usefulness of clomipramine and selective serotonin reuptake inhibitors (SSRIs) in obsessive-compulsive disorder (OCD) has been established, the efficacy of serotonin-norep-

inephrine reuptake inhibitors remains to be determined. This report describes the first randomized double-blind comparison study of an SNRI in patients with obsessive-compulsive disorder. The current study compares the efficacy and tolerability of venlafaxine with paroxetine. One hundred and fifty patients with primary OCD according to DSM-IV criteria were randomly assigned in a 12-week double-blind trial to receive dosages titrated upward to 300 mg/d of venlafaxine (n = 75) or 60 mg/d of paroxetine (n = 75). Primary efficacy was assessed by the change from baseline on the Yale-Brown obsessive-compulsive scale (Y-BOCS). Other assessments throughout the trial included the Hamilton depression rating scale, and the Hamilton anxiety rating scale. An intent-to-treat, last-observation-carried-forward analysis demonstrated a mean decrease on the Y-BOCS of 7.2 +/- 7.5 in the venlafaxine group and of 7.8 +/- 5.4 in the paroxetine group. In both treatment groups, a responder rate (decrease > 35% on the Y-BOCS) of approximately 40% was found. There were no significant differences between venlafaxine and paroxetine with regard to response or responder rates. The incidence of adverse events for venlafaxine and paroxetine was comparable. The most common side effects for venlafaxine were somnolence, insomnia, a dry mouth, and sweating; and for paroxetine somnolence, sweating, nausea, and headache. These results show that venlafaxine was equally effective to paroxetine in treating patients with OCD. Venlafaxine may be a useful therapy for obsessive-compulsive patients, but is not superior to SSRIs.

Denys D, van Megen HJ, et al. A double-blind switch study of paroxetine and venlafaxine in obsessive-compulsive disorder. J Clin Psychiatry. 2004;65(1):37-43.

BACKGROUND: The treatment guidelines for obsessive-compulsive disorder (OCD) propose to switch serotonin reuptake inhibitors (SRIs) in case of refractoriness. However, no controlled research has been published yet that prospectively examined the effects of changing SRIs. This article describes the first double-blind switch study of 2 SRIs in patients with OCD. METHOD: 150 patients with primary OCD, according to DSM-IV criteria, were randomly assigned in a 12-week, double-blind trial to receive dosages titrated upward to 300 mg/day of venlafaxine (N = 75) or 60 mg/day of paroxetine (N = 75). Primary efficacy was assessed by the change from baseline on the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), and nonresponse was defined as less than 25% reduction on the Y-BOCS. After a 4-week tapering phase, 43 nonresponders were switched to 12 additional weeks of the alternate antidepressant, of which 16 patients received venlafaxine and 27 received paroxetine. RESULTS: Eighteen of 43 patients benefited from a switch to the alternate SRI with a mean +/- SD decrease of at least 25% on the Y-BOCS. At the end of 12 weeks, responder rates were 56% for paroxetine (15/27) and 19% for venlafaxine (3/16). An intent-to-treat, last-observation-carried-forward analysis demonstrated a mean decrease on the Y-BOCS of 1.8 +/- 3.5 in the venlafaxine group and 6.5 +/- 7.1 in the paroxetine group. After 2 consecutive SRI trials, 109 of 150 patients (73%) achieved a Y-BOCS decrease of at least 25%. CONCLUSION: The results of the current study show that 42% of the nonresponders benefited from a crossover to the other SRI, and that paroxetine was more efficacious than venlafaxine in the treatment of nonresponders to a previous SRI trial. Switching SRIs in case of refractoriness may be considered a useful strategy for patients with OCD.

1.3.5. TCA *versus* IRSN (1 - 2002)

Albert U, Aguglia E, et al. Venlafaxine versus clomipramine in the treatment of obsessive-compulsive disorder: a preliminary single-blind, 12-week, controlled study. J Clin Psychiatry. 2002;63(11):1004-9.

BACKGROUND: The objective of this study was to investigate, in a single-blind manner over a period of 12 weeks, the efficacy and tolerability of venlafaxine versus clomipramine in the treatment of obsessive-compulsive disorder (OCD). METHOD: Patients with a DSM-IV diagnosis of OCD and a Yale-Brown Obsessive Compulsive Scale (YBOCS) score >/= 16 were randomly assigned to receive venlafaxine, 225 to 350 mg/day (26 patients), or clomipramine, 150 to 225 mg/day (47 patients), for 12 weeks, with dosage adjustments according to tolerability and response to treatment. All patients were medication-free from at least 2 months prior to study enrollment. Efficacy measures were the YBOCS and the Clinical Global Impressions scale (CGI), which were completed at baseline and every 4 weeks. We defined responders as patients who had an improvement from baseline in YBOCS score of >/= 35% and a CGI score </= 2. An investigator who was blinded to patients' current medication administered rating scales independently. Moreover, patients were instructed not to reveal their current treatment to this investigator. RESULTS: Twenty-five patients in the venlafaxine group and 40 in the clomipramine group completed the 12-week trial. Responder rates at the end of the 12 weeks were 36% for venlafaxine (9/25) versus 50% for clomipramine (20/40) according to the visitwise analysis and 34.6% (9/26) for venlafaxine versus 42.6% (20/47) for clomipramine ac-

cording to the last-observation-carried-forward analysis, with no statistically significant difference between the 2 drugs. Adverse experiences were reported by 61.5% of patients receiving venlafaxine (16/26) and by 91.5% of those receiving clomipramine (43/47). CONCLUSION: Our results indicate that venlafaxine might be as efficacious as clomipramine in the acute treatment of OCD, with fewer side effects.

1.3.6. Otras comparaciones (10 – 1983-2010)

Insel TR, Murphy DL, et al. Obsessive-compulsive disorder. A double-blind trial of clomipramine and clorgyline. Arch Gen Psychiatry. 1983;40(6):605-12.

Patients with obsessive-compulsive disorder who met DSM-III criteria and who had been ill for at least one year were studied in a double-blind, randomized, crossover comparison of the tricyclic antidepressant clomipramine hydrochloride and the monoamine oxidase inhibitor clorgyline hydrochloride. No significant improvement was evident after four weeks of treatment with placebo prior to the crossover study. Treatment with clomipramine was associated with significant improvement after both four and six weeks in measures of obsessions, anxiety, and depression. Antiobsessional responses to clomipramine did not depend on presence of depression. Improvement was correlated with plasma concentrations of clomipramine, but not with the plasma concentrations of any of its metabolites. No significant improvement was evident for the entire group with clorgyline treatment, although the conditions of individual patients did respond to the drug.

Prasad A. A double blind study of imipramine versus zimelidine in treatment of obsessive compulsive neurosis. Pharmacopsychiatry. 1984;17(2):61-2.

Six patients suffering from obsessive compulsive neurosis were randomly allocated into two groups of three patients each and commenced on either imipramine, a noradrenaline re-uptake inhibitor, or zimelidine, a serotonin re-uptake inhibitor. After 4 weeks, the group on zimelidine showed significant reduction of obsessional symptoms as compared to the other group. The response was rapid and sustained over a period of two months.

Joffe RT, Swinson RP, et al. Acute psychostimulant challenge in primary obsessive-compulsive disorder. J Clin Psychopharmacol. 1991;11(4):237-41.

The effects of acute oral administration of methylphenidate 40 mg versus dextroamphetamine 30 mg versus matched placebo were compared in 11 patients with primary obsessive-compulsive disorder. Dextroamphetamine but not methylphenidate had a significantly greater antiobsessive-compulsive effect as measured by the Comprehensive Psychiatric Rating Scale--Obsessive-Compulsive Subscale, as compared with placebo. This effect appeared unrelated to their effect on depression although a differential effect of the two psychostimulants on anxiety was observed. Although both these stimulants affect serotonin, the differences noted between dextroamphetamine and methylphenidate suggest that catecholamines may be implicated in the pathophysiology of obsessive-compulsive disorder.

Pato MT, Pigott TA, et al. Controlled comparison of buspirone and clomipramine in obsessive-compulsive disorder. Am J Psychiatry. 1991;148(1):127-9.

Eighteen outpatients with obsessive-compulsive disorder were treated with either buspirone, a partial serotonin agonist, or clomipramine, a serotonin uptake inhibitor, in a double-blind, random-assignment study. Both drugs led to statistically significant and similar improvements in scores on the Yale-Brown Obsessive-Compulsive Rating Scale and other obsessive-compulsive and depression scales. This preliminary result warrants further exploration with a larger sample and other serotonergic agents.

Hewlett WA, Vinogradov S, et al. Clomipramine, clonazepam, and clonidine treatment of obsessive-compulsive disorder. J Clin Psychopharmacol. 1992;12(6):420-30.

Serotonergic reuptake inhibitors have been the primary medications for treatment of obsessive-compulsive disorder (OCD); however, other serotonergic and alpha 2-adrenergic medications also have been reported to reduce obsessive-compulsive symptoms. In this study, we compare three medications with reported efficacy in OCD to a control medication, diphenhydramine, a medication without theoretical or demonstrated treatment benefit. The three active medications were clomipramine, a serotonergic reuptake inhibitor; clonazepam, a benezodiazepine with putative serotonergic properties; and clonidine, an alpha 2-adrenergic agonist. Twenty-eight subjects with DSM-III-R diagnosis of OCD rotated through 6-week trials of each of the four medications in a randomized, double-blind, multiple crossover protocol. Clomipramine and clonazepam were both effective relative to the con-

trol medication in reducing OCD symptoms. There was a significant cross-response between these two medications; however 40% of subjects failing clomipramine trials had a clinically significant response to clonazepam treatment. The control medication, diphenhydramine, itself produced a significant decrement in symptoms, whereas clonidine was ineffective in reducing OCD symptoms. Clonazepam improvement was unrelated to changes in anxiety and occurred early in treatment. Clonazepam was significantly more effective than the other medications during the first 3 weeks of treatment. The results confirm the efficacy of clomipramine in the treatment of OCD and suggest that clonazepam might be a useful alternative treatment for patients with this disorder.

Stein DJ, Hollander E, et al. Comparison of clomipramine, alprazolam and placebo in the treatment of obsessive-compulsive disorder. Human Psychopharmacology: Clinical and Experimental. 1992;7(6):389-95.

Compared the efficacy of clomipramine (CMI), alprazolam, and placebo in the treatment of obsessive-compulsive disorder (OCD). 44 patients (aged 18–65 yrs) with OCD were entered into a double-blind randomly assigned treatment protocol with CMI or placebo. Alprazolam was administered to 14 OCD patients in a separate open-treatment study. The response rate of patients completing treatment was 50% with CMI, 19% with placebo, and 18% with alprazolam. Self-ratings of OCD symptoms in both assigned patients and treatment completers demonstrated a significantly greater benefit with CMI than with alprazolam. Ratings of depression and clinician ratings of obsessionality did not, however, indicate differences between the treatment groups. (PsycINFO Database Record (c) 2013 APA, all rights reserved).

Vallejo J, Olivares J, et al. Clomipramine versus phenelzine in obsessive-compulsive disorder. A controlled clinical trial. Br J Psychiatry. 1992;161:665-70.

A double-blind clinical trial of clomipramine versus phenelzine was carried out on 30 patients suffering from DSM-III obsessive-compulsive disorder. The study period was 12 weeks, and the maximum doses used (from the fifth week on) were 225 mg/day for clomipramine (14 patients) and 75 mg/day for phenelzine (12 patients); four patients dropped out. Obsessive symptoms improved significantly in both drug groups, but there was no significant difference between groups. Depressive symptoms improved before obsessive ones.

Jenike MA, Baer L, et al. Placebo-controlled trial of fluoxetine and phenelzine for obsessive-compulsive disorder. Am J Psychiatry. 1997;154(9):1261-4.

OBJECTIVE: It is now well documented that fluoxetine is a viable treatment option for patients with obsessive-compulsive disorder (OCD), and there is a small body of evidence indicating that monoamine oxidase inhibitors may be effective in at least a subset of patients. The authors conducted a 10-week placebo-controlled trial of these two agents in patients who met DSM-III-R criteria for OCD. METHOD: Sixty-four subjects were randomly assigned to receive placebo, phenelzine (60 mg/day), or fluoxetine (80 mg/day). These doses were achieved by the end of week 3 of the active phase of the study. Outcomes were assessed with standardized instruments to measure OCD, mood, and anxiety. RESULTS: Fifty-four patients completed the study. There was a significant difference among the three treatments on one OCD scale, with fluoxetine-treated patients improving significantly more than those in the placebo or phenelzine group. A subgroup of OCD patients with symmetry obsessions did respond to phenelzine. CONCLUSIONS: This study provides no evidence to support the use of phenelzine in OCD except possibly for those patients with symmetry or other atypical obsessions. There was also no support for the hypothesis that patients with high levels of anxiety would respond preferentially to phenelzine.

Koran LM, Aboujaoude E, et al. Pulse-loaded intravenous clomipramine in treatment-resistant obsessive-compulsive disorder. J Clin Psychopharmacol. 2006;26(1):79-83.

INTRODUCTION: Small studies have suggested that intravenous clomipramine (CMI) may be more effective and induce faster improvement in obsessive-compulsive disorder than do orally administered serotonin reuptake inhibitors. OBJECTIVE: To test these hypotheses, we conducted a randomized, double-blind, double-dummy study of pulse-loaded intravenous versus oral CMI, followed by open-label oral CMI for 12 weeks. METHODS: We enrolled a volunteer and referred group of 34 adults with a primary diagnosis of Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition obsessive-compulsive disorder of > or =1-year duration and Yale-Brown Obsessive Scale score of > or =20. Eligible subjects had failed > or =2 adequate serotonin reuptake inhibitor trials. Subjects received pulse loaded CMI 150 mg by vein or by mouth on day 1 and 200 mg on day 2. Oral CMI began on day 6 at 200 mg/d and was increased by 25 mg every 4 days to 250 mg/d, as tolerated, for 12 weeks. RESULTS: Adverse events led to one withdrawal during oral pulse loading

and 5 during open-label oral treatment. Intravenous pulse loading did not induce a more rapid or greater Yale-Brown Obsessive Scale score decrease than oral pulse loading at day 6 or by week 12. Day 6 and week 12 improvement were unrelated to plasma drug or metabolite concentrations. Pulse loading itself seemed to induce more rapid and greater improvement than expected in treatment-resistant obsessive-compulsive disorder. CONCLUSIONS: Further investigation of oral pulse-loading regimens in treatment-resistant obsessive-compulsive disorder is warranted.

Sayyah M, Boostani H, et al. Comparison of Silybum marianum (L.) Gaertn. with fluoxetine in the treatment of Obsessive-Compulsive Disorder. Prog Neuropsychopharmacol Biol Psychiatry. 2010;34(2):362-5.

Obsessive-Compulsive Disorder (OCD) is a common neuropsychiatric condition. Although a variety of pharmaceutical agents is available for the treatment of OCD, psychiatrists often find that many patients cannot tolerate the side effects of these medications; do not respond properly to the treatment; or the medications lose their effectiveness after a period of treatment. Herbal medicine can be a solution to some of these problems. In fact many herbs with psychotropic effects exist which can have fewer side effects. They can provide an alternative treatment or be used to enhance the effectiveness of conventional anti-obsessive and compulsive symptoms. Silybum marianum (L.) Gaertn. is a well-known medicinal plant with a long history of usage in Iran. This plant is reported to be safe on humans. Our objective in this study was to compare the efficacy of the extract of S.marianum (L.) with fluoxetine in the treatment of OCD. The study was an 8-week pilot double-blind randomized trial. Thirty five adult outpatients who met the DSM-IV-TR criteria for OCD based on the structured clinical interview participated in the trial. The minimum score of Yale-Brown Scale for OCD was 21 for all patients. In this double-blind and randomized trial, patients were randomly assigned to receive either capsule of the extract (600 mg/day) or fluoxetine (30 mg/day) for 8 weeks. The results showed no significant difference between the extract and fluoxetine in the treatment of OCD. There was also no significant difference between the two groups in terms of observed side effects.

NOTA: Para 1.1, 1.2 y 1.3 señalar si se trata de:
- Adultos o ancianos.
- TOC leve-moderado o grave.
- *Naive* o no *naive*.

1.4. Relación dosis-respuesta de los tratamientos psicofarmacológicos (utilización de dosis elevadas) (5 - 1994-2009)

Tollefson GD, Rampey AH Jr., et al. A multicenter investigation of fixed-dose fluoxetine in the treatment of obsessive-compulsive disorder. Arch Gen Psychiatry. 1994;51(7):559-67.

OBJECTIVES: To determine the effectiveness of fluoxetine hydrochloride at fixed doses of 20 mg/d, 40 mg/d, and 60 mg/d in patients with obsessive-compulsive disorder (OCD) and to evaluate its safety. METHODS: Fixed-dose fluoxetine hydrochloride (20 mg/d, 40 mg/d, 60 mg/d) was compared with placebo in two randomized, double-blind, parallel, 13-week trials of identical design in 355 outpatients with OCD aged 15 to 70 years (DSM-III-R criteria; 1 year's duration or longer; depression secondary if present). RESULTS: Fluoxetine (all doses) was significantly (P < or = .001) superior to placebo on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) total score (mean baseline-to-end-point decrease, 4.6, 5.5, and 6.5 vs 0.9, respectively, studies pooled) and other efficacy measures (P < or = .01). A trend suggesting greater efficacy at 60 mg/d was observed. Most patients (79.2%) completed the study. Eight adverse events were statistically significantly more frequent with fluoxetine and one, with placebo. For some events, incidence tended to increase with increasing dosage; however, few patients discontinued treatment for any single event. CONCLUSION: Fluoxetine was associated with a statistically significant reduction in OCD severity, including time engaged in obsessional and/or compulsive behaviors. Adverse events infrequently led to study discontinuation.

Greist J, Chouinard G, et al. (1995) Double-blind parallel comparison of three dosages of sertraline and placebo in outpatients with obsessive-compulsive disorder. Archives of general psychiatry. 1995;52:289-95.

BACKGROUND: Anecdotal evidence suggests patients with obsessive-compulsive disorder (OCD) are treated with selective serotonin uptake inhibitors at dosages significantly higher than those used with depressed patients. The current study examined the efficacy, safety, and optimal dosing strat-

egy of sertraline in patients with OCD. METHODS: Three hundred twenty-four nondepressed outpatients with OCD from 11 sites followed identical protocols using a double-blind parallel design. Following 1 week of single-blind placebo, patients were randomly assigned to 12 weeks of treatment with one of three fixed dosages of sertraline (50, 100, or 200 mg/d) or placebo. RESULTS: Sertraline patients exhibited significantly greater improvement (P < .05) at end point than placebo patients on all three main efficacy measures in the 50-mg/d and 200-mg/d groups and on one measure in the 100-mg/d group. The placebo response was larger in this population of subjects with OCD than in those previously studied. Adverse experiences were common in the sertraline and placebo groups and appeared to be dose-related in the sertraline-treated patients. CONCLUSIONS: Results support the safety and efficacy of daily dosages of 50, 100, and 200 mg of sertraline in the short-term treatment of patients with OCD.

Zitterl W, Meszaros K, et al. Efficacy of fluoxetine in Austrian patients with obsessive-compulsive disorder. Wien Klin Wochenschr. 1999;111(11):439-42.

In an 8-week double-blind placebo-controlled trial we studied the efficacy of fluoxetine (FLX) in 53 Austrian patients with obsessive compulsive disorder (OCD) diagnosed according to DSM-III-R. The dosage of FLX was fixed at either 20, 40, or 60 mg per day. Response was prospectively defined as an at least 25% reduction on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) and an improvement on Clinical Global Impression (CGI) rating to at least "much improved" at the endpoint. Patients treated with at least 40 mg FLX per day showed significantly higher response rates than did those receiving either placebo or FLX 20 mg/day. Compulsions were more reduced than obsessions and we also observed a strong placebo effect which is largely attributable to an improvement in the Y-BOCS compulsion subscore.

Montgomery SA, Kasper S, et al. Citalopram 20 mg, 40 mg and 60 mg are all effective and well tolerated compared with placebo in obsessive-compulsive disorder. Int Clin Psychopharmacol. 2001;16(2):75-86.

Serotonin reuptake inhibitors appear to be uniquely effective treatments for obsessive-compulsive disorder (OCD). This double-blind, placebo-controlled study was the first trial to assess the efficacy of the most selective of the serotonin reuptake inhibitors, citalopram, in OCD. A total of 401 patients were randomized to receive citalopram 20, 40 or 60 mg/day or placebo for 12 weeks. All three doses of citalopram were significantly more effective than placebo measured on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) change score (P < 0.01). The highest response rate, defined as 25% improvement in Y-BOCS entry score, was observed in the 60 mg group (65%). This compared with 52% and 57.4% in the 40 mg and 20 mg groups. Response rate on placebo was 36.6% (P < 0.05 for all three doses of citalopram compared to placebo). There was no significant difference between the individual doses of citalopram. An advantage was seen for citalopram on the Sheehan Disability Scale compared with placebo (P < 0.05 on all three citalopram groups versus placebo for both the work situation and the family life and home responsibilities and P < 0.05 on citalopram 60 mg and 20 mg versus placebo for the social life and home activities). Citalopram was well tolerated; only 4 to 6 patients in each dose group discontinued the study prematurely due to adverse events.

Dougherty DD, Jameson M, et al. Open-label study of high (30 mg) and moderate (20 mg) dose escitalopram for the treatment of obsessive-compulsive disorder. Int Clin Psychopharmacol. 2009;24(6):306-11.

This study sought to investigate the efficacy of escitalopram at different dosages for the treatment of obsessive-compulsive disorder (OCD). Thirty individuals were enrolled in a 16-week, open-label trial of escitalopram and randomly assigned to the 20 or 30 mg study arm. Study measures assessing OCD symptoms, anxiety, depression, and quality of life were administered at baseline and weeks 2, 4, 8, 12, and 16. For the 23 study completers, pretreatment and posttreatment analyses revealed significant improvements (P<0.05) on clinician-rated and self-rated measures of OCD symptoms, quality of life, anxiety, and depression. Approximately half of the sample (n = 12) satisfied full medication response criteria and less than one-quarter (n = 5) were partial medication responders. Intention-to-treat analyses showed similar improvements (P<0.05) on all study measures. At study completion, a superior responder rate and more improvement on the Yale-Brown Obsessive Compulsive Scale (P<0.05) was reported for those in the 30 versus 20 mg study arm. The difference between the two groups, however, disappeared when initial differences in baseline depression and anxiety scores were used as analysis covariates. These results suggest that the 30 mg (vs. 20 mg) dose of escitalopram may provide a superior reduction in OCD symptoms for those sufferers with comorbid depression and/or anxiety.

1.5. Acelerar la respuesta (por ejemplo, gabapentina, mirtazapina) (8 – 1997-2010)

Koran LM, Sallee FR, et al. Rapid benefit of intravenous pulse loading of clomipramine in obsessive-compulsive disorder. Am J Psychiatry. 1997;154(3):396-401.

OBJECTIVE: The authors conducted a randomized, double-blind, placebo-controlled trial of intravenous versus oral pulse loading of clomipramine in patients with obsessive-compulsive disorder to test two hypotheses: 1) intravenous pulse loading will cause greater immediate improvement than oral pulse loading and 2) patients who respond to pulse loading will continue to improve during 8 weeks of oral clomipramine treatment. METHOD: Fifteen patients with DSM-III-R obsessive-compulsive disorder of at least 1 year's duration and baseline Yale-Brown Obsessive Compulsive Scale scores of 17 or higher were enrolled in the study. Yale-Brown scale ratings were made 4.5 days after double-blind oral or intravenous pulse loading of clomipramine, and patients were then given 150 mg/day of oral clomipramine with increases of 25 mg every 4 days to 250 mg/day as tolerated or, in two cases, other selective serotonin reuptake inhibitors (SSRIs). RESULTS: The first hypothesis was confirmed: 4.5 days after the second pulse-loaded dose, six of seven patients given intravenous clomipramine but only one of eight given oral medication responded to the drug. After 8 weeks of oral clomipramine, the results partially supported the second hypothesis: four of six patients who had responded to intravenous clomipramine continued their improvement, but those who had responded to pulse loading did not improve statistically significantly more than those who had not. CONCLUSIONS: Intravenous pulse loading of clomipramine may be a valuable new treatment for obsessive-compulsive disorder, particularly for patients who have failed oral treatment trials.

Mundo E, Guglielmo E, et al. Effect of adjuvant pindolol on the antiobsessional response to fluvoxamine: a double-blind, placebo-controlled study. Int Clin Psychopharmacol. 1998;13(5):219-24.

On the basis of recent results indicating that adjuvant pindolol has the positive effect of shortening latency to antidepressant response to selective serotonin reuptake inhibitors, the primary aim of our study was to evaluate the effect of pindolol on latency to antiobsessional response to fluvoxamine. Fifteen non-depressed obsessive-compulsive inpatients (six men and nine women) were consecutively recruited and randomly assigned to an 8-week standardized double-blind treatment with fluvoxamine and pindolol (group A) or fluvoxamine and placebo (group B). Patients were assessed weekly using rating scales for obsessive-compulsive disorder [Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), National Institute of Mental Health Obsessive-Compulsive Scale], co-occurent depressive symptoms (Hamilton Depression Scale) and global function (Clinical Global Improvement), from baseline to the end of the study. In accordance with data from the literature, response to treatment was defined as a reduction in YBOCS total scores of > or = 35% and a score on the 'global improvement' item of the Clinical Global Improvement of < 3. Data were analysed using analyses of variance with repeated measures performed on YBOCS and Hamilton Depression Scale scores to evaluate the mean quantitative response within and between groups and, additionally, employing a survival analysis to compute the percentage of responders within each group. Neither quantitative nor qualitative analysis revealed any differences between the two treatment groups, and pindolol did not shorten the latency of antiobsessional response to fluvoxamine. The results of this preliminary study indicate that different biological mechanisms underly the antiobsessional and antidepressant responses to fluvoxamine.

Koran LM, Pallanti S, et al. Sumatriptan, 5-HT(1D) receptors and obsessive-compulsive disorder. Eur Neuropsychopharmacol. 2001;11(2):169-72.

BACKGROUND: After considering the effects of 5-HT receptor agonists with different binding profiles on the symptoms of obsessive-compulsive disorder (OCD), Zohar and Kindler hypothesized that the 5-HT(1D) receptor was implicated in this disorder's pathophysiology. METHODS: We explored the 5-HT(1D) hypothesis in a 5-day, random, double-blind, placebo-controlled trial of oral sumatriptan 100 mg/day in medication-free adults with OCD. We hypothesized that sumatriptan, a 5-HT(1D) agonist, would diminish 5-HT release, thereby worsening OCD symptoms. We further hypothesized that by beginning to desensitize 5-HT(1D) receptors, sumatriptan pretreatment would promote a faster response or an increased likelihood of response to subsequent treatment with a selective serotonin reuptake inhibitor. RESULTS: The five sumatriptan subjects' OCD symptom worsening, as measured by the Yale-Brown scale (upward arrow 17.6% (S.D. 14.6)), was significant when compared to the slight symptom decrease in the five placebo subjects (downward arrow 5.2% (S.D. 4.9), P<0.015). The sumatriptan group did not exhibit a faster response or greater likelihood of response to a 90-day, open label trial of paroxetine. CONCLUSIONS: Longer term studies of the effects of 5-HT(1D) agonists on OCD symptoms are indicated. Zolmitriptan, a potent 5-HT(1D) receptor agonist with better penetration of the blood-brain barrier, may be a preferred challenge agent.

Bogetto F, Albert U, et al. Sertraline treatment of obsessive-compulsive disorder: efficacy and tolerability of a rapid titration regimen. Eur Neuropsychopharmacol. 2002;12(3):181-6.

The objective of this study was to compare in a single blind manner, over a period of 12 weeks, the efficacy and tolerability of two different titration regimens of sertraline in the treatment of OCD: 150 mg/day reached at day five from the beginning of therapy (rapid titration regimen) versus 150 mg/day reached at day 15 from the beginning (slow titration regimen). Patients with a DSM-IV diagnosis of OCD and a Y-BOCS greater or equal to 16 were randomly assigned to receive one of the two dosing regimens; an upper target dose of 150 mg/day was selected on the basis of a review of mean dosages used in flexible-dose sertraline studies. The primary efficacy measure was the Y-BOCS, which was completed at baseline and every 2 weeks. Thirty-two patients referred to the Anxiety and Mood Disorders Unit of the University of Turin were included in the study. Seventeen were assigned to the rapidly escalating dose regimen and 15 to the other titration regimen. Twenty-seven (84.4%) patients completed the 12 weeks of the study: 14 (82.4%) patients in the rapid and 13 (86.7%) in the slow titration regimen. The ANOVA analysis showed a significant difference between treatment groups at week 4 and 6 in favor of the rapid titration regimen group; this difference faded afterwards. Both titration regimens were effective in reducing OC symptoms and were well tolerated: no differences in drop-out or in adverse event rates emerged between the two groups. Limitations of the present study are the single-blind design and the lack of power to detect differences in tolerability.

Crockett BA, Churchill E, et al. A double-blind combination study of clonazepam with sertraline in obsessive-compulsive disorder. Ann Clin Psychiatry. 2004;16(3):127-32.

This double blind, randomized, parallel, placebo-controlled study investigates whether clonazepam accelerates and/ or increases the overall response in patients with obsessive compulsive disorder (OCD) who are treated with sertraline. Thirty-seven patients were randomized with 20 in the sertraline and clonazepam group and 17 in the sertraline and placebo groups. Male and female outpatients, age 18-65 years, met criteria for a primary diagnosis of obsessive compulsive disorder according to DSM-IV, as determined by the structured clinical MINI interview. Appropriate safety and efficacy parameters were measured throughout the study. The determination of efficacy was based primarily on changes from baseline to the last observation taken through week 12. Analysis revealed no significant difference between groups at endpoint on the main scale.

Pallanti S, Quercioli L, et al. Response acceleration with mirtazapine augmentation of citalopram in obsessive-compulsive disorder patients without comorbid depression: a pilot study. J Clin Psychiatry. 2004;65(10):1394-9.

BACKGROUND: Therapeutic action of selective serotonin reuptake inhibitors (SSRIs) is delayed from 8 to 12 weeks in patients with obsessive-compulsive disorder (OCD). Several different agents have been tested to reduce the SSRI therapeutic latency time. Mirtazapine, an antagonist at alpha2-adrenoceptors, does not enhance serotonin (5-HT) neurotransmission directly but disinhibits the norepinephrine activation of 5-HT neurons and thereby increases 5-HT neurotransmission by a mechanism that may not require a time-dependent desensitization of receptors. The present study was undertaken to determine whether the mirtazapine-citalopram combination could induce an earlier and/or greater effect on the 5-HT system in OCD subjects than citalopram alone. METHOD: Forty-nine patients with OCD (DSM-IV) without comorbid depression were randomly assigned to a 2-tailed, single-blind, 12-week clinical trial with citalopram (20-80 mg/day) plus placebo or citalopram plus mirtazapine (15-30 mg/day). Assessments were performed weekly with the Yale-Brown Obsessive Compulsive Scale (YBOCS), the Hamilton Rating Scale for Depression, and the Clinical Global Impressions scale. Data were collected from November 2001 to July 2003. RESULTS: The citalopram plus mirtazapine group achieved a reduction of at least 35% in YBOCS score and a "much improved" or "very much improved" rating on the Clinical Global Impressions-Improvement scale from the fourth week, while the citalopram plus placebo group obtained these results only from the eighth week. The number of responders was higher in the citalopram plus mirtazapine group at the fourth week of treatment, while no difference between groups in the response rate was noted at the eighth and twelfth weeks of treatment. CONCLUSIONS: We found an earlier onset of response action in OCD symptoms and reduced undesired side effects when mirtazapine was added to citalopram. This augmentation strategy deserves clinical and research consideration through further double-blind, placebo-controlled studies.

Onder E, Tural U, et al. Does gabapentin lead to early symptom improvement in obsessive-compulsive disorder? Eur Arch Psychiatry Clin Neurosci. 2008;258(6):319-23.

OBJECTIVE: The aim of this study was to compare efficacy of fluoxetine alone and co-administration of gabapentin and fluoxetine in patients with obsessive compulsive disorder (OCD). METH-

ODS: Forty outpatients with a DSM-IV diagnosis of OCD were randomized to open label treatment, 20 of whom were treated with fluoxetine alone and the remaining 20 with fluoxetine plus gabapentin during 8 weeks. The severity was assessed by Yale-Brown Obsessive Compulsive Scale (Y-BOCS) and Clinical Global Impression (CGI). RESULTS: Final CGI-I and Y-BOCS scores were not significantly different in both groups. However, in repeated measures ANOVA, compared to fluoxetine group, we found significantly a better improvement in the fluoxetine plus gabapentin group at week 2 by means of YBOCS and CGI-I scores. Comparisons on weeks 4, 6 and 8 revealed no statistical differences between the groups. There was no significant difference of adverse effects between two groups. CONCLUSIONS: Adding gabapentin to fluoxetine in the treatment of OCD seems to shorten the time to onset of fluoxetine's anti-obsessive effect without a significant increase in adverse effects. In order to accelerate the clinical response, co-administration of fluoxetine and gabapentin may be a preferable strategy. On the other hand, further controlled studies are needed to support this finding.

Chasson GS, Buhlmann U, et al. Need for speed: Evaluating slopes of OCD recovery in behavior therapy enhanced with D-cycloserine. Behaviour Research and Therapy. 2010;48(7):675-9.

Evidence suggests that the antibiotic D-cycloserine (DCS) enhances the treatment effects of exposure and response prevention (ERP) for Obsessive–Compulsive Disorder (OCD). Further, evidence suggests that the effects of DCS diminish partway through treatment, but it is unclear to what extent. In an effort to evaluate these issues, the current study re-analyzes data from a 10-session randomized controlled trial of ERP+DCS versus ERP+placebo in a sample of 22 adults with OCD. We analyzed repeated-measures mixed models with random slopes and intercepts across different intervals: sessions 1–10, 1–5, and 6–10. The results indicate that the course of ERP was 2.3 times faster over the full 10 sessions for the DCS compared to the placebo group, and nearly six times quicker in the first half of ERP. Further interpretation of the results suggests that DCS does not amplify the effects of ERP, but instead initiates treatment effects sooner in treatment. In addition, DCS does not necessarily lose its effect over repeated use, but instead may exhaust its maximum utility after effectively jump-starting ERP. Ultimately, DCS may provide a means for curtailing treatment costs, decreasing treatment dropout and refusal rates, and enhancing access to care. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract).

1.6. Otros tratamientos combinados (6 – 1998-2015)

Noorbala AA, Hosseini SH, et al. Combination of clomipramine and nortriptyline in the treatment of obsessive-compulsive disorder: a double-blind, placebo-controlled trial. J Clin Pharm Ther. 1998;23(2):155-9.

OBJECTIVE: There is growing interest in investigating noradrenergic functions in obsessive-compulsive disorder (OCD) because some antidepressants with strong effects on serotonin reuptake blockade fail to relieve obsessive-compulsive symptoms. We undertook a trial to investigate whether the combination of clomipramine with nortriptyline was more effective than clomipramine alone. METHOD: Thirty patients who met the DSM-IV criteria for OCD completed the study. Patients were allocated in a random fashion, 15 each to clomipramine 150 mg/ day plus nortriptyline 50 mg/ day and clomipramine 150 mg/day plus placebo. RESULTS: Although both protocols significantly decreased the scores of the Yale-Brown obsessive-compulsive scale over the trial period, the combination of clomipramine and nortriptyline showed a significant superiority over clomipramine alone in the treatment of OCD. CONCLUSION: As this study indicates, a rapid onset of action is one of the advantages of this combination. This study supports further investigation of the noradrenergic-serotonergic hypothesis in OCD.

Jie S, Jian-Qing T, et al. A Controlled Study of Morita Therapy Combined with Citalopram in the Treatment of Obsessive-Compulsive Disorder. Chinese Mental Health Journal. 2005;19(12):849-50.

Objective: To evaluate the efficacy and safety of Morita therapy combined with citalopram in the treatment of obsessive-compulsive disorder (OCD). Methods: Fifty-six patients with OCD were randomized to two groups. The patients (N=28) in observed group were treated with Morita therapy combined with citalopram. The patients (N=28) in control group were treated with citalopram alone. The efficacy and safety were assessed with Y-BOCS, CGI-SI, HAMD and TESS scales. Results: The scores of Y-BOCS, CGI-SI and HAMD scales in observed group were significantly lower than that in control group at the end of 4 weeks, 8 weeks and 6 month after the treatment ($P<0.05$, respectively). There was no significant difference in side effects between the two groups ($p>0.05$). Conclusion: Morita therapy combined with citalopram was more effective than citalopram mono-

therapy in the treatment of OCD. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract).

Vulink NC, Denys D, et al. Quetiapine augments the effect of citalopram in non-refractory obsessive-compulsive disorder: a randomized, double-blind, placebo-controlled study of 76 patients. J Clin Psychiatry. 2009;70(7):1001-8.

OBJECTIVE: To assess the efficacy of quetiapine addition to citalopram in treatment-naive or medication-free obsessive-compulsive disorder (OCD) patients. METHOD: Seventy-six patients who met DSM-IV criteria for OCD and who were drug-free or drug-naive at entry were randomly assigned in a 10-week, double-blind trial with citalopram (60 mg/day) plus quetiapine (300-450 mg/day) or placebo; treatment-refractory OCD patients were excluded. Of the 76 eligible patients, 66 patients completed the trial-31 in the quetiapine and 35 in the placebo group. The change from baseline to endpoint on the total Yale-Brown Obsessive Compulsive Scale (YBOCS) and the response to treatment in the quetiapine addition compared with the placebo addition group were the primary outcome measures. Response was defined as a 35% or greater reduction on the YBOCS and a Clinical Global Impressions-Improvement (CGI-I) score at endpoint of 1 or 2. The study was conducted from November 2003 to June 2005 at the University Medical Centre Utrecht, The Netherlands. RESULTS: As measured by the mean reduction in YBOCS scores following an intent-to-treat, last-observation-carried-forward analysis, quetiapine addition (11.9) was significantly superior to placebo (7.8; p = .009). Quetiapine addition was also significantly superior to placebo on the CGI-I scale, with a mean +/- SD CGI-I score of 2.1 +/- 1.3 versus 1.4 +/- 1.2, respectively (p = .023). Quetiapine addition (N = 22, 69%) was also associated with a significantly greater number of patients responding to treatment compared with placebo addition (N = 15, 41%; p = .019). More patients receiving quetiapine (N = 8) than placebo (N = 2; NS) discontinued treatment due to adverse events. CONCLUSIONS: The combination of quetiapine and citalopram was more effective than citalopram alone in reducing OCD symptoms in treatment-naive or medication-free OCD patients. TRIAL REGISTRATION: www.trialregister.nl Identifier NTR116.

Soltani F, Sayyah M, et al. A double-blind, placebo-controlled pilot study of ondansetron for patients with obsessive-compulsive disorder. Hum Psychopharmacol. 2010;25(6):509-13.

OBJECTIVE: To assess the efficacy and tolerability of ondansetron in combination with selective serotonin reuptake inhibitors (SSRIs) in patients with obsessive-compulsive disorder (OCD). METHODS: The study was an 8-week pilot double-blind randomized clinical trial. Forty-two adult outpatients who met the Diagnostic and Statistical Manual, Fourth Edition, Text Revision (DSM-IV-TR) criteria for OCD based on the structured clinical interview participated in the trial. In this study, patients were randomly assigned to receive either ondansetron (4 mg) plus fluoxetine or fluoxetine (20 mg/day) plus placebo. RESULTS: The results showed a significant difference between two groups in the treatment of OCD (based on t-test). There was not any significant difference between the two groups in terms of observed side effects. CONCLUSIONS: The results of this study show that ondansetron has positive effects on obsession and compulsion which start two weeks after the beginning of the treatment.

Zhong CL, Cui YH. A randomized controlled trial of sertraline combining with quetiapine in treatment of obsessive-compulsive disorder. Chinese Mental Health Journal. 2010;24(3):198-201.

Objective: To investigate the efficacy and safety of sertraline combining with quetiapine in the treatment of obsessive-compulsive disorder (OCD) . Methods: A total of 86 patients who met the criteria for OCD in International Classification of Diseases (ICD-10) were randomly assigned to two groups. One group was treated with sertraline combining with quetiapine and the other with sertraline only for 8 weeks. The efficacy was measured with the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) and the Hamilton Depression Scale (HAMD). The side effects were/assessed with the Treatment Emergent Symptoms Scale (TESS). Results: One patient in sertraline group fell off and was out of statistical analysis. At endpoint the significant improvement rate in the combining group was higher than that in the sertraline group (72.1% vs. 47.6%, P = 0.021). In combining group, the YBOCS score [(25.00 ± 5.19) vs. (11.74 ± 4.50), P < 0.01] and HAMD score [(14.47 ± 4.05) vs. (6.86 ± 2.61), P < 0.001] were decreased after treatment In sertraline group, the YBOCS score [(24.55 ± 3.60) vs. (14.38 ± 4.18), P < 0.001] and KAMA score [(14.79 ± 3.77) vs. (8.29 ± 3.04), P < 0.001] were also decreased after treatment. There were significant differences between the two groups (Ps < 0.05). There were no significant differences between the two groups in the TESS score at the end of 2, 4, 6 and 8 weeks (Ps > 0.05). The incidence of drowsiness and tachy-heart rate in the combining group was high than that in the control group (37.2% vs. 4. 8% , P < 0.001; 27.9% vs. 4.8% , P = 0.004). But most patients with these two kinds of side effects were disappeared in 2 weeks. There were no significant differences between the two groups in

other side effects such as nausea, anxiety, headache, and constipation (Ps > 0.05). Conclusion: The addition of quetiapine to sertraline therapy has been found to be effective and well-tolerated approach in patients with OCD. (PsycINFO Database Record (c) 2012 APA, all rights reserved)(journal abstract).

Bidabadi SS, Mehryar A. Music therapy as an adjunct to standard treatment for obsessive compulsive disorder and co-morbid anxiety and depression: A randomized clinical trial. Journal of Affective Disorders. 2015;184:13-7.

Background: Previous studies have highlighted the potential therapeutic benefits of music therapy as an adjunct to standard care, in a variety of psychiatric ailments including mood and anxiety disorders. However, the role of music in the treatment of obsessive–compulsive disorder (OCD) have not been investigated to date. Methods: In a single-center, parallel-group, randomized clinical trial (NCT02314195) 30 patients with OCD were randomly assigned to standard treatment (pharmacotherapy and cognitive-behavior therapy) plus 12 sessions of individual music therapy (n = 15) or standard treatment only (n = 15) for one month. Maudsley Obsessive–Compulsive Inventory, Beck Anxiety Inventory, and Beck Depression Inventory-Short Form were administered baseline and after one month. Results: Thirty patients completed the study. Music therapy resulted in a greater decrease in total obsessive score (post-intervention score: music therapy + standard treatment: 12.4 ± 1.9 vs standard treatment only: 15.1 ± 1.7, p < 0.001, effect size = 56.7%). For subtypes, significant between-group differences were identified for checking (p = 0.004), and slowness (p = 0.019), but not for washing or responsibility. Music therapy was significantly more effective in reducing anxiety (post-intervention score: music therapy+standard treatment: 16.9 ± 7.4 vs standard treatment only: 22.9 ± 4.6, p < 0.001, effect size = 47.0%), and depressive symptoms (post-intervention score: music therapy+standard treatment: 10.8 ± 3.8 vs standard treatment: 17.1 ± 3.7, p < 0.001, effect size = 47.0%). Limitations: Inclusion of a small sample size, lack of blinding due to the nature of the intervention, short duration of follow-up. Conclusion: In patients with OCD, music therapy, as an adjunct to standard care, seems to be effective in reducing obsessions, as well as co-morbid anxiety and depressive symptoms. (PsycINFO Database Record (c) 2015 APA, all rights reserved) (journal abstract).

2. INTERRUPCIÓN DEL TRATAMIENTO (DURACIÓN DEL TRATAMIENTO)

2.1. Estudios de interrupción del tratamiento (8 – 1988-2010)

Pato MT, Zohar-Kadouch R, et al. Return of symptoms after discontinuation of clomipramine in patients with obsessive-compulsive disorder. Am J Psychiatry. 1988;145(12):1521-5.

To evaluate the need for maintenance drug therapy in patients with obsessive-compulsive disorder, the authors assessed 21 patients with obsessive-compulsive disorder who manifested sustained improvement during 5 to 27 months of clomipramine treatment and who agreed to participate in a double-blind discontinuation study. Of 18 patients who completed the study, 16 had substantial recurrence of obsessive-compulsive symptoms by the end of the 7-week placebo period. In addition, 11 had a significant increase in depressive symptoms. Treatment duration before discontinuation of clomipramine was not related to the frequency or severity of obsessive-compulsive or depressive symptom appearance. These findings suggest that prolonged drug treatment may be warranted for obsessive-compulsive disorder.

Romano S, Goodman W, et al. Long-term treatment of obsessive-compulsive disorder after an acute response: a comparison of fluoxetine versus placebo. J Clin Psychopharmacol. 2001;21(1):46-52.

Few controlled studies have evaluated the long-term continuation of pharmacotherapy for relapse prevention in patients with obsessive-compulsive disorder (OCD). This study assessed efficacy and safety of fluoxetine versus placebo in preventing relapse of OCD during a 52-week period in responders to short-term administration of fluoxetine. Patients who met DSM-IV criteria for OCD and had a Yale-Brown Obsessive Compulsive Scale score > or = 19 were treated with single-blind fluoxetine 20, 40, or 60 mg/day (based on physician assessment of response and tolerability). After 20 weeks, responders were randomly assigned to receive continued treatment with fluoxetine or placebo and were monitored for relapse for up to 52 weeks. Of 130 patients who entered the study, 71 (55%) were randomly assigned to receive fluoxetine (N = 36) or placebo (N = 35). Patients who received fluoxetine had numerically lower relapse rates compared with those who received placebo, although the difference was not significant (Kaplan-Meier 1-year relapse rates: fluoxetine, 20.6%; placebo, 31.9%; one-tailed p value = 0.137). In additional analyses evaluating patients on the basis of fluoxetine dose at randomization, patients who continued treatment with fluoxetine 60 mg/day

(N = 52) had significantly lower rates of relapse than those who were switched to placebo (Kaplan-Meier 1-year relapse rates: fluoxetine, 17.5%; placebo, 38.0%; one-tailed p value = 0.041). Those who responded to the acute treatment phase with 40 (N = 18) or 20 (N = 1) mg/day had low overall rates of relapse, and the difference between continued fluoxetine and placebo treatment for these patients was not significant. For responders to the 60 mg/day dosage, those patients who continued treatment with fluoxetine were provided greater protection against relapse than those patients switched to placebo.

Koran LM, Hackett E, et al. Efficacy of sertraline in the long-term treatment of obsessive-compulsive disorder. Am J Psychiatry. 2002;159(1):88-95.

OBJECTIVE: Obsessive-compulsive disorder (OCD) typically begins early in life and has a chronic course. Despite the need for long-term treatment, the authors found no placebo-controlled studies that have examined the relapse-prevention efficacy of maintenance therapy. METHOD: Patients who met criteria for response after 16 and 52 weeks of a single-blind trial of sertraline were randomly assigned to a 28-week double-blind trial of 50-200 mg/day of sertraline or placebo. Primary outcomes after the double-blind trial were full relapse, dropout due to relapse or insufficient response, or acute exacerbation of OCD symptoms. RESULTS: Of 649 patients at baseline, 232 completed 52 weeks of the single-blind trial and met response criteria. Among the 223 patients in the double-blind phase of the study, sertraline had significantly greater efficacy than placebo on two of three primary outcomes: dropout due to relapse or insufficient clinical response (9% versus 24%, respectively) and acute exacerbation of symptoms (12% versus 35%). Sertraline resulted in improvement in quality of life during the initial 52-week trial and continued improvement, significantly superior to placebo, during the subsequent 28-week double-blind trial. Long-term treatment with sertraline was well tolerated. Over the entire study period, less than 20% of the patients stopped treatment because of adverse events. CONCLUSIONS: Sertraline demonstrated sustained efficacy among patients responding to treatment and was generally well tolerated during the 80-week study. During the study's last 28 weeks, sertraline demonstrated greater efficacy than placebo in preventing dropout due to relapse or insufficient clinical response and acute exacerbation of OCD symptoms.

Hollander E, Allen A, et al. Acute and long-term treatment and prevention of relapse of obsessive-compulsive disorder with paroxetine. J Clin Psychiatry. 2003;64(9):1113-21.

BACKGROUND: Limited information is available regarding optimal dosing or long-term pharmacotherapy with serotonin reuptake inhibitors in obsessive-compulsive disorder. This study evaluated the acute safety and efficacy and long-term efficacy, safety, and impact on relapse prevention of paroxetine in obsessive-compulsive disorder. METHOD: We enrolled 348 outpatients with DSM-III-R obsessive-compulsive disorder in phase 1, a 12-week randomized, double-blind, parallel study of fixed doses of paroxetine (20 mg/day, 40 mg/day, or 60 mg/day) and placebo. In phase 2, 263 phase 1 completers were enrolled in 6 months of flexibly dosed open-label paroxetine treatment. In phase 3, 105 responders to open-label paroxetine were randomized to 6-month double-blind, fixed-dose, parallel paroxetine/placebo treatment to evaluate long-term efficacy, safety, and impact on relapse prevention. The study was conducted from July 1991 to February 1994. RESULTS: Patients in phase 1 acute treatment receiving 40 mg/day or 60 mg/day of paroxetine improved significantly ($p < .05$) more than those receiving placebo; the mean reduction in Yale-Brown Obsessive-Compulsive Scale score was 25% on 40 mg/day of paroxetine and 29% on 60 mg/day compared with 13% on placebo. During phase 3, long-term treatment, a greater proportion of placebo- (59%) than paroxetine-treated (38%) patients relapsed. Paroxetine was well tolerated at all doses, with no significant increase in frequency of adverse events during long-term compared with short-term therapy. Greater adverse events in the placebo than in the paroxetine group in phase 3 probably represent a discontinuation effect. CONCLUSION: Paroxetine doses of 40 mg/day and 60 mg/day (but not 20 mg/day) are effective in treating acute obsessive-compulsive disorder. Long-term treatment with paroxetine is effective and safe, decreases the rate of relapse, and lengthens the time to relapse.

Koran LM, Gamel NN, et al. Mirtazapine for obsessive-compulsive disorder: an open trial followed by double-blind discontinuation. J Clin Psychiatry. 2005;66(4):515-20.

BACKGROUND: Many patients with obsessive-compulsive disorder (OCD) experience little response to standard treatment with serotonin reuptake inhibitors. Mirtazapine enhances serotonergic function by a mechanism distinct from reuptake inhibition. Because a pilot study suggested effectiveness of mirtazapine in OCD, we conducted a controlled trial. METHOD: We recruited 30 subjects, 15 treatmentnaive and 15 treatment-experienced, with DSM-IV OCD of > or =1 year's duration and a Yale-Brown Obsessive Compulsive Scale (YBOCS) score of > or =20. In the 12-week, open-label phase, subjects received mirtazapine starting at 30 mg/day and titrated over 2 weeks as toler-

ated to 60 mg/day. At week 12, responders (YBOCS score decrease > 25%) were randomly assigned, double-blind, to continue mirtazapine or switch to placebo for 8 weeks, including a 1-week, double-blind taper week for placebo subjects. RESULTS: In the open-label phase, the mean +/-SD YBOCS score fell from 28.3 +/-3.7 to 20.3 +/-8.5 (paired samples t = 4.81, p < .0001). Four subjects (13.3%) discontinued for side effects. Sixteen subjects (53.3%) (8 treatmentnaive, 8 treatment-experienced) were responders and 15 agreed to randomization. Response was independent of comorbid mood disorders. In the 8-week, double-blind, placebo-controlled discontinuation phase, the mirtazapine group's mean YBOCS score fell a mean +/-SD of 2.6 +/-8.7 points while the placebo group's mean score rose a mean +/-SD of 9.1 +/-7.5 points (Mann Whitney U = 6.5, p = .005, 1-tailed). All other outcome measures were consistent with mirtazapine's superiority versus placebo. CONCLUSION: Mirtazapine may be an effective pharmacotherapy for OCD. If our results are replicated, larger double-blind studies would be indicated.

Fineberg NA, Tonnoir B, et al. Escitalopram prevents relapse of obsessive-compulsive disorder. Eur Neuropsychopharmacol. 2007;17(6-7):430-9.

To examine the efficacy and tolerability of escitalopram in the prevention of relapse in patients with OCD, 468 patients with OCD were treated with open label escitalopram (10 mg or 20 mg) for 16 weeks, after which the 320 responders (Y-BOCS total score decrease > or =25%) were randomised to placebo or escitalopram (at the assigned dose) for 24 weeks double-blind treatment. The primary analysis (time to relapse) showed a significant advantage for escitalopram (p<0.001, log-rank test). The proportion of patients who relapsed was statistically significantly higher in the placebo group (52%) than in the escitalopram group (23%) (p<0.001, chi(2)-test). The risk of relapse was 2.74 times higher for placebo compared to escitalopram. Escitalopram was well tolerated and improvements in obsessive-compulsive symptoms reported during the open label period were sustained during the double-blind extension of treatment with active drug. These results demonstrate that escitalopram is effective for long-term treatment and relapse prevention in OCD.

Hatim A, Gill JS, et al. Escitalopram in the treatment of Malaysian patients with obsessive-compulsive disorder. Hong Kong Journal of Psychiatry. 2008;18(4):152-7.

Objective: This post-hoc analysis examined the efficacy and tolerability of escitalopram in the prevention of relapse in Malaysian patients with obsessive-compulsive disorder. Participants and Methods: In Malaysia, 47 patients with obsessive-compulsive disorder were treated with open-label escitalopram (10 mg or 20 mg/day) for 16 weeks, after which the 34 responders (Yale-Brown Obsessive Compulsive Scale total decrease score, ≥25%) were randomised to placebo or escitalopram for 24 weeks, using a double-blind protocol. Results: The primary efficacy analysis suggested a trend in favour of escitalopram treatment with respect to time to relapse (log-rank test, p = 0.07). A higher proportion of patients relapsed after placebo treatment (5 of 14, 36%) than with escitalopram treatment (2 of 20, 10%) [Fisher's exact test, 2-sided; p = 0.10]. The risk of relapse was 4-fold higher for placebo than escitalopram treatment (p = 0.09). During the double-blind period, the proportion of patients reporting treatment-emergent adverse events was comparable in the 2 groups (10% in the escitalopram group vs. 14% in the placebo group); no serious events being reported. Conclusions: This post-hoc subgroup analysis suggests that escitalopram is well tolerated in Malaysian patients with obsessive-compulsive disorder and appears to confer an advantage over placebo, in terms of time to relapse and other efficacy variables. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract).

Yang H, Chuzi S, et al. (2010) Type of residual symptom and risk of relapse during the continuation/maintenance phase treatment of major depressive disorder with the selective serotonin reuptake inhibitor fluoxetine. European archives of psychiatry and clinical neuroscience. 2010;260:145-50. DOI: 10.1007/s00406-009-0031-3.

UNLABELLED: Relapse of major depressive disorder (MDD) is a common clinical problem. Identifying relapse predictors could lead to strategies that reduce relapse risk. This study is designed to determine whether residual symptoms predict relapse risk during the continuation/maintenance treatment of MDD. 570 MDD patients received open-label fluoxetine for 12 weeks. Under double blind conditions, 262 patients who responded by week 12 were randomly assigned to continue fluoxetine or switch to placebo for 52 weeks or until relapse. Residual symptoms were measured using the Symptom Checklist-90 and the Symptom Questionnaire. The relationship between residual symptom severity and relapse risk was assessed. Without adjusting for overall residual symptom severity, a greater severity of residual obsessive-compulsive and phobic anxiety symptoms predicted greater relapse risk. After adjusting for overall residual symptom severity, only severity of phobic anxiety symptoms predicted relapse risk. The predictive value of phobic anxiety symptoms with re-

spect to relapse risk was independent of treatment assignment. The results indicated that there may be a specific pattern of residual symptoms associated with depressive relapse during antidepressant continuation/maintenance, which is unrelated to treatment assignment. Future studies are needed to further explore the relationship between residual symptoms and relapse risk in MDD. CLINICAL IMPLICATIONS: (1) It is important to treat residual symptoms among antidepressant responders/remitters in order to decrease relapse risk. (2) Clinicians should target residual phobic anxiety symptoms in order to decrease relapse risk. (3) Clinicians should target residual obsessive-compulsive symptoms in order to decrease relapse risk. LIMITATIONS: (1) limited generalizability due to inclusion/exclusion criteria; (2) lack of active comparator treatment group; (3) post hoc analysis.

2.2. Otros estudios de eficacia a largo plazo (13 – 1982-2011)

Mawson D, Marks IM, et al. Clomipramine and exposure for chronic obsessive-compulsive rituals: III. Two year follow-up and further findings. Br J Psychiatry. 1982;140:11-8.

Forty chronic ritualizers were given clomipramine or placebo from weeks 0 to 36; also all had exposure in vivo, half from weeks 4 to 10 (30 hours) and half from weeks 7 to 10 (15 hours). In the 37 patients available at week 114 there were substantial and maintained improvements in rituals, mood and social adjustment compared to week 0. Reduction of rituals was even greater in those who had 30 hours of exposure. There was no drug effect on rituals at two year follow-up. Greater initial anxiety or depression predicted the superiority of clomipramine over placebo from weeks 10 to 36 and more prescription of tricyclics in follow-up. However, two years outcome was not predicted by initial anxiety or depression, nor by sex, age, age of onset nor duration of rituals.

Mallya GK, White K, et al. Short- and long-term treatment of obsessive-compulsive disorder with fluvoxamine. Annals of Clinical Psychiatry. 1992;4(2):77-80.

28 patients with Diagnostic and Statistical Manual of Mental Disorders-III-Revised (DSM-III-R) diagnosis of obsessive-compulsive disorders (OCDs) completed a 10-wk double-blind placebo controlled trial of a serotonergic uptake blocker, fluvoxamine (FVX). Six Ss (43%) improved more than 35% in the FVX group, whereas only 1 S (7%) improved in the placebo group. Analysis of the change scores on the Yale-Brown Scale for OCD showed significantly greater improvement with FVX than with placebo. 21 of the Ss then participated in an open trial with FVX for a period of 2–22 mo. 12 Ss (57%) showed improvement. Seven of 9 relapsed within a few days to weeks of discontinuation of FVX. (PsycINFO Database Record (c) 2012 APA, all rights reserved)

Cottraux J, Mollard E, et al. Exposure therapy, fluvoxamine, or combination treatment in obsessive-compulsive disorder: one-year followup. Psychiatry Res. 1993;49(1):63-75.

Sixty outpatients with obsessive-compulsive disorder (OCD, 22 men, 38 women) were randomized to receive 6 months of antiexposure therapy with fluvoxamine (group F), exposure therapy with fluvoxamine (group Fe), or exposure therapy with placebo (group Pe). Patients in group F did not comply with antiexposure therapy, so it was in fact a neutral condition. Patients began with depressed mood (mean Hamilton depression score = 19). Fifty patients were reevaluated at week 8, 44 at week 24 (posttest), 37 at week 48, and 33 at 18 months, 1 year posttreatment (group F, n = 10; group Fe, n = 12; group Pe, n = 11). The three groups improved on rituals and depression. There was a drug effect on rituals at week 8 and on depression at week 24; both these effects disappeared at week 48. The 33 18-month completers had been comparable at baseline to those not followed up, apart from having more severe behavioral avoidance. At 18-month followup, patients as a whole remained improved with no between-group differences; over 80% of the Fe and Pe patients versus 40% of the F patients were not receiving antidepressant treatment (Fe vs. F: $p < 0.04$; Pe vs. F: $p = 0.053$; Fe vs. Pe: NS). In OCD fluvoxamine and exposure therapy were synergistic in the short term, and exposure reduced subsequent need for antidepressants in the followup year after they had been stopped.

Tollefson GD, Birkett M, et al. Continuation treatment of OCD: double-blind and open-label experience with fluoxetine. J Clin Psychiatry. 1994;55 Suppl: 69-76; discussion 77-68.

Recent advances in the pharmacotherapy of obsessive compulsive disorder (OCD) have led to a significant reduction in suffering and a return to productive living for many patients previously considered refractory to treatment. However, OCD can be a chronic disorder that significantly detracts from an individual's well-being. Potent inhibitors of 5-hydroxytryptamine (5-HT) reuptake have emerged as the first-line choice in the pharmacotherapy of OCD. These members of the therapeutic armamentarium for OCD, while associated with acute symptomatic improvement, have not been extensively studied during continuation therapy. In this study, 274 primary OCD subjects completed

a 13-week, double-blind, placebo-controlled trial of three fixed doses of fluoxetine. Treatment responders (n = 76) continued their blinded treatment, whereas acute fixed-dose nonresponders began an open-label trial on their maximally tolerated dose (up to 80 mg daily) for 24 weeks. Responders maintained their acute treatment gains; in addition, all three doses of fluoxetine (20, 40, and 60 mg) were associated with further Y-BOCS improvement over the 24-week extension. Fluoxetine 60 mg achieved a statistically significantly greater reduction in Y-BOCS than placebo during the continuation. Open-label study subjects (n = 198) benefited from dose titration, with two thirds achieving a clinical response during the subsequent 24 weeks. Fluoxetine was well tolerated during both 24-week continuation periods. Only 4 (5.7%) of 70 subjects treated with fluoxetine in the responder extension terminated early due to an adverse event. The open-label extension, fluoxetine (to 80 mg), also demonstrated a low rate of adverse events; the profile of events was consistent with the extensive fluoxetine experience in other clinical populations. In conclusion, fluoxetine continuation treatment in OCD was associated with a maintained/improved symptomatic profile in most cases. Further dose titration improved the outcome of many acute, fixed-dose nonresponders. Continuation treatment with fluoxetine appeared to be well tolerated with few late-emergent adverse events.

Greist JH, Jefferson JW, et al. (1995) A 1 year double-blind placebo-controlled fixed dose study of sertraline in the treatment of obsessive-compulsive disorder. International clinical psychopharmacology. 1995;10:57-65.

The objective of this study was to evaluate the safety and efficacy, over a 1 year treatment period, of three dose levels of sertraline and placebo in the treatment of non-depressed adult out-patients with obsessive-compulsive disorder (OCD). Following 1 week of single-blind placebo washout, patients (n = 325) from 11 sites following identical protocols were randomly assigned to 12 weeks of double-blind treatment with one of three fixed doses of sertraline (50, 100 or 200 mg) or placebo. At the end of 12 weeks, treatment responders (including placebo patients) were offered an additional 40 weeks of double-blind treatment at their assigned doses. Efficacy measures were the Yale-Brown Obsessive Compulsive Scale, the NIMH Global Obsessive Compulsive Scale, Clinical Global Impressions of Severity of Illness and Global Improvement and the Maudsley Obsessive Compulsive Inventory. Patients in the pooled sertraline group showed greater improvement than placebo-treated patients on all efficacy measures, based on the endpoint analyses. Moreover, pairwise comparisons at endpoint revealed a significant effect on all three investigator-rated scales in patients receiving 50 or 200 mg of sertraline; in the 100 mg group, there was a significant effect on the NIMH Global Obsessive Compulsive Scale only. Patients completing 3 months of sertraline treatment exhibited excellent toleration and sustained improvement during an additional 40 weeks of therapy. Results support the safety, efficacy and tolerability of daily doses of 50-200 mg of sertraline in the long-term treatment of patients with OCD.

Ravizza L, Barzega G, et al. Drug treatment of obsessive-compulsive disorder (OCD): long-term trial with clomipramine and selective serotonin reuptake inhibitors (SSRIs). Psychopharmacol Bull. 1996;32(1):167-73.

A 2-year, open-label followup was performed on 130 obsessive-compulsive patients who were responders to a previous 6-month treatment with clomipramine (150 mg/day), fluoxetine (40 mg/day), or fluvoxamine (300 mg/day). Continuation treatment with the same daily dose was compared to continuation with half doses or to discontinuation of pharmacotherapy. The Yale-Brown Obsessive Compulsive Scale (Y-BOCS) and the Clinical Global Impressions (CGI) scale were used every 3 months, or whenever a worsening of symptoms was experienced. Maintenance treatments were found significantly superior to discontinuation in preventing relapses, and no differences in efficacy were found between full and half doses. A comparison of the three subgroups of patients who were withdrawn from drug therapy failed to demonstrate any statistical difference.

Mundo E, Bareggi SR, et al. Long-term pharmacotherapy of obsessive-compulsive disorder: a double-blind controlled study. J Clin Psychopharmacol. 1997;17(1):4-10.

The aim of this study was to investigate whether obsessive-compulsive patients previously treated successfully with clomipramine or fluvoxamine could tolerate reduction of the daily dosage without worsening of the clinical condition. Thirty informed obsessive-compulsive patients, given a diagnosis according to DSM-III-R criteria, were recruited consecutively into the study. Patients were blindly assigned to one of the groups of treatment with different rates of reduction of the previously effective daily drug dosage: group 1 (control group, no reduction), group 2 (reduction of 33-40%), and group 3 (reduction of 60-66%). The entire study lasted 102 days. From baseline to the end of the study, the clinical condition was evaluated by the administration of standardized tests (Yale-Brown Obsessive-Compulsive Scale, Hamilton Rating Scale for Depression, Clinical Global Impression

[CGI] scale), and blood samples were collected for plasma drug level determinations. The criterion for discontinuation of the study was the worsening of obsessive-compulsive symptoms, arbitrarily defined by an increase of > 5% from the baseline total Yale-Brown Obsessive-Compulsive Scale score, as measured in two successive assessments, and a worsening of global clinical condition as measured by the CGI scale. The main result of the study was borne out from the survival analysis. There were no significant differences in the cumulative proportion of patients from each group of treatment who did not worsen during the 102 days of observation. This preliminary result, which needs to be confirmed in larger samples, suggests that long-term maintenance therapy for obsessive-compulsive disorder might be provided with lower dosages of the antiobsessional drug, with clear advantages for tolerability and compliance.

Rasmussen S, Hackett E, et al. A 2-year study of sertraline in the treatment of obsessive-compulsive disorder. Int Clin Psychopharmacol. 1997;12(6):309-16.

The present study investigated the tolerability, safety profile, and anti-obsessional efficacy of sertraline, a selective serotonin reuptake inhibitor, during long-term treatment of patients with obsessive-compulsive disorder (OCD). Fifty-nine OCD patients who had completed a 1 year double-blind, fixed dose study comparing sertraline and placebo subsequently entered a 1-year open extension. Among the 51 patients who had been treated with sertraline during the double-blind phase, the mean total duration of sertraline treatment was 690 days. Only treatment responders who completed the 52-week double-blind treatment phase were permitted to enter the open extension. The higher rate ($p < 0.02$) of sertraline patients (51 out of 241) than of placebo patients (eight out of 84), who responded to treatment and entered the open-label phase is therefore consistent with the greater mean improvement observed in the sertraline group during double-blind treatment. Placebo responders differed from sertraline responders in that they were less impaired at baseline of the double-blind study [Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) of 18.5 versus 23.4] and they exhibited less improvement during double-blind treatment (-6.1 versus -11.4). In the open-label phase all patients received sertraline at a starting dose of 50 mg once a day, titrated in 50 mg increments to a maximum dose of 200 mg according to clinical response. At end-point the mean Y-BOCS score for all patients decreased by a further 3.6 points. Patients previously treated with placebo showed greater improvement after being switched to sertraline than those who received continued sertraline treatment. Patients who completed the study and received 2 full years of sertraline treatment ($n = 38$) exhibited a mean improvement of 15.6 points using the Y-BOCS. Sertraline was well tolerated during both the double-blind phase and the open extension, and the incidence of adverse experiences was generally reduced during the second year of treatment. Three patients discontinued open treatment because of adverse experiences. Long-term sertraline treatment did not appear to be associated with the emergence, increased incidence, or increased severity of adverse experiences or clinically significant abnormalities in laboratory tests, vital signs, or the electrocardiogram. The study supports the long-term safety and tolerability of sertraline over a 2-year treatment course and the sustained efficacy of sertraline in patients with OCD.

Oppen P, Balkom AJ, et al. (2005) Cognitive therapy and exposure in vivo alone and in combination with fluvoxamine in obsessive-compulsive disorder: a 5-year follow-up. The Journal of clinical psychiatry. 2005;66:1415-22.

BACKGROUND: Information regarding the long-term effectiveness of the combination of pharmacotherapy and cognitive-behavioral therapy (CBT) in the treatment of obsessive-compulsive disorder (OCD) is limited. Our study is the first to examine the long-term effectiveness of cognitive therapy (CT) and to compare long-term effectiveness of CT alone, exposure in vivo with response prevention (ERP) alone, and CBT (either CT or ERP) in combination with fluvoxamine in the treatment of OCD. METHOD: Of 122 outpatients with primary DSM-III-R-defined OCD originally enrolled in 2 randomized controlled trials, 102 patients (45 male/57 female; mean +/- SD age = 36.2 +/- 10.7 years; range, 19-64 years) were available to be assessed for the presence and severity of OCD and comorbid psychopathology at follow-up. Follow-up data were collected from November 1996 to June 1999. RESULTS: After 5 years, 54% of the participants no longer met the DSM-III-R criteria for OCD. Long-term outcome did not differ between the 3 treatment groups. At follow-up, treatment dropouts appeared to have more severe OCD complaints compared with treatment completers. Compared with patients receiving CT alone, significantly ($p < .005$) more patients receiving CBT with fluvoxamine used antidepressants 5 years later. CONCLUSIONS: This study demonstrates that at 5-year follow-up (1) prevalence of OCD had declined in all 3 treatment conditions, (2) the clinical benefits of all 3 treatment conditions were maintained, (3) OCD complaints were more severe for treatment dropouts than for treatment completers, and (4) about half of the patients initially treated with fluvoxamine continued antidepressant use.

Rufer M, Hand I, et al. Long-term course and outcome of obsessive-compulsive patients after cognitive-behavioral therapy in combination with either fluvoxamine or placebo: a 7-year follow-up of a randomized double-blind trial. Eur Arch Psychiatry Clin Neurosci. 2005;255(2):121-8.

Longitudinal studies with very long follow-up periods of patients with obsessive-compulsive disorder (OCD) who have received adequate treatment are rare. In the current study, 30 of 37 inpatients (81%) with severe OCD were followed up 6-8 years after treatment with cognitive-behavioral therapy (CBT) in combination with either fluvoxamine or placebo in a randomized design. The significant improvements (with large effectsizes) in obsessive-compulsive symptoms from pre- to post-treatment (41% reduction on the Y-BOCS) remained stable at follow-up (45 %). Responder rates, defined as > or = 35% reduction on the Y-BOCS, were 67% and 60%, respectively. Depressive symptoms decreased significantly not only from pre- to post-treatment but also during follow-up. Re-hospitalization, which occurred in 11 patients (37 %), was associated with more severe depressive symptoms at pre-treatment and living without a partner. Full symptom remission at follow-up, defined as both Y-BOCS total score < or = 7 and no longer meeting diagnostic criteria for OCD, was achieved by 8 patients (27 %). Patients without full remission at follow-up had a significantly longer history of OCD, assessed at pretreatment, compared to remitted patients. The shortterm treatment outcome had no predictive value for the long-term course. Throughout the naturalistic follow-up, nearly all patients (29 patients) received additional psychotherapy and/or medication. This might indicate that such chronic OCD patients usually need additional therapeutic support after effective inpatient treatment to maintain their improvements over long periods.

Van Oppen P, van Balkom AJ, et al. Cognitive therapy and exposure in vivo alone and in combination with fluvoxamine in obsessive-compulsive disorder: a 5-year follow-up. J Clin Psychiatry. 2005;66(11):1415-22.

BACKGROUND: Information regarding the long-term effectiveness of the combination of pharmacotherapy and cognitive-behavioral therapy (CBT) in the treatment of obsessive-compulsive disorder (OCD) is limited. Our study is the first to examine the long-term effectiveness of cognitive therapy (CT) and to compare long-term effectiveness of CT alone, exposure in vivo with response prevention (ERP) alone, and CBT (either CT or ERP) in combination with fluvoxamine in the treatment of OCD. METHOD: Of 122 outpatients with primary DSM-III-R-defined OCD originally enrolled in 2 randomized controlled trials, 102 patients (45 male/57 female; mean +/- SD age = 36.2 +/- 10.7 years; range, 19-64 years) were available to be assessed for the presence and severity of OCD and comorbid psychopathology at follow-up. Follow-up data were collected from November 1996 to June 1999. RESULTS: After 5 years, 54% of the participants no longer met the DSM-III-R criteria for OCD. Long-term outcome did not differ between the 3 treatment groups. At follow-up, treatment dropouts appeared to have more severe OCD complaints compared with treatment completers. Compared with patients receiving CT alone, significantly ($p < .005$) more patients receiving CBT with fluvoxamine used antidepressants 5 years later. CONCLUSIONS: This study demonstrates that at 5-year follow-up (1) prevalence of OCD had declined in all 3 treatment conditions, (2) the clinical benefits of all 3 treatment conditions were maintained, (3) OCD complaints were more severe for treatment dropouts than for treatment completers, and (4) about half of the patients initially treated with fluvoxamine continued antidepressant use.

Koran LM, Bromberg D, et al. Extended-release fluvoxamine and improvements in quality of life in patients with obsessive-compulsive disorder. Compr Psychiatry. 2010;51(4):373-9.

OBJECTIVE: We hypothesized that subjects with obsessive-compulsive disorder (OCD) who received extended-release fluvoxamine (fluvoxamine ER) in a 12-week placebo-controlled trial would exhibit improvements in psychosocial domains of health-related quality of life (HRQOL) and that additional improvements would occur after a 40-week open-label extension trial. We also hypothesized that greater OCD symptom improvement in the first 12 weeks of treatment would be associated with greater HRQOL improvement after 52 weeks of treatment. METHODS: In the 12-week placebo-controlled trial, subjects were randomized to receive placebo or 100 mg/d of fluvoxamine ER and then titrated in weekly 50 mg increments to a final dose of 100 to 300 mg/d. All subjects enrolled in the 40-week extension trial followed a similar titration, during which they were maintained on their highest well-tolerated dose. RESULTS: After 12 weeks of treatment, fluvoxamine ER subjects experienced significantly greater decreases than placebo subjects in Yale-Brown Obsessive-Compulsive Scale scores ($P = .001$). Both the active drug and placebo groups exhibited significant improvements in psychosocial domains of HRQOL; further improvement occurred after 40 weeks of open-label treatment with active drug. The greater the improvement in OCD severity at 12 weeks, the greater the improvement at 52 weeks in the psychosocial domains (Social Functioning $r = -0.39$, $P = .027$; Emotional Problems $r = -0.37$, $P = .037$; Mental Health $r = -0.49$, $P = .004$). CONCLUSION:

Improvement in Yale-Brown Obsessive-Compulsive Scale severity scores during treatment with fluvoxamine ER was associated with improvements in psychosocial aspects of HRQOL that increased over an extended period of treatment.

Borges CP, Meyer E, et al. Cognitive-behavioral group therapy versus sertraline for obsessive-compulsive disorder: Five-year follow-up. Psychotherapy and Psychosomatics. 2011;80(4):249-50.

The present article reports a study that aimed to investigate whether the reduction in severity of obsessive-compulsive disorder (OCD) symptoms obtained with 12-weekly sessions of cognitive-behavioral therapy (CBGT) or with sertraline (100 mg/day) during the same period, in a randomized clinical trial, would be sustained over a 5-year period, as well as to compare the differences between the 2 treatments in the long term. Forty-six patients who were treated with CBGT or sertraline were evaluated 5 years after the end of the initial randomized clinical trial. In conclusion, this study has demonstrated the maintenance of efficacy of CBGT and sertraline for OCD after 5 years of followup. This was due to the fact that a portion of the patients from both initial groups sought continuation of the original treatment or made a natural 'crossover', as it was observed. As OCD is a chronic disorder, probably the continuation of any one of the treatment strategies is mainly responsible for the maintenance of outcomes in the long run. (PsycINFO Database Record (c) 2012 APA, all rights reserved)

3. PREDICTORES DE RESPUESTA AL TRATAMIENTO FARMACOLÓGICO (síntomas especiales) (38 – 1980–2015)

- Conductas de acumulación.
- Tics.
- Depresión.
- Bajo *insight*.
- Según subtipos.

NOTA: es posible que haya algún ensayo clínico específico, pero lo que habrá que buscar es información en los ensayos y revisiones sistemáticas sobre análisis de estos subgrupos.

Thoren P, Asberg M, et al. Clomipramine treatment of obsessive-compulsive disorder. I. A controlled clinical trial. Arch Gen Psychiatry. 1980;37(11):1281-5.

The effect of clomipramine hydrochloride in severe obsessive-compulsive disorder (OCD) was compared with that of nortriptyline hydrochloride and placebo in a five-week randomized, double-blind trial. Clomipramine, but not nortriptyline, was superior to placebo in interview-based ratings of severity of OCD. The effect was not clear-cut until after five weeks of treatment. When clomipramine was given openly to 22 patients after the end of the controlled trial, half of the patients responded to the drug. The response could not be predicted from severity or duration of illness, sex or age of the patient, or presence or absence of secondary depressive symptoms. The amelioration with clomipramine was not sustained if the drug was withdrawn.

Zahn TP, Insel TR, et al. Psychophysiological changes during pharmacological treatment of patients with obsessive compulsive disorder. Br J Psychiatry. 1984;145:39-44.

Twelve patients with obsessive compulsive disorder were studied with psychophysiological measures during a randomised, double-blind placebo-controlled drug trial. Significant clinical improvement followed six weeks of treatment with the tricyclic antidepressant clomipramine, but was not evident after an equal period of treatment with the monoamine oxidase inhibitor (MAOI) clorgyline. Compared to placebo, both drugs reduced skin conductance indices of baseline arousal, but only clomipramine reduced skin conductance and heart rate responses to loud tones and tonic and phasic skin conductance responses in a two-flash discrimination task. This suggests that reductions in autonomic responses to important and/or aversive stimuli may be critical to clinical improvement in obsessive compulsive disorder.

DeVeaugh-Geiss J, Katz R, et al. Clinical predictors of treatment response in obsessive compulsive disorder: exploratory analyses from multicenter trials of clomipramine. Psychopharmacol Bull. 1990;26(1):54-9.

Two multicenter, double-blind trials were conducted in adults with DSM-III (American Psychiatric Association 1980) defined Obsessive Compulsive Disorder (OCD), comparing clomipramine (Anafranil, CMI) up to 300 mg daily with placebo. Of 519 patients evaluated, 260 received CMI for up to

10 weeks. More than half of the CMI treated patients were significantly improved, approximately 30 percent were minimally improved, and 15 percent showed no improvement after CMI treatment. The Yale-Brown Obsessive Compulsive Scale (Y-BOCS) was used to assess treatment effects and attempts were made to correlate change in Y-BOCS score from baseline with a number of baseline characteristics, including age, sex, duration of OCD, baseline Y-BOCS score, baseline Hamilton Rating Scale for Depression (HAM-D) score, presence or absence of secondary depression, and predominance of obsessions or compulsions. Pearson and/or Spearman correlations failed to reveal any statistically significant correlations between outcome and any of the baseline characteristics studied. While the differences were not statistically significant, it did appear that male patients and patients with a longer duration of illness may be less likely to respond to CMI treatment; however, the overall conclusion from this analysis is that none of the variables studied is a reliable predictor of responses to treatment with CMI.

Baer L, Jenike MA, et al. (1992) Effect of axis II diagnoses on treatment outcome with clomipramine in 55 patients with obsessive-compulsive disorder. Archives of general psychiatry. 1992;49:862-6.

We used the Structured Interview for DSM-III Personality Disorders to diagnose DSM-III personality disorders systematically in 55 patients with obsessive-compulsive disorder in the active-treatment cell of a controlled trial of clomipramine hydrochloride. Patients with a cluster A personality disorder had significantly higher obsessive-compulsive disorder severity scores at baseline, and the number of personality disorders was strongly related to baseline severity of obsessive-compulsive disorder symptoms. At the conclusion of the 12-week study, we found no significant difference in treatment outcome with clomipramine between those patients with at least one personality disorder and those with no personality disorders. However, the presence of schizotypal, borderline, and avoidant personality disorders, along with total number of personality disorders, did predict poorer treatment outcome. These variables were strongly related to having at least one cluster A personality disorder diagnosis, which was also a strong predictor of poorer outcome. Implications of these findings are discussed.

Lax T, Başoğlu M, et al. Expectancy and compliance as predictors of outcome in obsessive-compulsive disorder. Behavioural Psychotherapy. 1992;20(3):257-66.

49 obsessive-compulsive ritualizers (aged 18–60 yrs) had clomipramine and live exposure in a randomized controlled design. The effect on outcome of pretreatment expectations from psychological and from drug treatment and of subsequent compliance with exposure instructions was studied. Exposure instructions led to greater pretreatment expectations than did anti-exposure instructions, but this did not affect outcome, suggesting that the effect of exposure was not due to expectation. Initially, more-ill patients expected more from the drug but improved less. Compliance with psychological treatment did not predict better improvement. (PsycINFO Database Record (c) 2012 APA, all rights reserved).

Cottraux J, Messy P, et al. Predictive factors in the treatment of obsessive-compulsive disorders with fluvoxamine and/or behaviour therapy. Behavioural Psychotherapy. 1993;21(1):45-50.

Conducted a stepwise discriminant analysis on 10 baseline variables searching for posterior prediction of success in 60 obsessive-compulsive outpatients. Ss' median score on the Hamilton Rating Scale for Depression was 19. Ss received either fluvoxamine with antiexposure (FAE), fluvoxamine with exposure (FLE), or placebo with exposure (PLE). In the whole sample, 5 variables accounted for 76% of Ss correctly classified: Avoidance score of the behavioral avoidance test, behavior therapy expectations, fluvoxamine expectations, Beck Depression Inventory score, and rituals repetition. High avoidance score predicted 68% of the correctly classified Ss, and was the best single predictor of failure. The discriminant function correctly classified 70% of FAE Ss, 75% of FLE Ss, and 85% of PLE Ss. (PsycINFO Database Record (c) 2013 APA, all rights reserved).

Hollander E, Stein DJ, et al. A pilot study of biological predictors of treatment outcome in obsessive-compulsive disorder. Biol Psychiatry. 1993;33(10):747-9.

Ackerman DL, Greenland S, et al. Predictors of treatment response in obsessive-compulsive disorder: multivariate analyses from a multicenter trial of clomipramine. J Clin Psychopharmacol. 1994;14(4):247-54.

There have been many attempts to find predictors of the therapeutic response to the clomipramine treatment of obsessive-compulsive disorder. The majority of studies have failed to identify such predictors. Possible reasons for this failure include the small sample size of most studies, samples homogeneous with respect to the study factors of interest, and the use of statistical procedures that

are insensitive to individual differences or that inadequately control for confounding. We have reanalyzed data from Ciba-Geigy's large, multicenter clinical trial of clomipramine for obsessive-compulsive disorder, using stratification and regression techniques to identify multiple prognostic factors and control for confounders. We assessed the relationship between therapeutic response and baseline measures such as severity of symptoms, type of symptoms (obsessions, compulsions, depression), length of illness, age of onset, and other demographic factors (age, race, and sex). We found age of onset to be a strong predictor of response to clomipramine: people who develop obsessive-compulsive disorder later in life have a better chance of responding than do those who become ill earlier, independent of length of illness. We also found that baseline depression is associated with response, but the association appears to be nonlinear.

Ravizza L, Barzega G, et al. Predictors of drug treatment response in obsessive-compulsive disorder. J Clin Psychiatry. 1995;56(8):368-73.

BACKGROUND: Although a large body of evidence indicates the efficacy of pharmacotherapy in the treatment of obsessive-compulsive disorder (OCD), a considerable percentage of these patients do not respond. Very few studies focus on factors related to treatment response of OCD. The purpose of this study was to investigate which clinical factors are related to drug treatment response in OCD. METHOD: We examined 53 OCD patients treated with either clomipramine or fluoxetine for a period of 6 months, dividing the sample into "responders" and "nonresponders" to treatment. At admission, patients were evaluated using a semistructured clinical interview, the Yale-Brown Obsessive Compulsive Scale (Y-BOCS), the Hamilton Rating Scale for Depression, and the Hamilton Rating Scale for Anxiety. We then compared acute-phase patient characteristics and response to drug treatment. Response was defined as a decrease of at least 40% in the Y-BOCS total score and a rating of "improved" or "very improved" on the Clinical Global Impressions scale within 16 weeks of treatment and maintained over three consecutive evaluations. RESULTS: By the sixth month of treatment, 31 patients (58.5%) responded to either clomipramine or fluoxetine. Nonresponders had lower age at onset and longer duration of the disorder; in addition, they showed higher frequency of compulsions, washing rituals, chronic course, concomitant schizotypal personality disorder, and previous hospitalizations. A worse response to drug treatment was predicted in a stepwise multiple regression by (1) concomitant schizotypal personality disorder, (2) presence of compulsions, and (3) longer illness length. CONCLUSION: Our findings suggest that there are distinct types of OCD with respect to drug treatment response. They provide indirect evidence of treatment specificity by identifying characteristics responsive to different modalities, which may be of value in the selection of patients for alternative treatments.

Ackerman DL, Greenland S, et al. Relationship between early side effects and therapeutic effects of clomipramine therapy in obsessive-compulsive disorder. J Clin Psychopharmacol. 1996;16(4):324-8.

Early adverse effects of a drug may be a manifestation of individual differences in drug metabolism or of different pathologic processes. These differences may influence therapeutic responsiveness. Using data from Ciba-Geigy's multicenter 10-week clinical trial, we studied the relationship between early side effects and subsequent therapeutic response to clomipramine (CMI) in obsessive-compulsive disorder. We used tabular analyses and multiple regression to evaluate associations between early complaints and change in score on the Yale-Brown Obsessive-Compulsive Scale. We also evaluated whether early complaints were drug related (i.e., true side effects). It appeared that dry mouth, constipation, dizziness, insomnia, male impotence, nervousness, palpitation, and tremor reported during the first 4 weeks were predictive of good response to CMI. Myoclonus and tinnitus appeared weakly associated with treatment success. Most of these complaints were reported more by the CMI group than the placebo group, and more during CMI treatment than before. The more common complaints may reflect an individual's ability to metabolize CMI appropriately so that adequate therapeutic blood levels are attained. The less common complaints may reflect a sensitivity to CMI's serotonergic actions.

Koran LM, Cain JW, et al. Are fluoxetine plasma levels related to outcome in obsessive-compulsive disorder? Am J Psychiatry. 1996;153(11):1450-4.

OBJECTIVE: In obsessive-compulsive disorder, the relationship between blood levels of serotonin reuptake inhibitors and clinical outcome is unclear. In a multicenter trial, the authors examined the relationship between steady state plasma levels of fluoxetine and norfluoxetine (determined after 7 weeks of treatment), and their sum, and clinical outcome. METHOD: Ratings of symptom severity of obsessive-compulsive disorder (Yale-Brown Obsessive Compulsive Scale scores) were obtained at baseline and after 13 weeks for 200 adult outpatients with moderately severe obsessive-compulsive disorder treated with fluoxetine doses of 20 mg/day (N = 68), 40 mg/day (N = 64), and 60 mg/day

(N = 68). RESULTS: Mean plasma levels of fluoxetine and norfluoxetine were statistically significantly higher with higher dose. Statistical analyses revealed no significant relationship for plasma level of either molecule or their sum in predicting endpoint percent change in obsessive-compulsive scores. Plasma levels of patients with a marked response (decrease of 50% or more in obsessive-compulsive score) did not differ significantly from those of nonresponders (less than a 25% decrease in obsessive-compulsive score). No hint was seen of a therapeutic window or of a relationship limited to one gender or within the lowest dose group (20 mg/day). However, since S-norfluoxetine is a much more potent serotonin reuptake inhibitor than R-norfluoxetine, the absence of chiral (stereospecific) assays in this study limits the results. CONCLUSIONS: Steady state plasma levels of fluoxetine and norfluoxetine are not related to clinical outcome in patients with obsessive-compulsive disorder. Individual patients can be told only that the optimum dose of fluoxetine for them will be the dose that produces the largest therapeutic effect with the smallest side effect burden. Future studies should examine the predictive utility of measures of serotonergic neuronal function and, if plasma levels of norfluoxetine are examined, the use of chiral assays.

Marazziti D, Pfanner C, et al. Changes in platelet markers of obsessive-compulsive patients during a double-blind trial of fluvoxamine versus clomipramine. Pharmacopsychiatry. 1997;30(6):245-9.

Abnormalities of platelet serotonin (5-HT) transporter, which are supposed to reflect similar dysfunctions in the central nervous system (CNS), have been reported in obsessive-compulsive disorder (OCD). Other platelet parameters altered in OCD are represented by phenolsulfotransferase (PST) activity, an enzyme involved in the catabolism of catecholic neuro-transmitters, and peripheral benzodiazepine receptors. Since no information is available on the behavior of these putative markers during antiobsessive treatments, the aim of the present study was to measure and compare 3H-imipramine (3H-IMI) binding, which labels the 5-HT transporter, PST activity, and 3H-PK 11,195 binding, which labels peripheral benzodiazepine receptors, in a group of 18 patients with obsessive-compulsive disorder (OCD) before and after a treatment with fluvoxamine versus clomipramine. The results showed that at baseline the patients had a decreased number of 3H-IMI binding sites, which correlated negatively with the Y-BOCS total score, an increased PST activity and no difference in 3H-PK 11,195 binding, as compared with healthy volunteers. After eight weeks of treatment with either clomipramine or fluvoxamine, which was effective in all patients, the number of 3H-IMI binding sites increased significantly toward normal values, while the PST showed no change. These findings suggest that the reduction in 3H-IMI binding sites in OCD may be related to the severity of the illness and possibly to a positive response to serotonin re-uptake inhibitors, and might be considered as a state-dependent marker, whereas the PST activity would seem to be a trait of the illness.

Ackerman DL, Greenland S, et al. Clinical characteristics of response to fluoxetine treatment of obsessive-compulsive disorder. J Clin Psychopharmacol. 1998;18(3):185-92.

Fluoxetine is effective in treating obsessive-compulsive disorder (OCD). Nonetheless, a substantial number of patients do not respond or have only partial improvement. Data generated by a multicenter, placebo-controlled, fixed-dose trial of fluoxetine were reanalyzed to identify characteristics of responders. Multiple regression methods were used to evaluate the relationship between therapeutic response and baseline measures such as severity of symptoms, type of symptoms (obsessions, compulsions, depression), course of illness, previous treatment, age of onset, and other demographic factors (age, race, and sex). Fluoxetine was more effective than placebo on all outcome measures. A 60-mg dosage was associated with a greater drop in Yale-Brown Obsessive-Compulsive Scale total score and a greater drop in Compulsion items than a 20-mg dosage. Response rates and overall improvement were greatest for patients with a history of remissions, with no previous drug treatment or with only prior behavior therapy, with more severe OCD (especially with greater interference and distress from obsessions), or with either low or high Hamilton Rating Scale for Depression scores. This study did not detect any associations between response and current age, age of OCD onset, gender, and race. None of the demographic or clinical factors evaluated was found to be related to improvement in the placebo group.

Black DW, Monahan P, et al. Hoarding and treatment response in 38 nondepressed subjects with obsessive-compulsive disorder. J Clin Psychiatry. 1998;59(8):420-5.

OBJECTIVE: The authors studied factors associated with short-term treatment response in 38 nondepressed subjects with DSM-III-R obsessive-compulsive disorder (OCD). METHOD: The subjects completed 12 weeks of treatment with paroxetine (N = 20), placebo (N = 8), or cognitive-behavioral therapy (N = 10). Clinician and self-rated measures were gathered at baseline, during treatment, and after treatment. RESULTS: Seventeen (45%) subjects had "much" or "very much" improvement and achieved at least a 40% decrease in their total Yale-Brown Obsessive Compulsive Scale (Y-BOCS)

score. Responders had lower obsessive-compulsive scores on the Symptom Checklist 90-Revised, had a lower checking score on the Maudsley Obsessive-Compulsive Inventory, were less likely to have had prior drug therapy, and in general suffered more obsessive-compulsive symptoms. They were significantly less likely to have hoarding obsessions and corresponding compulsions. The latter finding was confirmed using multiple regression analysis. CONCLUSION: Hoarding is an important symptom that predicts poor treatment response in patients with OCD.

Ackerman DL, Greenland S, et al. Side effects as predictors of drug response in obsessive-compulsive disorder. J Clin Psychopharmacol. 1999;19(5):459-65.

Differences between the side effect profiles of clomipramine (CMI) and the selective serotonin reuptake inhibitors may be important factors in both treatment outcome and patient selection in obsessive-compulsive disorder (OCD). Safety and efficacy data from an industry-sponsored, multicenter clinical trial of CMI were analyzed previously using tabular and multiple regression methods. Good response, defined as at least a 35% drop in final scores on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS), was associated with a later age of OCD onset and certain early side effects that may reflect a sensitivity of responders to CMI's serotonergic actions. The authors conducted a similar analysis of data from an industry-sponsored clinical trial of fluoxetine in OCD. Fluoxetine response did not seem to be associated with age of OCD onset. Good response to both drugs was associated with initial nervousness and sexual complaints. The common side effects of fluoxetine (headache, nausea, and gastrointestinal complaints) did not seem to be associated with treatment response. Slight differences in the protocols of the two clinical trials yielded patient populations that were different in factors found to be associated with treatment outcome: subjects in the fluoxetine study had lower scores on the Y-BOCS, higher scores on the Hamilton Rating Scale for Depression, and an earlier age of OCD onset.

Mataix-Cols D, Rauch SL, et al. Use of factor-analyzed symptom dimensions to predict outcome with serotonin reuptake inhibitors and placebo in the treatment of obsessive-compulsive disorder. Am J Psychiatry. 1999;156(9):1409-16.

OBJECTIVE: No consistent predictors of outcome have been identified for the pharmaco-therapy of obsessive-compulsive disorder (OCD). Recent factor analytic studies have identified meaningful symptom dimensions that may be related to response to serotonin reuptake inhibitors and other treatments. METHOD: A total of 354 outpatients with primary OCD were administered the Yale-Brown Obsessive Compulsive Scale Symptom Checklist, and its 13 main symptom categories were factor analyzed by using principal components analysis. The identified symptom dimensions were then entered into multiple regression models as outcome predictors of response to serotonin reuptake inhibitors and placebo response in a group of 150 nondepressed subjects who completed six double-blind, placebo-controlled trials with a serotonin reuptake inhibitor (clomipramine, fluvoxamine, fluoxetine, sertraline, and paroxetine). Eighty-four patients received a serotonin reuptake inhibitor and 66, placebo. RESULTS: The principal components analysis identified five factors that explained 65.5% of variance in outcome: symmetry/ordering, hoarding, contamination/cleaning, aggressive/checking, and sexual/religious obsessions. Serotonin reuptake inhibitors were significantly superior to placebo on all outcome measures. Initial severity of OCD was related to greater posttreatment severity of OCD. Higher scores on the hoarding dimension predicted poorer outcome following treatment with serotonin reuptake inhibitors, after control for baseline severity. No predictors of placebo response were identified. Exclusion of clomipramine did not modify the overall results, suggesting a cross-serotonin reuptake inhibitor effect. CONCLUSIONS: The identified symptom dimensions are largely congruent with those identified in earlier reports. Patients with OCD vary in their response to treatment with serotonin reuptake inhibitors. The presence of hoarding obsessions and compulsions is associated with poorer response to serotonin reuptake inhibitors.

Mundo E, Bareggi SR, et al. Effect of acute intravenous clomipramine and antiobsessional response to proserotonergic drugs: is gender a predictive variable? Biol Psychiatry. 1999;45(3):290-4.

BACKGROUND: Previous studies on serotonergic responsivity in obsessive-compulsive disorder (OCD) showed about 50% of patients experiencing an acute worsening of OC symptoms when administered meta-chlorophenylpiperazine or i.v. clomipramine. The aim of this study was to determine what variables influence the response to acute i.v. clomipramine. Could this response be predictive of the response to chronic treatment with two serotonergic drugs with differing selectivity profiles: clomipramine and fluvoxamine? METHODS: Fifty OC patients were consecutively recruited. All underwent a challenge with 25 mg i.v. clomipramine and placebo and were administered 10-week oral clomipramine or fluvoxamine according to a double-blind design. The efficacy of the antiobsessional treatment was evaluated by Yale-Brown Obsessive-Compulsive Scale and Clinical

Global Impression scale scores. RESULTS: Obsessions worsened in 42% patients as rated by change values in 100-mm visual analogue scale scores for the clomipramine vs. placebo infusion. There was a significant difference in gender distribution between "worsened" and "unchanged" patients, since female subjects were more frequently "unchanged." Thirty-one patients completed the 10-week treatment. According to both qualitative and quantitative evaluations, female subjects showed a better antiobsessional response, and this difference was enhanced in the clomipramine-treated group. CONCLUSIONS: Results suggest a role for reproductive hormones in the pathophysiology or treatment of OC patients.

Hoehn-Saric R, Schlaepfer TE, et al. Cerebral blood flow in obsessive-compulsive patients with major depression: effect of treatment with sertraline or desipramine on treatment responders and non-responders. Psychiatry Res. 2001;108(2):89-100.

We examined the effects of sertraline and of desipramine on patients with OCD and comorbid major depressive episodes at study entry. Sixteen patients, 9 receiving sertraline and 7 desipramine, received HMPAO SPECT scans while free of medication and after 12 weeks of treatment. Patients on sertraline showed significantly reduced regional cerebral blood flow (rCBF) in the right prefrontal and temporal regions. Patients on desipramine showed more diffuse rCBF reductions in frontal and temporal regions, more so in the left side. In a second analysis, patients who had a symptom reduction on the Yale-Brown Obsessive Compulsive Scale (YBOCS), irrespective of the type of medication, were retrospectively classified as 'responders' to treatment. Eleven patients were 'responders' and 5 'non-responders'. Before being medicated, responders differed from non-responders through higher rCBF in prefrontal regions, mostly on the left, and higher rCBF in the cingulate and basal ganglia bilaterally. After 12 weeks of treatment, responders showed a diffuse reduction of rCBF in prefrontal regions while non-responders showed only a few scattered low-frequency responses. Thus, higher prefrontal and subcortical activity was associated with better response to drug treatment. In addition, clinical change, but not the administration of medication as such, was associated with a decrease of prefrontal rCBF.

Humble M, Bejerot S, et al. Reactivity of serotonin in whole blood: relationship with drug response in obsessive-compulsive disorder. Biol Psychiatry. 2991;49(4):360-8.

BACKGROUND: Obsessive-compulsive disorder responds almost only to potent serotonin reuptake inhibitors. Previous studies have suggested a relation between serotonergic function and clinical outcome in serotonin reuptake inhibitor treatment of obsessive-compulsive disorder. METHODS: In a randomized, double-blind trial, comparing clomipramine, paroxetine, and a placebo in obsessive-compulsive disorder, serotonin levels in whole blood (WB-5-HT) were measured at baseline, after 1 week, and after 4 weeks of treatment and related to clinical outcome in 36 patients. RESULTS: In patients treated with serotonin reuptake inhibitors there was a pronounced decrease of WB-5-HT, variable after 1 week and uniformly maximal after 4 weeks. The decrease of WB-5-HT after 1 week of serotonin reuptake inhibitor treatment correlated negatively with clinical outcome after 12 weeks ($r = -.61$, $p = .0006$); hence, patients with slower WB-5-HT reactivity eventually responded better to treatment. Baseline WB-5-HT, but not WB-5-HT reactivity, was related to season. Depression, autistic traits, and previous serotonin reuptake inhibitor treatment predicted nonresponse. CONCLUSIONS: A fast decrease of WB-5-HT was associated with poor clinical outcome. This may be related to faster serotonin efflux from platelets, which has previously been linked to autism. Further studies are necessary to identify the underlying mechanism and discern whether serotonin reuptake inhibitor-induced WB-5-HT decrease is clinically useful.

Stein DJ, Montgomery SA, et al. Predictors of response to pharmacotherapy with citalopram in obsessive-compulsive disorder. Int Clin Psychopharmacol. 2001;16(6):357-61.

Although serotonin reuptake inhibitors (SRIs) are the medications of choice in the treatment of obsessive-compulsive disorder (OCD), only 50-60% of patients respond to a single trial of any of these agents. Improved knowledge of the predictors of response to treatment may have important clinical implications. Data from a large randomized placebo-controlled trial of citalopram in OCD was analysed using logistic regression to determine predictors of response. Demographic (age, sex), clinical (OCD severity and duration, depression severity, prior treatment) and trial variables (citalopram dose, treatment duration) were included. Subjects with longer duration of OCD, more severe OCD symptoms or previous selective SRI use were less likely to be responders in the citalopram trial. In contrast, subjects who received adequate medication doses for sufficient periods of time in the citalopram trial were more likely to be responders. Despite greater awareness of OCD in recent years, there is evidence that the disorder continues to be underdiagnosed and undertreated. The data here emphasize the crucial importance of early diagnosis and treatment of OCD, and of pharmacotherapy with appropriate dose and duration.

Denys D, Burger H, et al. (2003) A score for predicting response to pharmacotherapy in obsessive-compulsive disorder. International clinical psychopharmacology. 2003;18:315-22. DOI: 10.1097/01.yic.0000097036.25861.96.

Although there have been many attempts to find predictors of therapeutic response to antidepressant treatment of obsessive-compulsive disorder (OCD), few reports have evaluated the joint predictive value of a number of clinical characteristics. This study aimed to identify clinical predictors of outcome in OCD, and to develop an easily applicable method to predict response to drug treatment. One hundred and fifty patients with primary OCD according to DSM-IV criteria were randomly assigned in a 12-week, double-blind, comparison trial with a selective serotonin reuptake inhibitor (paroxetine), and a serotonin-noradrenaline reuptake inhibitor (venlafaxine). The primary efficacy parameter was the Yale-Brown obsessive-compulsive scale (Y-BOCS) score, and response to treatment was prospectively defined as a >/= 35% decrease from the beginning. A stepwise multivariate analysis was used to identify predictors. The absence of previous therapies, moderate baseline severity of obsessive-compulsive symptoms (Y-BOCS score < 23), and low Hamilton Depressive Rating Scale scores (6-15) were found to be prognostic determinants of good response to pharmacotherapy. The prognostic ability of the prediction model to discriminate between responders and non-responders was quantified as the area under the receiver operating/operator characteristic curve (ROC area), which was 0.71 (95% confidence interval 0.63-0.8), demonstrating a reasonable discriminatory power. This study is the first to present a model that can estimate by the use of prediction rules the probability of treatment response to antidepressants in patients with OCD.

Fontenelle LF, do Rosario-Campos MC, et al. Treatment-response by age at onset in obsessive-compulsive disorder. J Affect Disord. 2004;83(2-3):283-4.

Hollander E, Kaplan A, et al. Neurological soft signs as predictors of treatment response to selective serotonin reuptake inhibitors in obsessive-compulsive disorder. J Neuropsychiatry Clin Neurosci. 2005;17(4):472-7.

Neurological soft-sign abnormalities have been implicated in obsessive-compulsive disorder (OCD). This first comprehensive data analysis evaluated the association between baseline neurological soft signs and treatment response in 117 OCD patients treated with controlled-release fluvoxamine in a double-blind placebo-controlled trial. Total and right-sided soft signs for the responders and the nonresponders did not differ significantly. Left-sided visuospatial soft signs were significantly increased in treatment nonresponders compared to responders. These subtle neurological abnormalities may implicate a potential subgroup of OCD patients with poorer treatment response. This may have treatment implications and therefore serve as a screening tool in OCD.

Hollander E, Kaplan A, et al. Neurological soft signs as predictors of treatment response to selective serotonin reuptake inhibitors in obsessive-compulsive disorder. J Neuropsychiatry Clin Neurosci. 2005;17(4):472-7.

Neurological soft-sign abnormalities have been implicated in obsessive-compulsive disorder (OCD). This first comprehensive data analysis evaluated the association between baseline neurological soft signs and treatment response in 117 OCD patients treated with controlled-release fluvoxamine in a double-blind placebo-controlled trial. Total and right-sided soft signs for the responders and the nonresponders did not differ significantly. Left-sided visuospatial soft signs were significantly increased in treatment nonresponders compared to responders. These subtle neurological abnormalities may implicate a potential subgroup of OCD patients with poorer treatment response. This may have treatment implications and therefore serve as a screening tool in OCD.

Storch EA, Larson MJ, et al. Clinical predictors of early fluoxetine treatment response in obsessive-compulsive disorder. Depress Anxiety. 2006;23(7):429-33.

Despite wide use, relatively little is known about sociodemographic and clinical characteristics that predict early fluoxetine response. What research has been conducted has produced inconsistent findings, which may be due to the statistical procedures used, and no studies to date have examined predictors of early fluoxetine treatment response. Sixty adults with obsessive-compulsive disorder (OCD) completed an open-label fluoxetine trial for 8 weeks (up to 40 mg) after a 1-week, single-blind, placebo run-in before baseline assessment. The baseline and posttreatment assessment battery included the Yale-Brown Obsessive Compulsive Scale, the Hamilton Rating Scale for Depression, and the Yale Global Tic Severity Scale. Patient characteristics included illness duration, age, age of onset, gender, and pharmacological treatment history. Independent t-tests and multiple logistic regression analysis showed that longer illness duration, older age, and greater symptom severity were associated with nonresponse. Our findings highlight the impact of functional psychiatric impairment on

determining those who may respond to treatment. Furthermore, findings suggest early predictors of patients with certain characteristics who may ultimately need adjunctive care to facilitate response.

Denys D, Fineberg N, et al. Quetiapine addition in obsessive-compulsive disorder: is treatment outcome affected by type and dose of serotonin reuptake inhibitors? Biol Psychiatry. 2007;61(3):412-4.

BACKGROUND: The purpose of this study was to assess the effect of type and dose of serotonin reuptake inhibitors (SRIs) on treatment outcome in quetiapine addition trials for obsessive-compulsive disorder. METHODS: Results from all available, double blind, placebo-controlled quetiapine addition trials were pooled. Treatment outcome was assessed in a sample of 102 patients by change from baseline to end point on the Yale-Brown obsessive-compulsive scale (Y-BOCS). RESULTS: Quetiapine addition was superior with a mean Y-BOCS decrease of 6.8 +/- 6.7 compared with placebo with a decrease of 3.9 +/- 6.5 points. Patients with the lowest SRI dose showed the largest decrease on the Y-BOCS (11.6 +/- 7.7) compared with patients with the median dose (6.1 +/- 6.1) and highest dose (5.9 +/- 6.4). CONCLUSIONS: We found a superior response in the quetiapine addition group compared with the placebo group. The best response was achieved with the combination of clomipramine, fluoxetine, and fluvoxamine and with the lowest SRI doses.

Denys D, Nieuwerburgh F, et al. (2007) Prediction of response to paroxetine and venlafaxine by serotonin-related genes in obsessive-compulsive disorder in a randomized, double-blind trial. The Journal of clinical psychiatry. 2007;68:747-53.

OBJECTIVE: Serotonin reuptake inhibitors (SRIs) are the most effective pharmacologic treatment currently available for patients with obsessive-compulsive disorder (OCD). Still, up to 40% to 60% of OCD patients do not respond to SRI treatment. The purpose of the present study was to determine whether polymorphisms of the serotonin transporter (5-HTT), 5-HT1B, and 5-HT2A receptor genes affect the efficacy of SRI treatment in OCD. METHOD: 91 outpatients with OCD according to DSM-IV criteria consented to the study and were randomly assigned in a 12-week, double-blind trial to receive dosages titrated upward to 300 mg/day of venlafaxine or 60 mg/day of paroxetine. Primary efficacy was assessed by the change from baseline on the Yale-Brown Obsessive Compulsive Scale (YBOCS), and response was defined as a > or = 25% reduction on the YBOCS. Responders and nonresponders were stratified according to 5-HTT, 5-HT1B, and 5-HT2A genotypes and differentiated in paroxetine-or venlafaxine-treated groups. The study was conducted from August 1998 to July 2002. RESULTS: In the whole group, 64% of responders carried the S/L genotype of the 5-HTTLPR polymorphism (chi2 = 7.17, df = 2, p = .028). In the paroxetine-treated patients, the majority of responders carried the G/G genotype of the 5-HT2A polymorphism (chi2 = 8.66, df = 2, p = .013), whereas in the venlafaxine-treated patients, the majority of responders carried the S/L genotype of the 5-HTTLPR polymorphism (chi2 = 9.72, df = 2, p = .008). CONCLUSIONS: The results of this study suggest that response in venlafaxine-treated OCD patients is associated with the S/L genotype of the 5-HTTLPR polymorphism and in paroxetine-treated OCD patients with the G/G genotype of the 5-HT2A polymorphism.

Stein DJ, Andersen EW, et al. Response of symptom dimensions in obsessive-compulsive disorder to treatment with citalopram or placebo. Rev Bras Psiquiatr. 2007;29(4):303-7.

OBJECTIVE: There is increasing evidence that the symptoms of obsessive-compulsive disorder lie on discrete dimensions. Relatively little work has, however, explored the relationship between such factors and response to pharmacotherapy. METHOD: Data from a multi-site randomized placebo-controlled study of citalopram in obsessive-compulsive disorder were analyzed. Factor analysis of individual items and symptom categories of the Yale-Brown Obsessive-Compulsive Scale Checklist were undertaken, and the impact of symptom dimensions on treatment outcomes was analysed. RESULTS: Factor analysis of Yale-Brown Obsessive-Compulsive Scale Checklist individual items yielded 5 factors (contamination/cleaning, harm/checking, aggressive/sexual/religious, hoarding/symmetry, and somatic/hypochondriacal). Hoarding/symmetry was associated with male gender, longer duration of obsessive-compulsive disorder and early onset, whereas contamination/cleaning was associated with female gender. Citalopram was more effective than placebo, but high scores on the symmetry/hoarding and contamination/cleaning subscales predicted worse outcome at the end of study while high scores on the aggressive/religious/sexual subscale predicted better outcome. Factor analysis of Yale-Brown Obsessive-Compulsive Scale Checklist symptom clusters yielded a 4 factor solution, but confirmed that symmetry/ordering was associated with male gender, early onset, and long duration of obsessive-compulsive disorder while high scores on the hoarding subscale predicted worse response to pharmacotherapy. CONCLUSION: Citalopram shows good efficacy across the range of obsessive-compulsive disorder symptom dimensions. The relatively worse re-

sponse of symmetry/hoarding to a selective serotonin reuptake inhibitor is consistent with other evidence that this symptom dimension is mediated by the dopamine system. There may be associations between symmetry/hoarding, male gender, early onset, tics, and particular genetic variants; further work is, however, needed to delineate fully obsessive-compulsive disorder subtypes and their underlying neurobiology.

Stein DJ, Carey PD, et al. Escitalopram in obsessive-compulsive disorder: response of symptom dimensions to pharmacotherapy. CNS Spectr. 2008;13(6):492-8.

INTRODUCTION: There is a substantial body of evidence that obsessive-compulsive disorder (OCD) symptoms can be grouped into a series of discrete dimensions, and some evidence that not all OCD symptom dimensions respond equally well to pharmacologic or psychotherapeutic intervention. The response of OCD symptom dimensions to 12 weeks of treatment with escitalopram or placebo was investigated. METHODS: Data from a randomized, double-blind, placebo-controlled study of escitalopram in 466 adults with OCD were analyzed. Exploratory factor analysis of individual items of the Yale-Brown Obsessive-Compulsive Scale checklist was performed and subscale scores based on the extracted factors were determined. Analyses of covariance were undertaken to determine whether inclusion of each subscale score in these models impacted on the efficacy of escitalopram versus placebo. RESULTS: Exploratory factor analysis of individual Yale-Brown Obsessive-Compulsive Scale items yielded 5 factors (contamination/cleaning, harm/checking, hoarding/symmetry, religious/sexual, and somatic/hypochondriacal). Analyses of covariance including all the subscales demonstrated that escitalopram was more effective than placebo. There was a significant interaction for the hoarding/symmetry factor, which was associated with a poor treatment response. CONCLUSION: Escitalopram shows good efficacy across the range of OCD symptom dimensions. Nevertheless, hoarding/symmetry was associated with a poorer treatment response. Hoarding/symmetry may be particularly characteristic of an early-onset group of OCD patients, with the involvement of neurotransmitters other than serotonin. Further work is needed to delineate fully the subtypes of OCD, and their correlates with underlying psychobiology and treatment responsivity.

Landeros-Weisenberger A, Bloch MH, et al. Dimensional predictors of response to SRI pharmacotherapy in obsessive-compulsive disorder. J Affect Disord. 2010;121(1-2):175-9.

BACKGROUND: Obsessive-compulsive disorder (OCD) is clinically heterogeneous. Previous studies have reported different patterns of treatment response to serotonin reuptake inhibitors (SRI) based on symptom dimension. Our objective was to replicate these results in OCD patients who participated in one of four randomized, placebo-controlled, clinical trials (RCT). METHODS: A total of 165 adult OCD subjects participated in one or more eight-week RCT with clomipramine, fluvoxamine, or fluoxetine. All subjects were classified as having major or minor symptoms in four specific OC symptom dimensions that were derived in a previous factor analytic study involving many of these same patients. Ordinal logistic regression was used to test the association between OC symptom dimensions and SRI response. RESULTS: We found a significant association between the symptom dimension involving sexual, religious and harm-related obsessions as well as checking compulsions (AGG/SR) and improved SRI response. This increased rate of SRI response was experienced primarily by individuals with harm-related obsessions. Over 60% of patients with AGG/SR OCD symptoms were rated as very much improved after SRI treatment. LIMITATIONS: As some of the RCTs included were conducted prior to the development of the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), improvement in OCD severity was assessed using the Clinical Global Improvement (CGI) Scale. Data from the double-blind and open-label continuation phases of these trials was collapsed together to increase statistical power. CONCLUSIONS: Patients with OCD vary in their response to SRIs. The presence of AGG/SR symptoms is associated with an initial positive response to SRIs. These data add to the growing body of work linking central serotonin systems with aggressive behavior.

Maher MJ, Huppert JD, et al. Moderators and predictors of response to cognitive-behavioral therapy augmentation of pharmacotherapy in obsessive-compulsive disorder. Psychol Med. 2010;40(12): 2013-23.

BACKGROUND: Cognitive-behavioral therapy (CBT) consisting of exposure and response prevention (EX/RP) is efficacious as a treatment for obsessive-compulsive disorder (OCD). However, about half of patients have a partial or poor response to EX/RP treatment. This study examined potential predictors and moderators of CBT augmentation of pharmacotherapy, to identify variables associated with a poorer response to OCD treatment. METHOD: Data were drawn from a large randomized controlled trial that compared the augmenting effects of EX/RP to stress management training (SMT; an active CBT control) among 108 participants receiving a therapeutic dose of a serotonin reuptake inhibitor (SRI). Stepwise regression was used to determine the model specification.

RESULTS: Pretreatment OCD severity and gender were significant moderators of outcome: severity affected SMT (but not EX/RP) outcome; and gender affected EX/RP (but not SMT) outcome. Adjusting for treatment type and pretreatment severity, significant predictors included greater co-morbidity, number of past SRI trials, and lower quality of life (QoL). Significant moderators, including their main-effects, and predictors accounted for 37.2% of the total variance in outcome, comparable to the impact of treatment type alone (R2=30.5%). These findings were replicated in the subgroup analysis of EX/RP alone (R2=55.2%). CONCLUSIONS: This is the first randomized controlled study to examine moderators and predictors of CBT augmentation of SRI pharmacotherapy. Although effect sizes for individual predictors tended to be small, their combined effect was comparable to that of treatment. Thus, future research should examine whether monitoring for a combination of these risk factors and targeting them with multi-modular strategies can improve EX/RP outcome.

Carey PD, Lochner C, et al. Quetiapine augmentation of serotonin reuptake inhibitors in treatment-refractory obsessive-compulsive disorder: is response to treatment predictable? Int Clin Psychopharmacol. 2012;27(6):321-5.

Several studies have examined the predictors of treatment response in obsessive-compulsive disorder (OCD). Only limited information is available on the predictors of response to antipsychotic augmentation of serotonin reuptake inhibitors (SRIs). Data from placebo-controlled studies of augmentation with quetiapine were combined in a best subsets logistic regression to derive a predictive model for Yale-Brown obsessive-compulsive scale (YBOCS) change and the YBOCS endpoint. Data from the YBOCS checklist and a variety of clinical and demographic variables previously shown to predict treatment outcome in OCD were analysed. In univariate analyses, the failure of fewer previous SRI trials was associated with the YBOCS response. In the multivariate model, for YBOCS change, 45% of the variance was attributed to the fact that patients had failed fewer previous SRI treatments, had higher baseline obsession scores, and ordering and arranging compulsions. For the YBOCS endpoint scores, 50% of the variance was attributed to the fact that patients had fewer failed SRI trials, higher baseline compulsion scores, and counting/ordering and arranging compulsions. These data indicate a number of predictors of response to augmentation of SRIs in treatment-refractory OCD. These include fewer previously failed SRI trials and generally higher overall baseline scores for obsessions and compulsions as well as counting/ordering and arranging compulsions. Other factors are, however, also likely to play an important role in predicting outcome.

D'Alcante CC, Diniz JB, et al. Neuropsychological predictors of response to randomized treatment in obsessive-compulsive disorder. Prog Neuropsychopharmacol Biol Psychiatry. 2012;39(2):310-7.

OBJECTIVE: To identify neuropsychological predictors of treatment response to cognitive-behavioral therapy (CBT) and fluoxetine in treatment-naive adults with obsessive-compulsive disorder (OCD). METHOD: Thirty-eight adult outpatients with OCD underwent neuropsychological assessment, including tasks of intellectual function, executive functioning and visual and verbal memory, before randomization to a 12-week clinical trial of either CBT or fluoxetine. Neuropsychological measures were used to identify predictors of treatment response in OCD. RESULTS: Neuropsychological measures that predicted a better treatment response to either CBT or fluoxetine were higher verbal IQ (Wechsler Abbreviated Scale of Intelligence) ($p=0.008$); higher verbal memory on the California Verbal Learning Test ($p=0.710$); shorter time to complete part D (Dots) ($p<0.001$), longer time to complete part W (Words) ($p=0.025$) and less errors on part C (Colors) ($p<0.001$) in the Victoria Stroop Test (VST). Fewer perseverations on the California Verbal Learning Test, a measure of mental flexibility, predicted better response to CBT, but worse response to fluoxetine ($p=0.002$). CONCLUSION: In general, OCD patients with better cognitive and executive abilities at baseline were more prone to respond to either CBT or fluoxetine. Our finding that neuropsychological measures of mental flexibility predicted response to treatment in opposite directions for CBT and fluoxetine suggests that OCD patients with different neuropsychological profiles may respond preferentially to one type of treatment versus the other. Further studies with larger samples of OCD patients are necessary to investigate the heuristic value of such findings in a clinical context.

Vulink NC, Westenberg HG, et al. (2012) Catechol-O-methyltranferase gene expression is associated with response to citalopram in obsessive-compulsive disorder. International journal of psychiatry in clinical practice. 2012;16:277-83. DOI: 10.3109/13651501.2011.653375.

OBJECTIVE: To determine whether polymorphisms of the dopamine D(2) receptor (DRD2) and catechol-O-methyl-transferase (COMT) receptor genes affect the efficacy of quetiapine addition to citalopram in patients with OCD. METHODS: Sixty-four drug-free or drug-naïve patients meeting DSM-IV criteria for OCD were randomized to 10 weeks double-blind treatment with citalopram (60 mg/day) with quetiapine (300 -450 mg/day) or with placebo. The change from baseline to endpoint

on the total Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) and the response to treatment were the primary outcome measures. Response was defined as a 25% decrease in Y-BOCS score. Responders and nonresponders were stratified according to DRD2 TaqI A and COMT Val(158)Met genotypes. RESULTS: No significant differences in genotype distribution or allele frequencies of the COMT or DRD2 receptor were found between responders and nonresponders to citalopram with quetiapine. However, nearly half of responders to citalopram with placebo carried the Met/Met (48%) genotype of the COMT polymorphism compared to none of the nonresponders (?(2) = 10.06, df = 2, P = 0.007). CONCLUSIONS: The Met allele load of the COMT receptor gene was associated with response to 10 weeks of treatment with citalopram in drug-free or drug-naïve OCD patients.

Conceição Costa DL, Shavitt RG, et al. (2013) Can early improvement be an indicator of treatment response in obsessive-compulsive disorder? Implications for early-treatment decision-making. Journal of psychiatric research. 2013;47:1700-7. DOI: 10.1016/j.jpsychires.2013.07.006.

UNLABELLED: In major depression, early response to treatment has been strongly associated with final outcome. We aimed to investigate the ability of early improvement (4 weeks) to predict treatment response at 12 weeks in DSM-IV-defined obsessive-compulsive disorder (OCD) patients treated with serotonin reuptake inhibitors (SRI). We conducted an SRI practical trial with 128 subjects. INCLUSION CRITERIA: age range 18-65 years-old, baseline Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) score? 16, and absence of previous adequate pharmacological treatment. Systematic assessments were performed at baseline, 4 and 12 weeks of treatment. Treatment response at 12 weeks was defined as a 35% or greater reduction in baseline Y-BOCS score. Stepwise logistic regression was used to test the relationship between early improvement and treatment response at 12 weeks, taking into account additional potential predictive factors. Different thresholds of early improvement were tested and their predictive power was calculated. Early improvement, defined as a 20% or greater reduction from baseline Y-BOCS score at 4 weeks, predicted response at 12 weeks with 75.6% sensitivity and 61.9% specificity. According to a logistic regression including demographic and clinical features as explaining variables, early improvement was the best predictor of treatment response (OR = 1.05, $p < 0.0001$). Only 19.8% of patients who did not improve at 4 weeks were responders after 12 weeks. In contrast, 55.3% of the individuals who showed early improvement were responders at 12 weeks (Pearson Chi-Square = 17.06, $p < 0.001$). Early improvement predicted OCD treatment response with relatively good sensitivity and specificity, such that its role in early decision-making warrants further investigation in wider samples. TRIAL REGISTRATION: clinicaltrials.gov Identifier NCT00680602.

Da Conceicao Costa DL, Shavitt RG, et al. Can early improvement be an indicator of treatment response in obsessive-compulsive disorder? Implications for early-treatment decision-making. J Psychiatr Res. 2013;47(11):1700-7.

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Jakubovski E, Diniz JB, et al. Clinical predictors of long-term outcome in obsessive-compulsive disorder. Depress Anxiety. 2013;30(8):763-72.

BACKGROUND: The purpose of this study was to investigate demographic and clinical factors associated with the long-term outcome of obsessive-compulsive disorder (OCD). METHODS: A hundred ninety-six previously untreated patients with DSM-IV criteria OCD completed a 12-week

randomized open trial of group cognitive-behavioral therapy (GCBT) or fluoxetine, followed by 21 months of individualized, uncontrolled treatment, according to international guidelines for OCD treatment. OCD severity was assessed using the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) at different times over the follow-up period. Demographics and several clinical variables were assessed at baseline. RESULTS: Fifty percent of subjects improved at least 35% from baseline, and 21.3% responded fully (final Y-BOCS score < or = 8). Worse prognosis was associated with earlier age at onset of OCD (P = 0.045), longer duration of illness (P = 0.001) presence of at least one comorbid psychiatric disorder (P = 0.001), comorbidity with a mood disorder (P = 0.002), higher baseline Beck-Depression scores (P = 0.011), positive family history of tics (P = 0.008), and positive family history of anxiety disorders (P = 0.008). Type of initial treatment was not associated with long-term outcome. After correction for multiple testing, the presence of at least one comorbid disorder, the presence of a depressive disorder, and duration of OCD remained significant. CONCLUSIONS: Patients under cognitive-behavioral or pharmacological treatment improved continuously in the long run, regardless of initial treatment modality or degree of early response, suggesting that OCD patients benefit from continuous treatment. Psychiatric comorbidity, especially depressive disorders, may impair the long-term outcome of OCD patients.

Ducasse D, Boyer L, et al. D2 and D3 dopamine receptor affinity predicts effectiveness of antipsychotic drugs in obsessive-compulsive disorders: a metaregression analysis. Psychopharmacology (Berl). 2014;231(18):3765-70.

RATIONALE AND OBJECTIVE: The relationship between clinically effective antipsychotic drugs in obsessive-compulsive disorders (OCD) and binding affinities to cloned dopamine and serotonin receptor subtypes was analyzed in an effort to clarify the contribution of individual receptor subtypes to medication response. METHODS: Meta-analysis was used to update previous meta-analyses of effectiveness data of add-on antipsychotic drugs to selective serotonin reuptake inhibitors (SSRIs) in OCD. Twelve previously analyzed randomized controlled trials (RCTs) and one new RCT were included. We performed a metaregression using a mixed-effect model to examine the association between antipsychotic's effectiveness and receptor affinity. RESULTS: A total of 5 treatment arms obtained from 13 RCTs (431 patients) were included in our study. The results of our metaregression showed a significant association between D2 and D3 dopamine receptor affinities and effectiveness in OCD (respectively, slope = -0.36, p = 0.01; and slope = -0.50, p = 0.01) whereas other dopamine receptors and serotonin receptors were not significantly associated. CONCLUSIONS: These observations suggest that increasing D2 and D3 dopamine receptor binding affinities enhances antipsychotics' effectiveness in obsessive-compulsive disorders.

Wheaton MG, Rosenfield D, et al. Augmenting serotonin reuptake inhibitors in obsessive–compulsive disorder: What moderates improvement? Journal of Consulting and Clinical Psychology. 2015;83(5):926-37.

Objective: Patients with obsessive–compulsive disorder (OCD) often only partially respond to serotonin reuptake inhibitors (SRIs). In such cases, American Psychiatric Association practice guidelines suggest augmenting SRIs with cognitive–behavioral therapy consisting of exposure and ritual prevention (EX/RP) or antipsychotic medication (i.e., risperidone). We examined moderators and predictors of these 2 augmentation strategies. Method: Data came from a randomized controlled trial that compared adding EX/RP or risperidone to SRIs in adults with OCD. Patients entered the study on a stable SRI dosage and were randomized to EX/RP (N = 40), risperidone (N = 40), or placebo (N = 20). Data were analyzed using multilevel modeling. Results: Pretreatment OCD severity, age, and depression were significant moderators. Although OCD severity was unrelated to EX/RP response, individuals with more severe OCD had poorer outcomes and slower improvement with risperidone. Increasing age predicted better response to risperidone, but not EX/RP. Increased depression predicted poorer response to placebo, but not EX/RP or risperidone. Poorer functioning predicted worse outcome across all 3 conditions. Together, these moderators and predictor accounted for 33% of the variance in outcomes, above and beyond the 30.8% accounted for by treatment condition. Conclusions: SRI augmentation with EX/RP was more effective than risperidone across all of the demographic and clinical variables tested. EX/RP's superiority over risperidone increased with baseline OCD severity and with younger age. These data indicate that EX/RP should be the recommended SRI augmentation strategy, even for severe OCD. What determines the degree of EX/RP response in individual patients deserves further study. (PsycINFO Database Record (c) 2015 APA, all rights reserved) (journal abstract).

4. TRATAMIENTO FARMACOLÓGICO EN POBLACIONES ESPECIALES

4.1. Ancianos

4.2. Embarazo y lactancia (NOTA: requiere búsqueda específica)

4.3. Comorbilidades psiquiátricas

4.4. Otras

5. TRATAMIENTO DEL TOC CON RESPUESTA PARCIAL O FALTA DE RESPUESTA

5.1. Optimización del tratamiento (1 - 2006)

Ninan PT, Koran LM, et al. High-dose sertraline strategy for nonresponders to acute treatment for obsessive-compulsive disorder: a multicenter double-blind trial. J Clin Psychiatry. 2006;67(1):15-22.

OBJECTIVE: To evaluate the efficacy and safety of high-dose sertraline for patients with obsessive-compulsive disorder (OCD) who failed to respond to standard sertraline acute treatment. METHOD: Sixty-six nonresponders to 16 weeks of sertraline treatment who met DSM-III-R criteria for current OCD were randomly assigned, in a double-blind continuation phase of a multicenter trial, either to continue on 200 mg/day of sertraline or to increase their dose to between 250 and 400 mg/day for 12 additional weeks. Efficacy measures included the Yale-Brown Obsessive Compulsive Scale (YBOCS), the National Institute of Mental Health Global Obsessive Compulsive Scale (NIMH Global OC Scale), and the Clinical Global Impressions-Severity of Illness and -Improvement (CGI-I) scales. Data were collected from July 26, 1994, to October 26, 1995. RESULTS: The high-dose (250-400 mg/day, mean final dose = 357, SD = 60, N = 30) group showed significantly greater symptom improvement than the 200-mg/day group (N = 36) as measured by the YBOCS (p = .033), NIMH Global OC Scale (p = .003), and CGI-I (p = .011). Responder rates (decrease in YBOCS score of > or = 25% and a CGI-I rating < or = 3) were not significantly different for the 200-mg/day versus the high-dose sertraline group, either on completer analysis, 34% versus 52%, or on endpoint analysis, 33% versus 40%. Both treatments showed similar adverse event rates. CONCLUSION: Greater symptom improvement was seen in the high-dose sertraline group compared to the 200-mg/day dose group during continuation treatment. Both dosages yielded similar safety profiles. Administration of higher than labeled doses of selective serotonin reuptake inhibitors may be a treatment option for certain OCD patients who fail to respond to standard acute treatment.

5.2. Combinación (de dos antidepresivos) (3 – 1997-2011)

Barr LC, Goodman WK, et al. Addition of desipramine to serotonin reuptake inhibitors in treatment-resistant obsessive-compulsive disorder. Am J Psychiatry. 1997;154(9):1293-5.

OBJECTIVE: The purpose of this study was to determine whether combined treatment with a selective serotonin reuptake inhibitor (SSRI) and a norepinephrine reuptake inhibitor, desipramine, effectively reduces obsessive-compulsive symptoms in patients who do not respond to SSRIs. METHOD: In a double-blind study, desipramine or placebo was added for 6 or 10 weeks to the treatment of 30 patients with obsessive-compulsive disorder whose symptoms were refractory to SSRI treatment (fluvoxamine, fluoxetine, or sertraline) alone. RESULTS: There were no significant differences between the adjunctive desipramine and placebo groups in obsessive-compulsive or depressive symptoms. CONCLUSIONS: These data suggest that clomipramine's possibly superior efficacy in the treatment of obsessive-compulsive symptoms may not stem from its capacity to inhibit reuptake of norepinephrine.

Pallanti S, Quercioli L, et al. Citalopram for treatment-resistant obsessive-compulsive disorder. Eur Psychiatry. 1999;14(2):101-6.

We investigated the comparative efficacy of citalopram vs. citalopram administered with clomipramine, in treatment-resistant obsessive-compulsive disorder (OCD). Sixteen adult outpatients participated in a 90-day, randomized, open-label trial. Eligible patients were aged 18 to 45 years, had moderate to severe DSM-III-R OCD of >/= one year's duration, a baseline Yale-Brown scale (Y-BOCS) score of >/= 25 and no other active axis I diagnosis, and had failed adequate clomipramine and fluoxetine trials. The citalopram-plus-clomipramine group (n = 9) experienced a significantly larger percent decrease in mean Y-BOCS score by day 90 than the citalopram alone group (n = 7).

Only one citalopram patient decreased her score by >/= 35%, and two by >/= 25%. All nine citalopram-plus-clomipramine patients experienced decreases of 35%. Side effects were mild to moderate in both groups. We also treated with citalopram six OCD patients who had not tolerated fluoxetine alone and clomipramine alone; three achieved Y-BOCS score decreases of >/= 35% at 90 days. Since citalopram does not significantly affect clomipramine metabolism, the improvement in the combined drug group is unlikely to have resulted from increased plasma clomipramine levels. Double-blind controlled trials are needed of citalopram in OCD, and of combining citalopram with clomipramine in treatment-resistant OCD.

Diniz JB, Shavitt RG, et al. A double-blind, randomized, controlled trial of fluoxetine plus quetiapine or clomipramine versus fluoxetine plus placebo for obsessive-compulsive disorder. J Clin Psychopharmacol. 2011;31(6):763-8.

Obsessive-compulsive disorder patients who do not improve sufficiently after treatment with a selective serotonin reuptake inhibitor might improve further if other drugs were added to the treatment regimen. The authors present a double-blind, placebo-controlled trial comparing the efficacy of adding quetiapine or clomipramine to a treatment regimen consisting of fluoxetine. Between May 2007 and March 2010, a total of 54 patients with a primary diagnosis of obsessive-compulsive disorder, as defined by Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision, and a current Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) score of at least 16, the score having dropped by less than 35% after fluoxetine monotherapy, were allocated to 1 of 3 arms (n = 18 per arm): quetiapine + fluoxetine (</=200 and </=40 mg/d, respectively), clomipramine + fluoxetine (</=75 and </=40 mg/d, respectively), or placebo + fluoxetine (</=80 mg/d of fluoxetine). Follow-up was 12 weeks. The Y-BOCS scores were the main outcome measure. No severe adverse events occurred during the trial, and 40 patients (74%) completed the 12-week protocol. The Y-BOCS scores (mean [SD]) were significantly better in the placebo + fluoxetine and clomipramine + fluoxetine groups than in the quetiapine + fluoxetine group (final: 18 [7] and 18 [7], respectively, vs 25 [6], P < 0.001) (reduction from baseline: -6.7 [confidence interval {CI}, -9.6 to -3.8; and -6.5 [CI, -9.0 to -3.9], respectively, vs -0.1 [CI, -2.9 to 2.7], P < 0.001; number needed to treat = 2.4). The clomipramine-fluoxetine combination is a safe and effective treatment for fluoxetine nonresponders, especially those who cannot tolerate high doses of fluoxetine. However, the period of monotherapy with the maximum dose of fluoxetine should be extended before a combination treatment strategy is applied.

5.3. Potenciación

5.3.1. Con psicoterapia (2 – 2005-2008)

Tenneij NH, Megen HJ, et al. (2005) Behavior therapy augments response of patients with obsessive-compulsive disorder responding to drug treatment. The Journal of clinical psychiatry. 2005;66:1169-75.

OBJECTIVE: In many patients with obsessive-compulsive disorder (OCD), residual symptoms persist despite a clinically meaningful response. The objective of this study was to examine whether addition of behavior therapy would augment treatment outcome in these patients. METHOD: Ninety-six patients with DSM-IV OCD who had responded to 3 months of drug treatment were randomly assigned to either receive addition of behavior therapy or continue on drug treatment alone for 6 months. Patients who continued on drug treatment alone eventually received addition of behavior therapy for 6 months. Data were gathered from October 1998 to June 2002. RESULTS: OCD patients who received addition of behavior therapy showed a greater improvement in obsessive-compulsive symptoms (Yale-Brown Obsessive Compulsive Scale [Y-BOCS] score change = -3.9 in the completers sample) than those who continued on drug treatment alone (Y-BOCS score change = +3.9 for completers). Significantly more patients who received addition of behavior therapy were in remission compared with those who continued on drug treatment alone (p < .0001 for completers). Patients who received behavior therapy after 6 months of drug treatment alone showed a nonsignificant decline in obsessive-compulsive symptoms (Y-BOCS score change = -2.7 for completers); however, the remission rate found in this group was comparable to the remission rate found in the group of patients receiving addition of behavior therapy directly after responding to drug treatment. CONCLUSION: The results indicate that addition of behavior therapy is beneficial for patients who have responded to drug treatment. The data also suggest that the effect is greater when behavior therapy is added immediately after attainment of the drug response.

Simpson HB, Foa EB, et al. A randomized, controlled trial of cognitive-behavioral therapy for augmenting pharmacotherapy in obsessive-compulsive disorder. Am J Psychiatry. 2008;165(5):621-30.

OBJECTIVE: Although serotonin reuptake inhibitors (SRIs) are approved for the treatment of obsessive-compulsive disorder (OCD), most OCD patients who have received an adequate SRI trial continue to have clinically significant OCD symptoms. The purpose of this study was to examine the effects of augmenting SRIs with exposure and ritual prevention, an established cognitive-behavioral therapy (CBT) for OCD. METHOD: A randomized, controlled trial was conducted at two academic outpatient clinics to compare the effects of augmenting SRIs with exposure and ritual prevention versus stress management training, another form of CBT. Participants were adult outpatients (N=108) with primary OCD and a Yale-Brown Obsessive Compulsive Scale total score > or = 16 despite a therapeutic SRI dose for at least 12 weeks prior to entry. Participants received 17 sessions of CBT (either exposure and ritual prevention or stress management training) twice a week while continuing SRI pharmacotherapy. RESULTS: Exposure and ritual prevention was superior to stress management training in reducing OCD symptoms. At week 8, significantly more patients receiving exposure and ritual prevention than patients receiving stress management training had a decrease in symptom severity of at least 25% (based on Yale-Brown Obsessive Compulsive Scale scores) and achieved minimal symptoms (defined as a Yale-Brown Obsessive Compulsive Scale score < or = 12). CONCLUSIONS: Augmentation of SRI pharmacotherapy with exposure and ritual prevention is an effective strategy for reducing OCD symptoms. However, 17 sessions were not sufficient to help most of these patients achieve minimal symptoms.

5.3.2. Con antipsicóticos (22 – 1994-2013)

McDougle CJ, Goodman WK, et al. Haloperidol addition in fluvoxamine-refractory obsessive-compulsive disorder. A double-blind, placebo-controlled study in patients with and without tics. Arch Gen Psychiatry. 1994;51(4):302-8.

BACKGROUND: To determine the efficacy of adding haloperidol to the treatment of patients with obsessive-compulsive disorder (OCD), with or without a comorbid chronic tic disorder, who were refractory to adequate treatment with the serotonin-uptake inhibitor fluvoxamine alone. It was hypothesized that OCD patients with a concurrent chronic tic disorder would preferentially respond to this treatment. METHODS: Sixty-two patients with a primary DSM-III-R diagnosis of OCD received placebo fluvoxamine for 1 week, followed by 8 weeks of active fluvoxamine. Thirty-four of these patients were refractory to fluvoxamine and were randomized in a double-blind fashion to 4 weeks of treatment with either haloperidol (n = 17) or placebo (n = 17) added to ongoing fluvoxamine treatment. The placebo-treated group included five women and 12 men, six inpatients and 11 outpatients, and eight patients with a comorbid chronic tic disorder. The haloperidol-treated group consisted of two women and 15 men, three inpatients and 14 outpatients, and seven patients with a comorbid chronic tic disorder. All 34 patients completed the entire study. The Yale-Brown Obsessive Compulsive Scale (Y-BOCS) and the Clinical Global Impression scale were the principal measures of treatment outcome. RESULTS: Haloperidol addition was significantly better than placebo in reducing the severity of obsessive-compulsive symptoms as measured by the Y-BOCS. Eleven of 17 patients responded to the haloperidol, compared with none of 17 patients given placebo. Eight of eight patients with comorbid chronic tic disorders, such as Tourette's disorder, responded to double-blind haloperidol addition to ongoing fluvoxamine treatment. Haloperidol addition was of little benefit in treating OCD patients without tics. Fluvoxamine blood levels were not related to treatment response. CONCLUSIONS: The results of this study suggest that OCD patients with a comorbid chronic tic disorder constitute a clinically meaningful subtype of OCD that might require conjoint serotonin-uptake inhibitor/neuroleptic therapy for effective symptom reduction.

McDougle CJ, Epperson CN, et al. A double-blind, placebo-controlled study of risperidone addition in serotonin reuptake inhibitor-refractory obsessive-compulsive disorder. Arch Gen Psychiatry. 2000;57(8):794-801.

BACKGROUND: To date, only 1 controlled study has found a drug (haloperidol) to be efficacious in augmenting response in patients with obsessive-compulsive disorder (OCD) refractory to serotonin reuptake inhibitor (SRI) monotherapy; patients with comorbid chronic tic disorders showed a preferential response. This report describes the first controlled study of risperidone addition in patients with OCD refractory to treatment with SRI alone. METHODS: Seventy adult patients with a primary DSM-IV diagnosis of OCD received 12 weeks of treatment with an SRI. Thirty-six patients were refractory to the SRI and were randomized in a double-blind manner to 6 weeks of risperidone (n = 20) or placebo (n = 16) addition. Behavioral ratings, including the Yale-Brown Obsessive Compul-

sive Scale, were obtained at baseline and throughout the trial. Placebo-treated patients subsequently received an identical open-label trial of risperidone addition. RESULTS: For study completers, 9 (50%) of 18 risperidone-treated patients were responders (mean daily dose, 2.2 +/-0.7 mg/d) compared with 0 of 15 in the placebo addition group (P<. 005). Seven (50%) of 14 patients who received open-label risperidone addition responded. Risperidone addition was superior to placebo in reducing OCD (P<.001), depressive (P<.001), and anxiety (P =.003) symptoms. There was no difference in response between OCD patients with and without comorbid diagnoses of chronic tic disorder or schizotypal personalty disorder. Other than mild, transient sedation, risperidone was well tolerated. CONCLUSION: These results suggest that OCD patients with and without comorbid chronic tic disorders or schizotypal personality disorder may respond to the addition of low-dose risperidone to ongoing SRI therapy.

Atmaca M, Kuloglu M, et al. Quetiapine augmentation in patients with treatment resistant obsessive-compulsive disorder: A single-blind, placebo study. International Clinical Psychopharmacology. 2002;17(3):115-9.

Recently, atypical antipsychotics have been used for the management of the patients with refractory obsessive-compulsive disorder (OCD). The aim of the present study was to evaluate the results of quetiapine augmentation to a serotonin reuptake inhibitor (SRI) in the patients with refractory OCD. 52 patients with OCD (aged 18-44 yrs) according to Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) entered 3 months of an open-label phase treatment with a SRI with or without concomitant adjunctive treatment regimen. Of them, 27 patients were refractory OCD. These patients were randomly divided into two groups, SRI plus quetiapine and SRI plus placebo, for an 8-wk single-blind phase, The course of OCD was evaluated by Vale-Brown Obsession-Compulsion (Y-BOCS) and Clinical Global Impression-Severity of Illness and Improvement (CGI-SI and 1) Scales every other week for 8 weeks. Of the 14 patients in group 1, nine (64.4%) showed significant improvement with 60% or greater improvement on the Y-BOCS and one (7.1%) partial improvement with 30% or greater improvement on the Y-BOCS, whereas no improvement was observed in group 11. The addition of quetiapine to ongoing SRI therapy has been found to be effective and well-tolerated approach in patients with refractory OCD. (PsycINFO Database Record (c) 2012 APA, all rights reserved).

Hollander E, Baldini Rossi N, et al. Risperidone augmentation in treatment-resistant obsessive-compulsive disorder: a double-blind, placebo-controlled study. Int J Neuropsychopharmacol. 2003;6(4):397-401.

This double-blind, placebo-controlled trial was performed to determine the efficacy and tolerability of 8 wk of risperidone augmentation of serotonin reuptake inhibitor (SRI) treatment in adult subjects with treatment-resistant obsessive-compulsive disorder (OCD) (failure of at least two SRI trials). Sixteen adult treatment-resistant OCD patients were randomly assigned to augmentation with 8 wk of either risperidone (n=10) (0.5-3.0 mg/d) or placebo (n=6) following at least 12 wk of SRI treatment. Four patients on risperidone (40%) and none (0%) on placebo were responders with both a Clinical Global Impression - Improvement (CGI-I) score of 1 or 2 and a Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) decrease >/=25%. Risperidone was generally well tolerated: there were 3 dropouts, 1 on risperidone and 2 on placebo. Better Y-BOCS insight score at baseline significantly correlated with a greater CGI-I score at endpoint on risperidone augmentation. Risperidone may be an effective and well-tolerated augmentation strategy in treatment-resistant OCD subjects, but larger sample size studies are required to demonstrate this.

Hollander E, Rossi NB, et al. Risperidone augmentation in treatment-resistant obsessive-compulsive disorder: A double-blind, placebo-controlled study. International Journal of Neuropsychopharmacology. 2003;6(4):397-401.

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Bystritsky A, Ackerman DL, et al. Augmentation of serotonin reuptake inhibitors in refractory obsessive-compulsive disorder using adjunctive olanzapine: a placebo-controlled trial. J Clin Psychiatry. 2004;65(4):565-8.

BACKGROUND: The purpose of this study was to explore the efficacy of adding an atypical antipsychotic, olanzapine, to a serotonin reuptake inhibitor (SRI) in treatment-refractory obsessive-compulsive disorder (OCD). METHOD: Twenty-six patients aged between 18 and 65 (mean = 41.2, SD = 11.9) years meeting DSM-IV criteria for OCD, who had not responded to SRIs, were treated for 6 weeks in a double-blind, placebo-controlled augmentation study with either olanzapine (up to 20 mg/day) or placebo. Severity of illness was assessed biweekly by the Yale-Brown Obsessive Compulsive Scale (Y-BOCS). Analysis of covariance with baseline Y-BOCS score included as a covariate was used to compare improvement in Y-BOCS scores in the 2 groups. Response was defined as a 25% or greater improvement in Y-BOCS score. Data were collected between April 2001 and May 2003. RESULTS: Outcome was assessed for all patients using the last observation carried forward. Subjects in the olanzapine group had a mean decrease of 4.2 (SD = 7.9) in Y-BOCS score compared with a mean increase in score of 0.54 (SD = 1.31) for subjects in the placebo group (F = 4.85, df = 2,23; p =.04). Six (46%) of 13 subjects in the olanzapine group showed a 25% or greater improvement in Y-BOCS score compared with none in the placebo group. The final mean dose of olanzapine was 11.2 (SD = 6.5) mg/day. Medication was well tolerated. Only 2 (15%) of 13 subjects who received olanzapine discontinued because of side effects: sedation (N = 1) or weight gain (N = 1). CONCLUSION: These results provide preliminary evidence that adding olanzapine to SRIs is potentially efficacious and well tolerated in the short-term treatment of patients with refractory OCD. Controlled studies with larger sample sizes are necessary to more definitively address this treatment strategy.

Denys D, de Geus F, et al. A double-blind, randomized, placebo-controlled trial of quetiapine addition in patients with obsessive-compulsive disorder refractory to serotonin reuptake inhibitors. J Clin Psychiatry. 2004;65(8):1040-8.

BACKGROUND: Although serotonin reuptake inhibitors (SRIs) are the most effective pharmacologic treatment currently available for patients with obsessive-compulsive disorder (OCD), 40% to 60% of patients do not respond to this treatment. This study was conducted to evaluate the efficacy and tolerability of quetiapine in addition to an SRI for treatment-refractory patients with OCD. METHOD: Forty patients (10 men/30 women, mean +/- SD age = 35.2 +/- 12.1 years; range, 18-60 years) with primary OCD according to DSM-IV criteria who were recruited between February 2001 and December 2002 were randomly assigned in an 8-week, double-blind, placebo-controlled trial to receive dosages titrated upward to 300 mg/day of quetiapine (N = 20) or placebo (N = 20) in addition to their SRI treatment. At entry, all patients were unresponsive to courses of treatment with at least 2 different SRIs at a maximum tolerated dose for 8 weeks. During the study, primary efficacy was assessed according to change from baseline on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS). A responder was defined as having a final Clinical Global Impressions-Improvement scale rating of "very much improved" or "much improved" and a decrease of > or = 35% in Y-BOCS score. RESULTS: An intent-to-treat, last-observation-carried-forward analysis demonstrated a mean +/- SD decrease in Y-BOCS score of 9.0 +/- 7.0 (31%) in the quetiapine group and 1.8 +/- 3.4 (7%) in the placebo group (F=16.99, df=1,38; p <.001). Eight (40%) of 20 patients in the quetiapine group and 2 (10%) of 20 patients in the placebo group were responders (chi2=4.8, df=1, p=.028). The most common side effects in the quetiapine group were somnolence, dry mouth, weight gain, and dizziness. CONCLUSION: The results of this study show that quetiapine in addition to an SRI is beneficial for patients with OCD who do not respond to SRI treatment alone.

Denys D, Geus F, et al. (2004) A double-blind, randomized, placebo-controlled trial of quetiapine addition in patients with obsessive-compulsive disorder refractory to serotonin reuptake inhibitors. The Journal of clinical psychiatry. 2004;65:1040-8.

BACKGROUND: Although serotonin reuptake inhibitors (SRIs) are the most effective pharmacologic treatment currently available for patients with obsessive-compulsive disorder (OCD), 40% to 60% of patients do not respond to this treatment. This study was conducted to evaluate the efficacy and tolerability of quetiapine in addition to an SRI for treatment-refractory patients with OCD. METHOD: Forty patients (10 men/30 women, mean +/- SD age = 35.2 +/- 12.1 years; range, 18-60 years) with primary OCD according to DSM-IV criteria who were recruited between February 2001 and December 2002 were randomly assigned in an 8-week, double-blind, placebo-controlled trial to receive dosages titrated upward to 300 mg/day of quetiapine (N = 20) or placebo (N = 20) in addition to their SRI treatment. At entry, all patients were unresponsive to courses of treatment with at least 2 different SRIs at a maximum tolerated dose for 8 weeks. During the study, primary efficacy was assessed according to change from baseline on the Yale-Brown Obsessive Compulsive Scale (Y-

BOCS). A responder was defined as having a final Clinical Global Impressions-Improvement scale rating of "very much improved" or "much improved" and a decrease of > or = 35% in Y-BOCS score. RESULTS: An intent-to-treat, last-observation-carried-forward analysis demonstrated a mean +/- SD decrease in Y-BOCS score of 9.0 +/- 7.0 (31%) in the quetiapine group and 1.8 +/- 3.4 (7%) in the placebo group (F=16.99, df=1,38; p <.001). Eight (40%) of 20 patients in the quetiapine group and 2 (10%) of 20 patients in the placebo group were responders (chi2=4.8, df=1, p=.028). The most common side effects in the quetiapine group were somnolence, dry mouth, weight gain, and dizziness. CONCLUSION: The results of this study show that quetiapine in addition to an SRI is beneficial for patients with OCD who do not respond to SRI treatment alone.

Shapira NA, Ward HE, et al. A double-blind, placebo-controlled trial of olanzapine addition in fluoxetine-refractory obsessive-compulsive disorder. Biol Psychiatry. 2004;55(5):553-5.

BACKGROUND: One of the few combination approaches to the treatment of obsessive-compulsive disorder (OCD) with encouraging support is the addition of an antipsychotic to a serotonin reuptake inhibitor. METHODS: The study consisted of a 6-week, placebo-controlled addition of olanzapine 5-10 mg (6.1 +/- 2.1 mg, mean +/- SD) to fluoxetine in OCD subjects who were partial or nonresponders to an 8-week, open-label fluoxetine trial (40 mg in 43 subjects, 20 mg in 1 subject). RESULTS: Both the fluoxetine-plus-olanzapine (n = 22) and fluoxetine-plus-placebo (n = 22) groups improved significantly over 6 weeks [F(3,113) = 11.64, p <.0001] according to Yale-Brown Obsessive Compulsive Scale scores with repeated-measures analysis of variance; however, the treatment x time interaction was not significant for olanzapine versus placebo addition to fluoxetine. CONCLUSIONS: These findings indicate no additional advantage of adding olanzapine for 6 weeks in OCD patients who have not had a satisfactory response to fluoxetine for 8 weeks, compared with extending the monotherapy trial.

Carey PD, Vythilingum B, et al. (2005) Quetiapine augmentation of SRIs in treatment refractory obsessive-compulsive disorder: a double-blind, randomised, placebo-controlled study [ISRCTN83050762]. BMC psychiatry.2005;5:5. DOI: 10.1186/1471-244X-5-5.

BACKGROUND: Although serotonin reuptake inhibitors are effective in the treatment of OCD, many patients fail to respond to these agents. Growing evidence from open-label and placebo-controlled trials suggests a role for augmentation of SRIs with atypical antipsychotics in OCD. Quetiapine is generally well tolerated and previous open-label data has produced mixed results in OCD and additional controlled data is needed. METHODS: We undertook a double-blind, randomised, parallel-group, flexible-dose, placebo-controlled study of quetiapine augmentation in subjects who had responded inadequately to open-label treatment with an SRI for 12 weeks. Following informed consent and screening, forty-two subjects were randomised to either placebo or quetiapine for six weeks. RESULTS: There was significant improvement from baseline to endpoint on the Yale-Brown Obsessive-Compulsive Scale in both the quetiapine and placebo groups (quetiapine, n = 20, p < 0.0001; placebo, n = 21, p = 0.001) with 40% (n = 8) of quetiapine and 47.6% (n = 10) of placebo treated subjects being classified as responders. Quetiapine did not demonstrate a significant benefit over placebo at the end of the six-week treatment period (p = .636). Similarly quetiapine failed to separate from placebo in the subgroup of subjects (n = 10) with co-morbid tics. Quetiapine was generally well tolerated. CONCLUSIONS: In this study, quetiapine augmentation was no more effective than placebo augmentation of SRIs. A number of limitations in study design make comparisons with previous studies in this area difficult and probably contributed to our negative findings. Future work in this important clinical area should address these limitations.

Erzegovesi S, Guglielmo E, et al. Low-dose risperidone augmentation of fluvoxamine treatment in obsessive-compulsive disorder: a double-blind, placebo-controlled study. Eur Neuropsychopharmacol. 2005;15(1):69-74.

According to previous data, the addition of risperidone in obsessive-compulsive patients refractory to serotonin reuptake inhibitors (SRIs) is shown to be a safe and effective treatment strategy. The aims of our study were to evaluate the efficacy of risperidone addition, in comparison to placebo, in fluvoxamine-refractory obsessive-compulsive patients and to investigate whether risperidone could boost the efficacy of fluvoxamine in fluvoxamine-responder patients. Subjects were 45 obsessive-compulsive inpatients, consecutively recruited at the Department of Neurosciences at the San Raffaele Hospital, Milan. Thirty-nine patients completed the study. All patients received 12 weeks of a standardized open-label fluvoxamine monotherapy and then continued for 6 weeks with placebo or risperidone in a double-blind design. Results showed a significant effect of risperidone addition, at the end of the double-blind phase (18th week), only for fluvoxamine-refractory patients. Five patients on risperidone (50%) and two (20%) on placebo became responders, with a Yale-Brown Ob-

sessive-Compulsive Scale (Y-BOCS) decrease > or =35%. Risperidone was generally well tolerated, except for a mild transient sedation and a mild increase in appetite. This preliminary study suggests that even very low (0.5 mg) risperidone doses are effective in OC patients who were nonresponders to a standardized treatment with fluvoxamine.

Fineberg NA, Sivakumaran T, et al. Adding quetiapine to SRI in treatment-resistant obsessive-compulsive disorder: a randomized controlled treatment study. Int Clin Psychopharmacol. 2005;20(4):223-6.

This study aimed to determine the efficacy and tolerability of adding quetiapine to a serotonin reuptake inhibitor in treatment-resistant obsessive-compulsive disorder (OCD). Twenty-one adult treatment-resistant OCD patients were randomized to 16 weeks of augmentation with either quetiapine (n = 11) or placebo (n = 10). Patients with significant comorbidities, including tic-spectrum disorders, were not included. The treatment was well tolerated, with only one premature dropout in each treatment-group. The primary analysis showed that individuals in the quetiapine-treated group showed a 14% mean improvement in baseline Yale-Brown Obsessive-Compulsive Scale scores at study endpoint compared with a 6% improvement in those treated with placebo, but this difference did not reach statistical significance (F<1). Three patients treated with quetiapine met criteria for clinical response, compared to one patient who was treated with placebo. Larger studies are needed to explore the efficacy of second generation antipsychotics, such as quetiapine, when used as adjunct treatment in resistant OCD.

Li X, May RS, et al. Risperidone and haloperidol augmentation of serotonin reuptake inhibitors in refractory obsessive-compulsive disorder: a crossover study. J Clin Psychiatry. 2005;66(6):736-43.

BACKGROUND: Although serotonin reuptake inhibitors (SRIs) are the first-line treatment for obsessive-compulsive disorder (OCD), approximately half of patients with OCD do not respond adequately to SRI monotherapy. Patients with predominant obsessions are common in OCD and are often difficult to treat, necessitating adjunctive treatment. METHOD: This was a 9-week, double-blind, placebo-controlled, crossover study comparing the benefits of 2-week adjunctive treatments with risperidone, haloperidol, and placebo in patients with OCD (DSM-IV criteria) who continued to have severe symptoms despite taking a stable dose of an SRI. Eligible patients must have been receiving a therapeutic dose of an SRI for at least 12 weeks and at the screening visit had a score > or = 10 on items 1-5 (obsession) and a total score > or = 16 on the Yale-Brown Obsessive Compulsive Scale (YBOCS). Data were collected from January 1999 through April 2002. RESULTS: Sixteen patients were enrolled and 12 completed the study. On the YBOCS, both risperidone and haloperidol significantly reduced obsession ($p < .05$) when compared with placebo. There was a tendency that haloperidol, and to a lesser degree risperidone, also reduced the compulsion and the total YBOCS scores. These results were accompanied by a reduction in the Hopkins Symptom Checklist 90-revised (SCL-90R) anxiety scale score. According to the 17-item Hamilton Rating Scale for Depression, the SCL-90R depression scale, and the Profile of Mood States, risperidone, but not halo-peridol, also improved depressed mood. Neither risperidone nor haloperidol changed neurocogni-tive function during the 2-week treatment. All 12 patients completed the 2-week risperidone treatment, but 5 of the 12 terminated haloperidol treatment early owing to intolerable side effects. CONCLUSION: Adjunctive risperidone improved obsessions and depressed mood and was well tolerated in patients with SRI-refractory OCD.

De Geus F, Denys D, et al. Effects of quetiapine on cognitive functioning in obsessive-compulsive disorder. Int Clin Psychopharmacol. 2007;22(2):77-84.

In recent years, growing evidence supports the efficacy of antipsychotic addition to serotonin reuptake inhibitors in patients with treatment-refractory obsessive-compulsive disorder. This study is the first to investigate the effects of antipsychotic addition on cognitive functioning in obsessive-compulsive disorder patients. Cognitive functioning was evaluated at baseline and at endpoint of an 8-week double-blind, placebo-controlled quetiapine addition trial. Neurocognitive performance was compared between the placebo and quetiapine group and between responders and nonresponders. The neuropsychological test battery consisted of the national adult reading test, the Wisconsin Card Sorting Test, the Trail Making Test, verbal fluency, the Stroop Color Word Test, the California Verbal Learning Test, the Rey Complex Figure Task, the Continuous Performance Test, and the Digit Symbol Substitution. The results of this study suggest that quetiapine addition to serotonin reuptake inhibitors has no major effects on cognitive functioning in obsessive-compulsive disorder patients, apart from some evidence for a failure to maintain set on the Wisconsin Card Sorting Test. It is proposed that this failure may be caused by attention difficulties owing to somnolence.

Kordon A, Wahl K, et al. Quetiapine addition to serotonin reuptake inhibitors in patients with severe obsessive-compulsive disorder: a double-blind, randomized, placebo-controlled study. J Clin Psychopharmacol. 2008;28(5):550-4.

OBJECTIVE: Although many patients with obsessive-compulsive disorder (OCD) benefit from treatment with serotonin reuptake inhibitors (SRIs), it is estimated that 40% to 60% of them do not respond. The objective of the present study was to evaluate the efficacy of quetiapine added to baseline treatment with SRIs for the treatment of OCD in severely ill adult subjects. METHOD: Forty patients (21 men, 19 women) with primary OCD according to Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria participated in a 12-week, double-blind, placebo-controlled trial. They were randomly assigned to dosages of quetiapine titrated up to 400 mg/d (n = 20) or to placebo (n = 20) in addition to their SRI treatment. During the continuation phase (weeks 6-12), subjects received different dosages between 400 and 600 mg/d depending on clinical response. At entry, all patients were unresponsive to at least 1 course of at least 12 weeks of treatment with SRIs at defined doses. The total Yale-Brown Obsessive-Compulsive Scale score was the primary efficacy parameter. RESULTS: Intention-to-treat, last-observation-carried-forward analysis demonstrated a mean +/- SD decrease in Yale-Brown Obsessive-Compulsive Scale score of 5.2 +/- 5.4 in the quetiapine group and 3.9 +/- 4.9 in the placebo group. The analysis of treatment effects between the 2 groups showed no significant difference. There were no significant group differences in any of the other self-rating scales or clinician-administered rating scales. CONCLUSIONS: In this study, augmentation of SRI treatment with quetiapine in severe OCD had no additional effect.

Maina G, Pessina E, et al. 8-week, single-blind, randomized trial comparing risperidone versus olanzapine augmentation of serotonin reuptake inhibitors in treatment-resistant obsessive-compulsive disorder. Eur Neuropsychopharmacol. 2008;18(5):364-72.

The aim of the present pilot study was to investigate in a single-blind manner, over a period of 8 weeks, the comparative efficacy and tolerability of risperidone versus olanzapine addition in the treatment of OCD patients who did not show a >or=35% decrease in the YBOCS score after 16-week SRI treatment (defined as resistant). The study consisted of two different phases: a 16-week open-label prospective phase to ascertain resistance to SRI treatment and an 8-week single-blind addition phase for resistant subjects only. Ninety-six subjects with DSM-IV OCD (YBOCS>or=16) entered the open-label prospective phase; at the end of the 16-week period, 50 (52%) were judged to be resistant and were randomized to receive risperidone (1 to 3 mg/d) or olanzapine (2.5 to 10 mg/d) addition for 8 weeks. Overall, patients in both groups responded significantly, without differences between the two treatment groups; although no differences emerged for the proportion of patients reporting at least an adverse event, the profiles of adverse experiences differed significantly, being risperidone associated with amenorrhoea and olanzapine with weight gain.

Matsunaga H, Nagata T, et al. A long-term trial of the effectiveness and safety of atypical antipsychotic agents in augmenting SSRI-refractory obsessive-compulsive disorder. J Clin Psychiatry. 2009;70(6):863-8.

OBJECTIVE: Although atypical antipsychotic agents have been found effective in the augmentation of serotonin reuptake inhibitors (SRIs) for treatment-resistant obsessive-compulsive disorder (OCD) in short-term trials, there are few data on the effectiveness and safety of these agents in clinical settings over the long term. METHOD: Subjects (N = 46) who responded to selective SRIs (SSRIs) in an initial 12-week trial were continued on SSRI monotherapy plus cognitive-behavioral therapy (CBT) for 1 year. Subjects (N = 44) who failed to respond to SSRIs were randomly assigned to 1 of 3 atypical antipsychotics -- olanzapine, quetiapine, or risperidone -- and were consecutively treated using SSRI + atypical antipsychotics combined with CBT for 1 year. This study was conducted from January 2006 to November 2007 at Osaka City University Graduate School of Medicine Hospital, Japan. RESULTS: Augmentation with atypical antipsychotics reduced mean +/- SD Yale-Brown Obsessive Compulsive Scale (YBOCS) total scores in SSRI-refractory OCD patients (at initial assessment = 29.3 +/- 9.9, after 1 year = 19.3 +/- 6.8). However, compared to SSRI responders (at initial assessment = 25.8 +/- 11.4, after 1 year = 13.7 +/- 4.6), total YBOCS scores in those who required atypical antipsychotic augmentation were initially higher, and they remained at higher levels than those of SRI responders after 1 year of the treatments. CONCLUSIONS: Our work does not sufficiently support the long-term effectiveness of the atypical antipsychotics in the augmentation of SSRIs for treatment-resistant OCD patients. Even though this approach seems useful for some types of OCD patients, such as those with symmetry/ordering and hoarding symptoms, these data emphasize the limitations of the current pharmacotherapeutic options in treatment-refractory OCD, and their chronic use raises a number of safety concerns. TRIAL REGISTRATION: (ClinicalTrials.gov) Identifier NCT00854919.

Diniz JB, Shavitt RG, et al. A double-blind, randomized, controlled trial of fluoxetine plus quetiapine or clomipramine versus fluoxetine plus placebo for obsessive-compulsive disorder. J Clin Psychopharmacol. 2011;31(6):763-8.

Obsessive-compulsive disorder patients who do not improve sufficiently after treatment with a selective serotonin reuptake inhibitor might improve further if other drugs were added to the treatment regimen. The authors present a double-blind, placebo-controlled trial comparing the efficacy of adding quetiapine or clomipramine to a treatment regimen consisting of fluoxetine. Between May 2007 and March 2010, a total of 54 patients with a primary diagnosis of obsessive-compulsive disorder, as defined by Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision, and a current Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) score of at least 16, the score having dropped by less than 35% after fluoxetine monotherapy, were allocated to 1 of 3 arms (n = 18 per arm): quetiapine + fluoxetine (</=200 and </=40 mg/d, respectively), clomipramine + fluoxetine (</=75 and </=40 mg/d, respectively), or placebo + fluoxetine (</=80 mg/d of fluoxetine). Follow-up was 12 weeks. The Y-BOCS scores were the main outcome measure. No severe adverse events occurred during the trial, and 40 patients (74%) completed the 12-week protocol. The Y-BOCS scores (mean [SD]) were significantly better in the placebo + fluoxetine and clomipramine + fluoxetine groups than in the quetiapine + fluoxetine group (final: 18 [7] and 18 [7], respectively, vs 25 [6], P < 0.001) (reduction from baseline: -6.7 [confidence interval {CI}, -9.6 to -3.8; and -6.5 [CI, -9.0 to -3.9], respectively, vs -0.1 [CI, -2.9 to 2.7], P < 0.001; number needed to treat = 2.4). The clomipramine-fluoxetine combination is a safe and effective treatment for fluoxetine nonresponders, especially those who cannot tolerate high doses of fluoxetine. However, the period of monotherapy with the maximum dose of fluoxetine should be extended before a combination treatment strategy is applied.

Muscatello MR, Bruno A, et al. Effect of aripiprazole augmentation of serotonin reuptake inhibitors or clomipramine in treatment-resistant obsessive-compulsive disorder: a double-blind, placebo-controlled study. J Clin Psychopharmacol. 2011;31(2):174-9.

Based on the evidence that aripiprazole added to serotonin reuptake inhibitors (SRIs) or clomipramine in treatment-resistant obsessive-compulsive disorder (OCD) has reported promising results, the present 16-week, double-blind, randomized, placebo-controlled trial had the aim to explore the efficacy of aripiprazole add-on pharmacotherapy on clinical symptoms and cognitive functioning in a sample of treatment-resistant OCD patients receiving SRIs. After clinical and neurocognitive assessments, patients were randomly allocated to receive, in a double-blind design, 15 mg/d of aripiprazole or a placebo. A final sample of 30 patients completed the study. The results obtained indicate that aripiprazole added to stable SRI treatment substantially improved obsessive-compulsive symptoms as measured by changes on the Yale-Brown Obsessive Compulsive Scale total score and subscores (obsessions, P = 0.007; compulsions, P = 0.001; total score, P < 0.0001). Regarding cognitive functions, improvement was observed in some explored areas, such as attentional resistance to interference (Stroop score, P = 0.001) and executive functioning (perseverative errors, P = 0.015). The findings provide evidence that aripiprazole augmentation of SRIs/clomipramine treatment is well tolerated and may be proposed as an effective therapeutic strategy to improve outcome in treatment-resistant OCD.

Selvi Y, Atli A, et al. The comparison of aripiprazole and risperidone augmentation in selective serotonin reuptake inhibitor-refractory obsessive-compulsive disorder: a single-blind, randomised study. Hum Psychopharmacol. 2011;26(1):51-7.

OBJECTIVE: To investigate the comparative efficacy of aripiprazole and risperidone as augmenting agents in the treatment of obsessive-compulsive disorder (OCD) patients who did not show a >/=35% decrease in the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) after 12-week monotherapy with selective serotonin reuptake inhibitors (SSRIs). METHODS: The study consists of two different periods of treatment: a 12-week prospective period to determine resistance to SSRI treatment and an 8-week single-blind addition period for refractory patients only. Ninety patients were randomly assigned to receive one of the SSRI treatments. Sixty-nine patients (76.6%) completed the 12-week SSRI monotherapy period. Forty-one patients (59.4%) were considered refractory and were randomised to receive either risperidone (20 patients, 3 mgr daily) or aripiprazole (21 patients, 15 mgr daily) as augmentation to SSRI treatment. Sixteen patients (76.2%) in the aripiprazole group and 18 patients (84%) in the risperidone group completed the 8-week treatment period. RESULTS: Eight patients (50%) in aripiprazole and 13 patients (72.2%) in risperidone group met response criteria of Y-BOCS decrease >/=35% at the end of the study. The risperidone group showed a significant improvement in Y-BOCS obsession scores compared with aripiprazole. CONCLUSIONS: The present findings suggest that risperidone may be more effective than aripiprazole.

Sayyah M, Sayyah M, et al. Effects of aripiprazole augmentation in treatment-resistant obsessive-compulsive disorder (a double blind clinical trial). Depress Anxiety. 2012;29(10):850-4.

BACKGROUND: Obsessive-compulsive disorder (OCD) is a chronic disorder with unknown etiology. Failure in OCD treatmentcompulsive is common and finding effective augmentations in treatment of OCD will benefit patients. Antipsychotic augmentation is a common strategy for treatment resistant OCD. This trial evaluated the efficacy of adding aripiprazole in patients whose OCD was insufficiently responsive to an adequate SSRI treatment. METHODS: Thirty-nine adult outpatients, who met the DSM-IV-TR criteria for OCD and had treatment resistant OCD were evaluated in a double-blind randomized clinical trial. The patients received either aripiprazole 10 mg/day or placebo, for 12 weeks. Data were analyzed using intention-to-treat analysis with last observation carried forward. All statistical tests were two-sided, and were considered statistically significant at $P < 0.05$. RESULTS: A significant reduction in total scores of Y-BOCS ($P < 0.0001$) was found in the aripiprazole group. Aripiprazole was generally well tolerated. There was no significant difference between the two groups in terms of observed side effects. CONCLUSION: Results of the present study indicate that aripiprazole could be an effective augmentation medicine in treatment resistant OCD.

Storch EA, Goddard AW, et al. Double-blind, placebo-controlled, pilot trial of palipendone augmentation in serotonin reuptake inhibitor-resistant obsessive-compulsive disorder. Journal of Clinical Psychiatry. 2013;74(6):e527-32.

Objective. This pilot study explored the efficacy and tolerability of paliperidone augmentation of serotonin reuptake inhibitors (SRIs) in adults with treatment-resistant obsessive-compulsive disorder (OCD). Method: Thirty-four patients aged 24-67 years (mean = 43.7 years, SD = 11.4) who met DSM-IV criteria for OCD and remained symptomatic following 2 or more past adequate SRI trials (including their current medication) were enrolled from May 2008 to March 2012. Participants were treated for 8 weeks in a double-blind study with either paliperidone (up to 9 mg/d) or matching placebo in addition to their SRI Blinded raters conducted outcome assessments. The primary outcome, obsessive-compulsive symptom severity, was assessed using the Yale-Brown. Obsessive Compulsive Scale (YBOCS). Secondary outcomes included the Clinical Global Impressions-Severity of Illness and-Improvement scales. Results: Paliperidone administration resulted in significant baseline-to-posttreatment reductions in obsessive-compulsive symptoms as measured by the YBOCS ($P < 01$, $d = 0.66$), although placebo administration also resulted in medium-sized, trend-level significant YBOCS changes ($P = 05$, $d = 0.53$). In exploratory analyses examining between-group differences, tests for paliperidone superiority relative to placebo were not significant ($P = .14$, $d = 0.34$), however, a numerical trend toward significant between-group differences was found, with a reduction of 7.98 points on the YBOCS for the paliperidone group compared to a reduction of 4.02 points for the placebo group. Paliperidone was generally well tolerated and not associated with significant weight gain (mean [SD] weight paliperidone, pretreatment 84.70 [27.08] kg, posttreatment 84.84 [18.99] kg, vs placebo, pretreatment 77.50 [25.33] kg, posttreatment 77.43 [19.90] kg, $P = 21$). Conclusions: These results suggest that paliperidone augmentation is well tolerated and has potential efficacy in the short-term treatment of some patients with SRI-resistant OCD. Well-powered, randomized, controlled studies are necessary to more definitively address the efficacy of this treatment strategy. (PsycINFO Database Record (c) 2013 APA, all rights reserved)(journal abstract)

5.3.3. Con estimulantes (1 – 2009)

Koran LM, Aboujaoude E, et al. Double-blind study of dextroamphetamine versus caffeine augmentation for treatment-resistant obsessive-compulsive disorder. J Clin Psychiatry. 2009;70(11):1530-5.

INTRODUCTION: Two small, double-blind, placebo-controlled, single-dose, crossover studies found dextroamphetamine (d-amphetamine) 30 mg clearly superior to placebo in relieving symptoms of obsessive-compulsive disorder (OCD). We conducted a 5-week, double-blind, caffeine-controlled study to test the hypothesis that d-amphetamine, added after an adequate selective serotonin reuptake inhibitor (SSRI) or serotonin-norepinephrine reuptake inhibitor (SNRI) trial, would be more effective than caffeine in reducing residual OCD symptoms of moderate or greater severity. METHOD: Between August 2006 and February 2008, we enrolled adults with DSM-IV OCD and a Yale-Brown Obsessive Compulsive Scale (Y-BOCS) score of >or= 20 after >or= 12 weeks of adequate treatment with an SSRI or SNRI. Subjects were randomly assigned to double-blind d-amphetamine 30 mg/d or caffeine 300 mg/d added to their SSRI/SNRI and other medications. Responders (first week mean Y-BOCS score decrease of >or= 20%) entered the study's 4-week double-blind extension phase. RESULTS: We enrolled 24 subjects, 11 women and 13 men, with a mean (SD) age of 40

(13.2) years and mean baseline Y-BOCS scores of 26.5 (4.1) for the d-amphetamine group (n = 12) and 29.1 (4.0) for the caffeine group (n = 12). At the end of week 1, 6 of 12 d-amphetamine subjects (50%) and 7 of 12 caffeine subjects (58%) were responders. At week 5, the responders' mean Y-BOCS score decreases were, for the d-amphetamine group (last observation carried forward), 48% (range, 20%-80%); and, for the caffeine group, 55% (range, 27%-89%). Obsessive-compulsive disorder and depression improvement were independent. The double-blind remained intact. No subject discontinued the study due to side effects. CONCLUSIONS: Larger, double-blind, placebo-controlled trials of both d-amphetamine and caffeine augmentation are needed in OCD subjects inadequately responsive to adequate doses of an SSRI or SNRI. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT00363298.

5.3.4. Con moduladores glutamatérgicos (riluzol, topiramato, lamotrigina, N-acetilcisteína, etc.) (14 – 2005-2015)

Coric V, Taskiran S, et al. Riluzole augmentation in treatment-resistant obsessive-compulsive disorder: an open-label trial. Biol Psychiatry. 2005;58(5):424-8.

BACKGROUND: Most patients with obsessive-compulsive disorder (OCD) show only partial reduction of symptoms with standard therapy. Recent imaging data suggests glutamatergic dysfunction in the corticostriatal pathway in OCD. We investigated the efficacy of augmentation therapy with riluzole, a glutamate-modulating agent, in treatment-resistant OCD. METHODS: Thirteen patients aged between 18 and 65 years with a primary diagnosis of OCD that had proven resistant to standard treatment were treated with the addition of riluzole to their existing pharmacotherapy. Yale-Brown Obsessive Compulsive Scale (Y-BOCS), Hamilton Depression Inventory (HAM-D), and Hamilton Anxiety Inventory (HAM-A) scores were obtained weekly. RESULTS: Thirteen treatment-resistant OCD patients received riluzole 50 mg twice a day. Y-BOCS scores improved significantly over time. Of 13 patients, 7 (54%) demonstrated a >35% reduction in Y-BOCS scores, and 5 (39%) were categorized as treatment responders. HAM-D and HAM-A scores for the group also significantly improved over time. Riluzole was well tolerated with no serious adverse effects noted. CONCLUSIONS: Riluzole appears to have significant antiobsessional, antidepressant, and antianxiety properties. The addition of this agent may be of practical clinical benefit in patients with OCD.

Kushner MG, Kim SW, et al. D-cycloserine augmented exposure therapy for obsessive-compulsive disorder. Biol Psychiatry. 2007;62(8):835-8.

BACKGROUND: D-cycloserine (DCS), a glutamatergic partial N-methyl-d-aspartate (NMDA) agonist, can facilitate extinction learning related to cued fear in animals and humans. We predicted that DCS would accelerate obsession-related distress reduction in patients with obsessive-compulsive disorder (OCD) undergoing extinction-based exposure therapy. METHODS: We administered DCS (125 mg) or placebo in a double-blind fashion to individuals with OCD approximately 2 hours before each exposure session. RESULTS: D-cycloserine decreased both the number of exposure sessions required to achieve clinical milestones and the rate of therapy dropout. After four exposure sessions, patients in the DCS group reported significantly greater decreases in obsession-related distress compared with the placebo group; however, after additional sessions, the placebo group tended to catch up. CONCLUSIONS: D-cycloserine augmentation has the potential to increase the efficiency, palatability, and overall effectiveness of standard exposure therapy for OCD.

Greenberg WM, Benedict MM, et al. Adjunctive glycine in the treatment of obsessive-compulsive disorder in adults. J Psychiatr Res. 2009;43(6):664-70.

BACKGROUND: Recent preclinical findings, case reports and non-blinded studies have suggested that glutamatergic interventions may be efficacious for Obsessive-Compulsive Disorder (OCD). METHODS: We enrolled 24 adult outpatients with OCD on stabilized treatment regimens in a double-blind trial of adjunctive glycine, an NMDA glutamate receptor agonist. Participants were randomly assigned 1:1 to either placebo or glycine titrated to 60g/day, with follow-up visits scheduled at 4, 8 and 12 weeks. Yale-Brown Obsessive Compulsive Scale (Y-BOCS) was the principal outcome measure. RESULTS: Regimen non-adherence, principally related to complaints about the taste and/or nausea, resulted in only 14 individuals who were evaluable by predetermined criteria. Those receiving glycine (n=5) experienced a mean decrease of 6.04 points in Y-BOCS score, compared with a 1.00 point decrease for those receiving placebo (n=9). Using a hierarchical linear model, compared with placebo, individuals who received glycine had an average 0.82 decrease in Y-BOCS score for each week they remained in the study, not quite reaching statistical significance (p=0.053). Two of those receiving glycine were responders, versus none receiving placebo (p=0.11, ns, Fisher exact).

Despite the dropouts, two participants were known to have subsequently continued taking glycine through their regular treating psychiatrist for over a year. CONCLUSIONS: The glycine condition approached efficacy for treatment of OCD in this study, with the high dropout rate related to problems with palatability and small sample size the principal caveats. This may indicate a new strategy for treatment of OCD, although confirmatory studies are clearly needed. (ClinicalTrials.gov NCT00405535.).

Stewart SE, Jenike EA, et al. A single-blinded case-control study of memantine in severe obsessive-compulsive disorder. J Clin Psychopharmacol. 2010;30(1):34-9.

BACKGROUND: Obsessive-compulsive disorder (OCD) is a common debilitating psychiatric illness that typically improves but does not remit with first-line medication and behavioral treatments. Serotonergic agents including selective serotonin reuptake inhibitors and clomipramine have provided the mainstay of OCD medication management for decades. Combined dopamine/serotonergic agents such as atypical antipsychotics are presently the only OCD-augmenting strategies proven effective via randomized controlled trials. Despite increasing evidence for a pathogenic role of glutamate in OCD, no controlled trials of glutamatergic augmenting agents have been reported. METHODS: An intent-to-treat sample included 44 subjects receiving standard treatment at the McLean/Massachusetts General Hospital Intensive Residential Treatment (IRT) program, 22 of whom also received memantine augmentation. Admission, monthly and discharge measures of OCD, depression, and psychosocial functioning were collected by raters blinded to augmentation status. Matched controls were selected based on sex, initial OCD severity, psychosocial functioning, and timing of admission. The Clinical Global Improvement Scale captured global clinical change. RESULTS: Mean (SD) Yale-Brown Obsessive Compulsive Scale score decreases were 7.2 (6.4) among the cases and 4.6 (5.9) among the matched controls, reflecting mean clinical improvement among the cases (27.0% decrease) but not the controls (16.5% decrease). Mean (SD) depression severity score decreases were 5.8 (9.5) among the cases and 4.7 (9.9) among the controls. Initial intrusive obsessions were significantly more severe among marked responders compared with limited response or nonresponse cases (4.4 vs 2.9; t = 2.15; P = 0.048). CONCLUSIONS: This study provides preliminary supportive evidence for the effectiveness of memantine as a glutamatergic augmenting agent in severe OCD. Future randomized double-blind placebo-controlled trials are warranted.

Berlin HA, Koran LM, et al. Double-blind, placebo-controlled trial of topiramate augmentation in treatment-resistant obsessive-compulsive disorder. J Clin Psychiatry. 2011;72(5):716-21.

BACKGROUND: From 40% to 60% of obsessive-compulsive disorder (OCD) patients fail to tolerate or respond to selective serotonin reuptake inhibitors (SSRIs). Preclinical and neuroimaging studies have shown abnormally high glutamatergic concentrations in OCD patients and an association between decreased caudate glutamatergic concentrations and reduced OCD symptom severity after SSRI treatment. Topiramate inhibits glutamatergic conduction. METHOD: Thirty-six adult patients with DSM-IV-defined OCD were randomly assigned to topiramate (n = 18) and placebo (n = 18) groups in this 12-week, double-blind, placebo-controlled, parallel-groups trial. Subjects were taking the maximum SSRI dose they could tolerate for at least 12 weeks and their current dose for at least 6 weeks, which was maintained throughout the study. Primary outcome measures were changes in the Yale-Brown Obsessive Compulsive Scale (YBOCS) total score and compulsions and obsessions subscores. Patients were recruited and followed up between April 1, 2003, and April 13, 2006. RESULTS: Using mixed regression models (time [weeks] x treatment), we found a significant treatment effect on the YBOCS compulsions (P = .014) subscale, but not the obsessions (P = .99) subscale or the total score (P = .11). Over the 12-week trial, the topiramate group (mean endpoint dose = 177.8 +/- 134.2 mg/d; range, 50-400 mg/d) showed an average linear decrease of 5.38 points on the compulsions subscale compared to 0.6 points in the placebo group. Thirteen topiramate and 14 placebo subjects completed the study. Topiramate was not well tolerated in this trial: 28% (5/18) of the subjects discontinued the drug for adverse effects, and 39% (7/18) had a dose reduction for this reason. CONCLUSIONS: The results of this first double-blind, placebo-controlled trial of topiramate augmentation for treatment-resistant OCD suggest that topiramate may be beneficial for compulsions, but not obsessions. Modifications in glutamatergic function may be responsible, at least in part, for the improved response in compulsions seen with topiramate. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT00211744.

Afshar H, Roohafza h, et al. N-acetylcysteine add-on treatment in refractory obsessive-compulsive disorder: a randomized, double-blind, placebo-controlled trial. J Clin Psychopharmacol. 2012;32(6):797-803.

OBJECTIVE: This study aimed to evaluate the efficacy and safety of N-acetylcysteine, a glutamate-modulating agent, in patients with treatment-refractory obsessive-compulsive disorder as an ad-

junct to serotonin reuptake inhibitor treatment. METHODS: Forty-eight patients (36 women; mean +/- SD age, 30.93 +/- 4.99) with obsessive-compulsive disorder who failed to respond to a course of serotonin reuptake inhibitor treatment were randomized to a 12-week intervention period of N-acetylcysteine (up to 2400 mg/d) or placebo. Primary outcome measures were the change in Yale-Brown Obsessive Compulsive Scale (Y-BOCS) score from baseline to end point and the rate of full response in each group at the end of trial. Full response was defined as 35% or greater reduction in Y-BOCS score from baseline. RESULTS: Changes of Y-BOCS score were different over time ($P < 0.001$) and between groups ($P < 0.001$). N-acetylcysteine-assigned patients showed significantly improved mean Y-BOCS score ($P = 0.003$) and Clinical Global Impression-Severity of Illness scale score ($P = 0.01$) but not Clinical Global Impression-Improvement scale score at study end point. Of the patients in the N-acetylcysteine group, 52.6% were full responders at the end of the study, which was significantly higher than 15% of the patients in the placebo group ($P = 0.013$). CONCLUSION: This trial suggests that N-acetylcysteine may be a safe and effective option to augment standard treatment in patients with refractory obsessive-compulsive disorder.

Bruno A, Micò u, et al. Lamotrigine augmentation of serotonin reuptake inhibitors in treatment-resistant obsessive-compulsive disorder: A double-blind, placebo-controlled study. Journal of Psychopharmacology. 2012;26(11):1456-62.

The present 16-week double-blind, randomized, placebo-controlled trial had the aim to explore the efficacy of lamotrigine add-on pharmacotherapy on clinical symptomatology and cognitive functioning in a sample of patients with treatment-resistant obsessive–compulsive disorder (OCD) receiving serotonin reuptake inhibitors (SRIs). After clinical and neurocognitive assessments, patients were randomly allocated to receive, in a double-blind design, 100 mg/day of lamotrigine or a placebo. A final sample of 33 patients completed the study. The results obtained indicate that lamotrigine added to stable SRI treatment substantially improved obsessive–compulsive (Yale–Brown Obsessive Compulsive Scale: obsessions, $p < 0.0001$; compulsions, $p < 0.0001$; total score, $p < 0.0001$), and affective symptoms (Hamilton Rating Scale for Depression $p < 0.0001$). Regarding cognitive functions, improvement was observed only in Semantic Fluency ($p = 0.004$). The findings provide evidence that lamotrigine augmentation of SRI treatment is well tolerated and may be proposed as an effective therapeutic strategy to improve outcome in treatment-resistant OCD. (PsycINFO Database Record (c) 2014 APA, all rights reserved) (journal abstract).

Ghaleiha A, Entezari N, et al. Memantine add-on in moderate to severe obsessive-compulsive disorder: randomized double-blind placebo-controlled study. J Psychiatr Res. 2013;47(2):175-80.

There is a growing body of evidence for the efficacy of memantine augmentation in patients with obsessive-compulsive disorder (OCD). However, to date, no double-blind study has addressed this issue. The objective of the present randomized double-blind placebo-controlled study was to evaluate efficacy and tolerability of memantine add-on treatment in patients with moderate to severe OCD. Forty-two patients with the diagnosis of OCD based on DSM-IV-TR who had a Yale-Brown Obsessive Compulsive Scale (Y-BOCS) score of >/=21 were randomly assigned to memantine (10 mg/day for the first week, and 20 mg/day for the rest of the trial) or placebo in addition to fluvoxamine for eight weeks. Patients were assessed using Y-BOCS every two weeks. Thirty-eight patients completed the study. Repeated measure ANOVA showed significant effect for time x treatment interaction in total scale [$F (2.096, 75.470) = 5.280$, $P = 0.006$] and obsession [$F (2.340, 94.547) = 5.716$, $P = 0.002$] and near significant effect for compulsion subscales [$F (2.005, 79.179) = 2.841$, $P = 0.065$]. By week eight, all patients in the memantine group and six (32%) patients in the placebo group [P value of Fisher's exact test <0.001] met the criteria for partial and complete response. At the end of the trial, 17 (89%) patients in the memantine group compared with six (32%) patients in the placebo group achieved remission ($chi(2)(1) = 13.328$, $P < 0.001$). Frequency of side-effects was not significantly different between the two groups. In summary, we showed that memantine add-on to fluvoxamine significantly improved short-term outcomes in patients with moderate to severe OCD.

Haghighi M, Jahangard L, et al. In a double-blind, randomized and placebo-controlled trial, adjuvant memantine improved symptoms in inpatients suffering from refractory obsessive-compulsive disorders (OCD). Psychopharmacology (Berl). 2013;228(4):633-40.

BACKGROUND: There is growing evidence that memantine, a noncompetitive N-methyl-D-aspartate receptor antagonist, may be applied as an add-on in treating patients suffering from obsessive-compulsive disorders (OCD). The aim of the present study was therefore to assess the effect of adjuvant memantine in a double-blind, randomized, and placebo-controlled study of the treatment of patients suffering from OCD. METHOD: A total of 40 inpatients (32 females (80 %); mean age = 31.25

years) suffering from OCD were randomly assigned to a treatment (administration of memantine) or a control group (placebo). Treatment lasted for 12 consecutive weeks. All patients were treated with selective serotonin re-uptake inhibitors or clomipramine. Patients completed the Yale-Brown Obsessive Compulsive Scale four times. Experts' ratings consisted in clinical global impression (clinical global impressions (CGI), illness severity and illness improvement; two to three times). Liver enzymes SGOT and SGPT were also assessed (twice). RESULTS: Of the 40 inpatients approached, 29 completed the 12 consecutive weeks of the study. Of the 11 dropouts, 6 were in the target group and five in the control group. Symptoms significantly decreased across the period of the study, but particularly in the treatment compared with the control group (significant time x group interaction). Illness severity (CGI severity) also significantly decreased over time but more so in the treatment than in the control group (significant time x group interaction). Illness improvements (CGI improvements) were not significant. CONCLUSIONS: The pattern of results from the present double-blind, randomized, and placebo-controlled study for the treatment of patients suffering from OCD suggests that adjuvant memantine does significantly and favorably impact on OCD.

Grant PJ, Joseph LA, et al. 12-week, placebo-controlled trial of add-on riluzole in the treatment of childhood-onset obsessive-compulsive disorder. Neuropsychopharmacology. 2014;39(6):1453-9.

Many children with childhood-onset obsessive-compulsive disorder (OCD) fail to respond adequately to standard therapies. Evidence from preclinical and clinical studies suggests that the glutamatergic neurotransmitter system might be an alternative treatment target. This study examined the efficacy of riluzole, a glutamatergic modulator, as an adjunctive therapy for children with treatment-resistant OCD. In a 12-week, double-blind, placebo-controlled study, 60 treatment-resistant children and adolescents (mean age=14.5 +/- 2.4 years), with moderate to severe OCD (mean Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS)=28.2 +/- 3.7), 17 of whom also had concomitant autism spectrum disorder, were randomized to receive riluzole (final dose of 100 mg/day) or placebo in addition to the existing treatment regimen. Fifty-nine subjects completed the randomized trial. Primary outcome measures were changes on the CY-BOCS, the Clinical Global Impressions Scale, and the Children's Global Assessment Scale. Riluzole was fairly well tolerated, although it was associated with one case of pancreatitis and five instances of slight increases in transaminases. All subjects showed significant reductions in CY-BOCS scores during treatment; however, there was no significant difference between placebo and riluzole on any of the primary or secondary outcome measures. The study failed to demonstrate superiority of riluzole over placebo as an adjunctive treatment for children with childhood-onset OCD. However, future studies may show benefits for less treatment-refractory children with fewer concomitant medications.

Sahraian A, Bigdeli M, et al. Topiramate as an adjuvant treatment for obsessive compulsive symptoms in patients with bipolar disorder: a randomized double blind placebo controlled clinical trial. J Affect Disord. 2014;166:201-5.

BACKGROUND: It has not been examined trialed whether obsessive compulsive symptoms in patients with bipolar disorder respond to topiramate as an adjuvant treatment. METHODS: This 4-month double-blind placebo-controlled randomized clinical trial examined the efficacy and safety of augmentation with topiramat for treating the patients with bipolar disorder, manic phase type-I, and obsessive compulsive disorder symptoms. Both groups received lithium+olanzapine+clonazepam. However, one group received topiramate and the other group placebo as adjuvant medications. Yale Brown obsessive compulsive behavior scale was used to assess the outcome. Adverse effects were also recorded. RESULTS: A total of 32 patients completed this trial. The mean score decreased from 24.2(4.8) to 17.6(8.7) in the topiramate group (P<0.003) and from 20.9(2.9) to 9.6(3.5) in the placebo group during this trial (P<0.0001). Additionally, 9(52.9%) out of 17 patients in the topiramate group and 2(12.5%) out of 16 patients in the placebo group showed more than 34% decline in YBOC score (x2=6.0, df=1, P<0.01). No serious adverse effects were detected. LIMITATIONS: The limitations of the present study were its small sample size and the fact that it was conducted in a single center. CONCLUSIONS: The combination of lithium+olanzapine+clonazepam decreased the symptoms of obsessive compulsive disorder in the patients with bipolar disorder type I. However, topiramate had a more significant effect than placebo on improvement of the patients with bipolar disorder and obsessive compulsive symptoms. This combination seems to be without serious adverse effects.

Andersson E, Hedman E, et al. D -cycloserine vs placebo as adjunct to cognitive behavioral therapy for obsessive-compulsive disorder and interaction with antidepressants: A randomized clinical trial. JAMA Psychiatry. 2015;72(7):659-67.

Importance: It is unclear whether D-cycloserine (DCS), a partial N-methyl-D-aspartate agonist that enhances fear extinction, can augment the effects of exposure-based cognitive behavioral

therapy (CBT) for obsessive-compulsive disorder (OCD). OBJECTIVES: To examine whether DCS augments the effects of CBT for OCD and to explore (post hoc) whether concomitant antidepressant medication moderates the effects of DCS. Design, setting, and participants: A 12-week, double-blind randomized clinical trial with 3-month follow-up conducted at an academic medical center between September 4, 2012, and September 26, 2013. Participants included 128 adult outpatients with a primary diagnosis of OCD and a Yale-Brown Obsessive Compulsive Scale (Y-BOCS) score of 16 or higher. Concurrent antidepressant medication was permitted if the dose had been stable for at least 2 months prior to enrollment and remained unchanged during the trial. The main analysis was by intention-to-treat population. Interventions" All participants received a previously validated Internet-based CBT protocol over 12 weeks and were randomized to receive either 50 mg of DCS or placebo, administered 1 hour before each of 5 exposure and response prevention tasks. Main outcomes and measures: Clinician-administered Y-BOCS score at week 12 and at 3-month follow-up. Remission was defined as a score of 12 or lower on the Y-BOCS. Result: In the primary intention-to-treat analyses, DCS did not augment the effects of CBT compared with placebo (mean [SD] clinician-rated Y-BOCS score, DCS: 13.86 [6.50] at week 12 and 12.35 [7.75] at 3-month follow-up; placebo: 11.77 [5.95] at week 12 and 12.37 [6.68] at 3-month follow-up) but showed a significant interaction with antidepressants (clinician-rated Y-BOCS, B = −1.08; Z = −2.79; P = .005). Post hoc analyses revealed that antidepressants significantly impaired treatment response in the DCS group but not the placebo group, at both posttreatment and follow-up (clinician-rated Y-BOCS: t62 = −3.00; P = .004; and t61 = −3.49; P < .001, respectively). In the DCS group, a significantly greater proportion of antidepressant-free patients achieved remission status at follow-up (60% [95%CI, 45%-74%]) than antidepressant-medicated patients (24%[95%CI, 9%-48%]) (P = .008). Antidepressants had no effect in the placebo group (50% [95%CI, 36%-64%] remission rate in both groups). Conclusions and relevance: The findings suggest that antidepressants may interact with DCS to block its facilitating effect on fear extinction. Use of DCSmay be a promising CBT augmentation strategy but only in antidepressant-free patients with OCD. (PsycINFO Database Record (c) 2015 APA, all rights reserved) (journal abstract).

Pittenger C, Bloch MH, et al. Riluzole augmentation in treatment-refractory obsessive-compulsive disorder: a pilot randomized placebo-controlled trial. J Clin Psychiatry. 2015;76(8):1075-84.

OBJECTIVE: Obsessive-compulsive disorder (OCD) affects approximately 2.5% of the population and is associated with significant morbidity. Many patients receive little benefit from the best available treatments, and even those who do respond often suffer from significant residual symptoms. Convergent evidence suggests that abnormalities in glutamate homeostasis and neurotransmission may contribute to OCD and that glutamate-modulating medications may be of benefit in patients whose symptoms are refractory to standard interventions. Small open-label trials of augmentation of serotonin reuptake inhibitor (SRI) pharmacotherapy with the glutamate modulator riluzole have suggested benefit in adults with refractory symptoms. We report a pilot randomized placebo-controlled trial of riluzole augmentation of ongoing SRI treatment in SRI-refractory patients. METHOD: Outpatients (n = 27) and inpatients (n = 11) with DSM-IV OCD on stable SRI pharmacotherapy were randomized between November 2006 and December 2012 to receive riluzole 50 mg or placebo twice a day and followed for 12 weeks after a 2-week placebo lead-in phase. RESULTS: Riluzole was well tolerated; 1 patient experienced moderate nausea, but none discontinued treatment due to side effects. While there was nominally greater Y-BOCS improvement in the riluzole group (our primary outcome) compared to placebo, it did not reach statistical significance. In the outpatient subsample, a trend suggesting benefit from riluzole augmentation for obsessions (P = .056, 2-tailed, uncorrected) was found in a secondary analysis. Among outpatients, more achieved at least a partial response (> 25% improvement) with riluzole than with placebo (P = .02 in a secondary analysis). CONCLUSIONS: Riluzole may be of benefit to a subset of patients. Larger samples would be required to detect effects of the order suggested by the nominal improvement in our outpatient subsample. TRIAL REGISTRATION: ClinicalTrials.gov identifier: NCT00523718.

Sarris J, Oliver G, et al. N-acetyl cysteine (NAC) in the treatment of obsessive-compulsive disorder: A 16-week, double-blind, randomised, placebo-controlled study. CNS Drugs. 2015;29(9):801-9.

Background: Obsessive-compulsive disorder (OCD) is a disabling mental illness for which pharmacological and psychosocial interventions are all too often inadequate. Recent preclinical and clinical studies have implicated dysfunction of glutamatergic neurotransmission in the pathophysiology of OCD. The amino acid-based nutraceutical N-acetyl cysteine (NAC) is a safe and readily available agent that has been found to modify the synaptic release of glutamate in subcortical brain regions via modulation of the cysteine-glutamate antiporter. Objective: The aim of this study was to assess the efficacy and safety of NAC in treating OCD. Methods: A 16-week, double-blind, placebo-

controlled, randomised trial using 3 g/day of NAC (1.5 g twice daily) in 44 participants (aged 18–70 years) with Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5)-diagnosed OCD, during 2013–2015. The primary outcome measure was the Yale–Brown Obsessive Compulsive Scale (YBOCS), conducted every 4 weeks.Results: Analysis of the full sample (intention-to-treat) with repeated measures mixed linear modelling revealed a nonsignificant time × treatment interaction for the YBOCS scale total score (p = 0.39). A per-protocol analysis removing protocol violators also failed to show a significant time × treatment interaction for YBOCS total score (p = 0.15). However, a significant time × treatment interaction was observed for the YBOCS 'Compulsions' subscale in favour of NAC (p = 0.013), with a significant reduction observed at week 12 (dissipating at week 16). At 16 weeks, only four (20 %) participants were considered 'responders' (YBOCS ≥35 % reduction at endpoint) versus four (27 %) in the placebo group. The NAC was well-tolerated, aside from more cases of heartburn occurring compared with placebo (p = 0.045). Conclusion: Further research involving NAC for OCD may require larger samples to detect moderate or small effect sizes, involve dosage or formulation differences, use in concert with exposure therapy, or an additional post-study observational period to mitigate study withdrawal. (PsycINFO Database Record (c) 2015 APA, all rights reserved) (journal abstract).

5.3.5. Otros fármacos (por ejemplo, ondansetrón) (17 – 1984-2015)

Rasmussen SA. Lithium and tryptophan augmentation in clomipramine-resistant obsessive-compulsive disorder. Am J Psychiatry. 1984;141(10):1283-5.

Obsessive-compulsive patients with symptoms resistant to clomipramine were treated by lithium or L-tryptophan augmentation. The improvement noted supports the hypothesis that increasing serotonergic neurotransmission ameliorates obsessive symptoms.

McDougle CJ, Price LH, et al. A controlled trial of lithium augmentation in fluvoxamine-refractory obsessive-compulsive disorder: lack of efficacy. J Clin Psychopharmacol. 1991;11(3):175-84.

Two- and 4-week double-blind placebo-controlled trials of lithium augmentation of ongoing fluvoxamine treatment trials were conducted in 20 and 10 patients, respectively, with primary obsessive-compulsive disorder (OCD) who had failed to respond to fluvoxamine alone. Although 2 weeks of double-blind lithium augmentation produced a small but statistically significant reduction in obsessive-compulsive symptoms, most patients did not have a clinically meaningful response. Furthermore, there was no statistical or clinical improvement in obsessive-compulsive symptoms during the subsequent 4-week double-blind, placebo-controlled trial of lithium augmentation. On the basis of treatment response criteria, only 18% and 0% of the patients responded to lithium augmentation of fluvoxamine during the 2- and 4-week treatment trials, respectively. In light of the previously reported 44% response rate to lithium augmentation in treatment-resistant depressed patients on fluvoxamine, the results of this study suggest that pathophysiological differences may exist between OCD and depression. The routine use of lithium augmentation in the management of patients with OCD who are refractory to serotonin reuptake inhibitors is not supported by these findings.

Pigott TA, Pato MT, et al. A controlled comparison of adjuvant lithium carbonate or thyroid hormone in clomipramine-treated patients with obsessive-compulsive disorder. J Clin Psychopharmacol. 1991;11(4):242-8.

In this study, 16 patients with obsessive-compulsive disorder (OCD) who had partially improved during at least 6 months of treatment with clomipramine were sequentially treated with triiodothyronine and lithium carbonate in an 8-week double-blind cross-over study. Both triiodothyronine and lithium carbonate have been reported to be efficacious in open trials as adjunctive agents when combined with tricyclics in the treatment of OCD and depressed patients. However, in our controlled study, OCD and depressive symptoms, as assessed by standardized rating scales in the patient group as a whole, did not significantly change after either adjuvant treatment. Further analysis on an individual patient basis revealed that neither adjuvant medication was associated with a clinically meaningful change (greater than 25%) in OCD symptoms. However, lithium, but not triiodothyronine, adjuvant therapy was associated with a 25% or greater reduction in depression scores in 44% of the patients. This controlled study lends further support to the contention that OCD may represent a disorder with characteristics distinct from affective disorders.

Pigott TA, L'Heureux F, et al. A double-blind study of adjuvant buspirone hydrochloride in clomipramine-treated patients with obsessive-compulsive disorder. J Clin Psychopharmacol. 1992;12(1):11-8.

In this study, 14 patients with obsessive-compulsive disorder (OCD) who had received at least 3 months of treatment with clomipramine were treated with the anxiolytic agent buspirone in a 10-week, double-blind study. Before the addition of buspirone, these patients as a group had shown a partial but incomplete reduction (averaging 28%) in OCD symptoms during clomipramine treatment alone. Because buspirone has been reported to be efficacious as a sole agent and as an adjunct agent in combination with fluoxetine in patients with OCD, we were interested in assessing whether buspirone added to clomipramine treatment would be associated with further significant reductions in OCD or depressive symptoms. Although adjuvant buspirone treatment was well tolerated in most subjects, mean OCD and depressive symptoms, as evaluated by standardized rating scales, did not significantly change from baseline scores achieved on clomipramine treatment alone, either after the addition of placebo for 2 weeks or buspirone (57 +/- 7 mg/day) for an additional 10 weeks. However on an individual basis, 4 (29%) of the 14 patients did have an additional 25% reduction in OCD symptoms after adjuvant buspirone treatment. This double-blind study suggests that adjunctive buspirone therapy is not generally associated with significant further clinical improvement in OCD or depressive symptoms compared with clomipramine monotherapy, but that there may be a subgroup of patients who do benefit from adjuvant buspirone therapy.

Grady TA, Pigott TA, et al. Double-blind study of adjuvant buspirone for fluoxetine-treated patients with obsessive-compulsive disorder. Am J Psychiatry. 1993;150(5):819-21.

In a double-blind, crossover study, 13 fluoxetine-treated patients with obsessive-compulsive disorder were given adjuvant buspirone and placebo for 4 weeks each. There were no significant differences between buspirone and placebo in obsessive-compulsive, depressive, or anxiety symptoms.

McDougle CJ, Goodman WK, et al. Limited therapeutic effect of addition of buspirone in fluvoxamine-refractory obsessive-compulsive disorder. Am J Psychiatry. 1993;150(4):647-9.

The authors found that buspirone added to the treatment of 33 patients with obsessive-compulsive disorder who were refractory to the serotonin reuptake inhibitor fluvoxamine was no better than placebo in reducing obsessive-compulsive, depressive, or anxiety symptoms. This finding suggests that addition of buspirone to ongoing fluvoxamine therapy is not an effective treatment strategy for most patients with obsessive-compulsive disorder.

Fux M, Benjamin J, et al. Inositol versus placebo augmentation of serotonin reuptake inhibitors in the treatment of obsessive–compulsive disorder: A double-blind cross-over study. International Journal of Neuropsychopharmacology. 1999;2(3):193-5.

Current serotonin reuptake inhibitor (SRI) treatments for obsessive–compulsive disorder (OCD) provide only partial benefit. A previous study suggested that inositol alone is efficacious in OCD. Ten Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) OCD patients (mean age 30.3 yrs) completed a study of 18 g inositol or placebo for 6 wks each in addition to ongoing SRI treatment in a double-blind randomized cross-over design. Weekly assessments included the Yale–Brown Obsessive–Compulsive Scale and Hamilton Depression and Anxiety scales. Assessments were taken at baseline, 2 wks, 4 wks, and 6 wks after receiving treatment. No significant difference was found between the 2 treatment phases. (PsycINFO Database Record (c) 2012 APA, all rights reserved).

Dannon PN, Sasson Y, et al. Pindolol augmentation in treatment-resistant obsessive compulsive disorder: a double-blind placebo controlled trial. Eur Neuropsychopharmacol. 2000;10(3):165-9.

OBJECTIVE: To evaluate the efficacy of pindolol augmentation in treatment-resistant obsessive compulsive disorder (OCD) patients who were unsuccessfully treated with serotonin reuptake inhibitors. METHOD: Fourteen treatment-resistant OCD patients were treated with paroxetine for 17.4+/-2.1 weeks up to 60 mg/d after they failed at least two other serotonin reuptake inhibitor trials. The patients, who did not respond to open-label paroxetine treatment, were assigned to a double-blind, placebo-controlled pindolol (2.5 mgx3/d) augmentation. All the subjects were evaluated biweekly for a six-week period with the Yale-Brown Obsessive Compulsive Scale (Y-BOCS), Hamilton Anxiety Scale (HAM-Anx), and Montgomery Asberg Depression Rating Scale (MADRS). Data was analyzed by paired t-test, and ANOVA with repeated measures. RESULTS: Pindolol augmentation to paroxetine (n=8) as compared to placebo augmentation (n=6), was associated with a significant (P<0.01) improvement in Y-BOCS as measured by paired t-test after the fourth week of the treatment and by ANOVA with repeated measures (df: 4.9, f: 3,3, P<0.006). Although no significant differences were found between placebo and pindolol groups on HAM-Anx and MADRS, a

trend for improvement in the pindolol group was noted. CONCLUSIONS: The results of our study demonstrated that pindolol may augment the therapeutic effect of paroxetine in treatment-resistant OCD patients.

Fux M, Benjamin J, et al. A placebo-controlled cross-over trial of adjunctive EPA in OCD. J Psychiatr Res. 2004;38(3):323-5.

Several clinical studies showed beneficial effects of omega-3 fatty acids in major affective disorders, including resistant depression. Some antidepressants are also effective, albeit less so, in obsessive-compulsive disorder (OCD). We therefore undertook a preliminary placebo-controlled cross-over trial of adjunctive eicosapentaenoic acid (EPA) in OCD. Eleven patients with current obsessive-compulsive disorder, who were on a stable maximally tolerated dose of SSRI with no further improvement over at least the last two months, were recruited. Subjects were randomly allocated to begin 6 weeks of placebo (2 g liquid paraffin per day) followed by 6 weeks of 2 g of EPA or EPA followed by placebo. Patients continued their prior SSRIs at the same dose. Assessments were performed with the Yale-Brown Obsessive-Compulsive Scale (YBOCS), and the Hamilton Rating Scales for depression (HAM-D) and anxiety (HAM-A). There were no effects of order of treatment. Time had a main effect of YBOCS scores; mean scores declined from 26.0 (+/-5) to 17.6 (+/-6) by week 6 on placebo and to 18.5 (+/-4) on EPA. There were no effects on HAM-D and HAM-A. No clinically relevant side effects were reported. The results of this study suggest that adjunctive EPA is ineffective against OCD.

Koran LM, Aboujaoude E, et al. Double-blind treatment with oral morphine in treatment-resistant obsessive-compulsive disorder. J Clin Psychiatry. 2005;66(3):353-9.

BACKGROUND: Obsessive-compulsive disorder (OCD) often responds inadequately to serotonin reuptake inhibitors (SRIs). A case series reported substantial response to once-weekly oral morphine. We conducted a placebo-controlled, double-blind trial to investigate whether once-weekly oral morphine is effective in SRI-resistant OCD. METHOD: Subjects with DSM-IV-defined OCD for > or =3 years who had failed > or =2 adequate SRI trials and had a Yale-Brown Obsessive Compulsive Scale (Y-BOCS) score of > or =20 were recruited. Current medications were continued. Subjects were randomly assigned to random-order, 2-week blocks of once-weekly morphine, lorazepam, and placebo. Week 2 dosage was increased, decreased, or maintained depending on response and side effects. RESULTS: We enrolled 23 subjects, who had failed 2 to 6 SRI trials. The median screening Y-BOCS score was 29. The median Y-BOCS score after morphine (highest dose) was 25 (median decrease = 13%). Seven subjects (30%) were responders (Y-BOCS decreases > or =25%). The median Y-BOCS score after lorazepam (highest dose) was 27 (median decrease = 6%). Four subjects (17%) responded to lorazepam; 1 was a morphine responder. The median Y-BOCS score after placebo (highest dose) was 27 (median decrease = 7%), and no subject responded. Responses differed significantly among the 3 conditions (Friedman 2-way analysis of variance, chir(2) = 13.92, df = 2, p = .01). Wilcoxon matched-pairs signed-rank tests (T = 56.5, p = .05) showed significance for morphine versus placebo but not lorazepam versus placebo. CONCLUSION: Our results support the hypothesis that once-weekly oral morphine can reduce symptoms in some treatment-resistant OCD patients. The mechanism of action is unknown. Further studies of mu-agonists and glutamate antagonists are warranted.

Amiaz R, Fostick L, et al. Naltrexone augmentation in OCD: a double-blind placebo-controlled cross-over study. Eur Neuropsychopharmacol. 2008;18(6):455-61.

Current treatments for Obsessive Compulsive Disorder (OCD) rely primarily on serotonergic mechanisms. However, approximately 30% of patients do not respond to serotonin reuptake inhibitors and remain chronically ill. Given the behavioral similarities between some of the compulsive behaviors in OCD and addiction, we hypothesized that the opioid antagonist naltrexone might attenuate compulsions in OCD as well. The effect of naltrexone augmentation to SRI was compared to placebo in 10 OCD outpatients who had not responded to an adequate dose of SSRI or clomipramine for at least 2 months. Participants underwent 5 weeks of treatment with naltrexone or placebo (and 1 week of tapering) in a randomized, double-blind, cross-over design. Patients were evaluated weekly using the Y-BOCS, CGI, HAM-A, and MADRS scales. A two-way repeated measures MANOVA revealed no significant effect for Y-BOCS. However, while receiving naltrexone, patients had significantly higher scores on CGI, MADRS and HAM-A as compared to placebo. The lack of significant findings on OC symptoms could be due to either ceiling effect or alternatively, due to a non-specific exacerbation on anxiety and depression but not on OC symptoms.

Pallanti S, Bernardi S, et al. Ondansetron augmentation in treatment-resistant obsessive-compulsive disorder: a preliminary, single-blind, prospective study. CNS Drugs. 2009;23(12):1047-55.

Serotonin and dopamine neuronal systems have been implicated in the modulation of obsessive-compulsive disorder (OCD) symptoms. About 40% of OCD patients do not respond to first-line selective serotonin reuptake inhibitor (SSRI) treatment; among those, dopamine blocker augmentation has been reported to improve the rate of response by an additional one-third. Given that serotonin 5-HT(3) receptors are indirect inhibitors of cortico-mesolimbic dopamine release, augmentation with the 5-HT(3) receptor antagonist ondansetron in combination with SSRIs and antipsychotics has potential efficacy in treatment-resistant OCD patients. To assess the efficacy and tolerability of ondansetron in combination with SSRIs and antipsychotics in patients with treatment-resistant OCD. In total, 14 patients with a DSM-IV diagnosis of OCD, who were treatment resistant and receiving stable treatment with SSRIs and antipsychotic augmentation, entered a 12-week, single-blind trial of ondansetron. The drug was initiated at a dosage of 0.25 mg twice daily for 6 weeks and was then titrated to 0.5 mg twice daily for 6 weeks. Of the 14 patients, nine (64.3%) experienced a treatment response (> or =25% reduction in the Yale-Brown Obsessive Compulsive Scale [YBOCS] score and a Clinical Global Impressions-Improvement [CGI-I] score of 1 or 2) at 12 weeks. The average reduction in YBOCS-rated symptoms for the whole group was 23.2%. None of the treated patients experienced symptom exacerbation or significant adverse effects. These results suggest that low-dose ondansetron may have promise as an augmentation strategy for some patients with OCD resistant to SSRIs and antipsychotic augmentation, but further controlled trials are required. Trial registration number (ClinicalTrials.gov): NCT00796497.

Sayyah M, Boostani H, et al. A preliminary randomized double-blind clinical trial on the efficacy of celecoxib as an adjunct in the treatment of obsessive-compulsive disorder. Psychiatry Res. 2011;189(3):403-6.

Obsessive-compulsive disorder is a common neuropsychiatric condition. Although a variety of pharmaceutical agents is available for its treatment, psychiatrists have found that many patients cannot tolerate the side effects, do not respond to treatment adequately, and may finally discontinue their treatment. However, augmentation strategies have been shown to have some benefits in the treatment of OCD. These include reducing both the overall cost of treatment and the side effects. The purpose of this study was to assess the efficacy of celecoxib as an adjuvant agent in the treatment of OCD in an 8-week, double-blind, placebo controlled trial. To this end, 25 patients were assigned to a study group and were given fluoxetine 20mg/day plus celecoxib 400mg/day (200mg BID). The control group included 25 patients who were given fluoxetine 20mg/day plus placebo. Both protocols significantly lowered scores on the Yale-Brown Obsessive-Compulsive Scale over the trial period. The combination of fluoxetine and celecoxib decreased the symptoms of obsessions and compulsions significantly more than fluoxetine plus placebo. The results of this study suggest that celecoxib can be an effective adjuvant agent in the management of patients with OCD; therefore, anti-inflammatory therapies should be further investigated.

Askari N, Moin M, et al. Granisetron adjunct to fluvoxamine for moderate to severe obsessive-compulsive disorder: a randomized, double-blind, placebo-controlled trial. CNS Drugs. 2012;26(10):883-92.

BACKGROUND: Several small studies have shown beneficial effects of ondansetron, a serotonin 5-HT(3) receptor antagonist, in the treatment of obsessive-compulsive disorder (OCD). The efficacy of other 5-HT(3) receptor antagonists in patients with OCD is still unclear. Granisetron does not alter cytochrome P450 activity and might have a lower risk of drug interactions, a longer duration of action and a better tolerability profile than other 5-HT(3) receptor antagonists. OBJECTIVE: The objective of this study was to assess the efficacy and tolerability of granisetron augmentation of fluvoxamine in patients with OCD. STUDY DESIGN: This was a two-centre, randomized, double-blind, placebo-controlled, parallel-group study conducted from November 2011 to March 2012. STUDY SETTING: The study setting was outpatient clinics of two large referral centres. PATIENTS: Study participants were men and women, aged 18-60 years, who met the diagnostic criteria of OCD based on the DSM-IV-TR and who had a Yale-Brown Obsessive Compulsive Scale (Y-BOCS) score of at least 21. INTERVENTIONS: Participants were randomly assigned to granisetron (Kytril((R)); SmithKline Beecham, Philadelphia, PA, USA) 1 mg every 12 hours or placebo every 12 hours in addition to fluvoxamine for 8 weeks. MAIN OUTCOME MEASURE: Patients were assessed using the Y-BOCS at baseline, second, fourth, sixth and eighth weeks. The primary outcome measure was the difference in the score change of Y-BOCS total score from baseline to week 8 between the two groups. We also compared changes in the obsession and compulsion subscales of the Y-BOCS, and frequencies of partial response (>/=25% reduction in Y-BOCS score), complete response (>/=35% reduction in

Y-BOCS score) and remission (Y-BOCS score </=16) between the two groups. RESULTS: Of the 42 included patients, 39 (20 in the placebo group, 19 in the granisetron group) completed the study. Significant time X treatment interaction was observed for total Y-BOCS (F [2.097, 79.678] = 4.941, p = 0.009), obsession (F [2.337, 88.799] = 4.938, p = 0.006) and compulsion (F [2.050, 77.899] = 4.674, p = 0.012) subscales. By week 8, complete response and remission were achieved by 20 (100%) and 18 (90%) patients in the granisetron group and by 7 (35%) patients in the placebo group (p-value of Fisher's exact test <0.001, risk ratio (RR) [95% CI] = 3.857 [2.039, 7.297]). There was no significant difference in the tolerability between the two regimens. CONCLUSION: Granisetron is an efficacious adjunct for the short-term treatment of patients with moderate to severe OCD and is well tolerated. CLINICAL TRIAL REGISTRATION NUMBER: IRCT201202041556N32.

Sayyah M, Olapour A, et al. Evaluation of oral zinc sulfate effect on obsessive-compulsive disorder: a randomized placebo-controlled clinical trial. Nutrition. 2012;28(9):892-5.

OBJECTIVE: Obsessive-compulsive disorder is a common neuropsychiatric condition. Although various pharmaceutical agents are available for the treatment of obsessive-compulsive disorder, psychiatrists often find that many patients cannot tolerate the side effects of these medications, the patients do not respond properly to the treatment, or the medications lose their effectiveness after a period of treatment. The augmentation with safe supplementation of medication, such as with trace elements, may be a solution to some of these problems. METHODS: This study was a prospective, double-blinded, 8-wk trial. Twelve patients were given fluoxetine (20 mg/d) plus zinc (440 mg/d) and 11 patients were given fluoxetine plus placebo for 8 wk. RESULTS: Both groups showed a decrease in the mean Yale-Brown Obsessive-Compulsive Scale score. Based on t tests, in weeks 2 and 8, patients treated with fluoxetine plus zinc had significantly lower scores than those treated with fluoxetine plus placebo. CONCLUSION: The results show that zinc, as adjuvant agent for obsessive-compulsive disorder, produces improved outcomes.

Heidari M, Zarei M, et al. Ondansetron or placebo in the augmentation of fluvoxamine response over 8 weeks in obsessive-compulsive disorder. Int Clin Psychopharmacol. 2014;29(6):344-50.

The aim of this study was to investigate the efficacy and safety of ondansetron as an augmentative agent to fluvoxamine in the treatment of patients with obsessive-compulsive disorder (OCD). Forty-six men and women, aged 18-60 years, who fulfilled the diagnostic criteria of OCD on the basis of the DSM-IV-TR and had a Yale-Brown Obsessive Compulsive Scale (Y-BOCS) score of at least 21 were recruited into the study. The patients randomly received either ondansetron (8 mg/day) or placebo for 8 weeks. All patients received fluvoxamine (100 mg/day) for the first 4 weeks, followed by 200 mg/day for the rest of the trial. The patients were assessed using the Y-BOCS and the adverse event checklists at baseline, and the second, fourth, sixth, and eighth week. Forty-four patients completed the study. The Y-BOCS total score as well as the Y-BOCS obsession subscale score and compulsion subscale score showed significantly greater reduction in the ondansetron group than in the placebo group. There was no significant difference in adverse events between the two groups. In this 8-week double-blind randomized-controlled trial, ondansetron showed significant beneficial effect as an augmentative agent with fluvoxamine in patients with moderate to severe OCD and it was generally well tolerated.

Shalbafan M, Mohammadinejad P, et al. Celecoxib as an adjuvant to fluvoxamine in moderate to severe obsessive-compulsive disorder: A double-blind, placebo-controlled, randomized trial. Pharmacopsychiatry. 2015;48(4-5):136-40.

Introduction: A growing body of evidence implicates inflammatory cascades in the pathophysiology of obsessive-compulsive disorder (OCD), making this pathway a target for development of novel treatments. Methods: 50 outpatients with moderate to severe OCD participated in the trial, and underwent 10 weeks of treatment with either celecoxib (200 mg twice daily) or placebo as an adjuvant to fluvoxamine. Participants were investigated using Yale-Brown Obsessive Compulsive Scale (Y-BOCS). The main outcome measure was to assess the efficacy of celecoxib in improving the OCD symptoms. Results: General linear model repeated measures demonstrated significant effect for time × treatment interaction on the Y-BOCS total scores [F (1.38, 66.34) = 6.91, p = 0.005]. Kaplan-Meier estimation with log-rank test demonstrated significantly more rapid response in the celecoxib group than the placebo group (p < 0.001). There was no significant difference in adverse event frequencies between the groups. Discussion: The results of the current study suggest that celecoxib could be a tolerable and effective adjunctive treatment for more rapid and more satisfying improvements in OCD symptoms. (PsycINFO Database Record (c) 2015 APA, all rights reserved) (journal abstract).

5.3.6. Otras terapias físicas (17 -2001-2015)

Sachdev PS, McBride R, et al. Right versus left prefrontal transcranial magnetic stimulation for obsessive-compulsive disorder: a preliminary investigation. J Clin Psychiatry. 2001;62(12):981-4.

BACKGROUND: There is preliminary evidence that repetitive transcranial magnetic stimulation (rTMS) may be useful for the treatment of obsessive-compulsive disorder (OCD), but no definitive study has been published, and the effect of laterality of stimulation is uncertain. METHOD: Subjects (N = 12) with resistant OCD were allocated randomly to either right or left prefrontal rTMS daily for 2 weeks and were assessed by an independent rater at 1 and 2 weeks and 1 month later. RESULTS: Subjects had an overall significant improvement in the obsessions ($p < .01$), compulsions ($p < .01$), and total ($p < .01$) scores on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) after 2 weeks and at 1-month follow-up. This improvement was significant for obsessions ($p < .05$) and tended to significance for total Y-BOCS scores ($p = .06$) after correction for changes in depression scores on the Montgomery-Asberg Depression Rating Scale. There was no significant difference between right- and left-sided rTMS on any of the parameters examined. Two subjects (33%) in each group showed a clinically significant improvement that persisted at I month but with relapse later in I subject. CONCLUSION: A proportion (about one quarter) of patients with resistant OCD appear to respond to rTMS to either prefrontal lobe, although in the absence of a sham treatment group in this study, we cannot rule out the possibility of this being a placebo response. This treatment warrants further investigation to better establish its efficacy and examine the best parameters for response.

Nuttin BJ, Gabriels LA, et al. Long-term electrical capsular stimulation in patients with obsessive-compulsive disorder. Neurosurgery. 2003;52(6):1263-72; discussion 1272-4.

OBJECTIVE: Because of the irreversibility of lesioning procedures and their possible side effects, we studied the efficacy of replacing bilateral anterior capsulotomy with chronic electrical capsular stimulation in patients with severe, long-standing, treatment-resistant obsessive-compulsive disorder. METHODS: We stereotactically implanted quadripolar electrodes in both anterior limbs of the internal capsules into six patients with severe obsessive-compulsive disorder. Psychiatrists and psychologists performed a double-blind clinical assessment. A blinded random crossover design was used to assess four of those patients, who underwent continuous stimulation thereafter. RESULTS: The psychiatrist-rated Yale-Brown Obsessive Compulsive Scale score was lower in the stimulation-on condition (mean, 19.8 +/- 8.0) than in the postoperative stimulator-off condition (mean, 32.3 +/- 3.9), and this stimulation-induced effect was maintained for at least 21 months after surgery. The Clinical Global Severity score decreased from 5 (severe; standard deviation, 0) in the stimulation-off condition to 3.3 (moderate to moderate-severe; standard deviation, 0.96) in the stimulation-on condition. The Clinical Global Improvement scores were unchanged in one patient and much improved in the other three during stimulation. During the stimulation-off period, symptom severity approached baseline levels in the four patients. Bilateral stimulation led to increased signal on functional magnetic resonance imaging studies, especially in the pons. Digital subtraction analysis of preoperative [(18)F]2-fluoro-2-deoxy-d-glucose positron emission tomographic scans and positron emission tomographic scans obtained after 3 months of stimulation showed decreased frontal metabolism during stimulation. CONCLUSION: These observations indicate that capsular stimulation reduces core symptoms 21 months after surgery in patients with severe, long-standing, treatment-refractory obsessive-compulsive disorder. The stimulation elicited changes in regional brain activity as measured by functional magnetic resonance imaging and positron emission tomography.

Prasko J, Paskova B, et al. The effect of repetitive transcranial magnetic stimulation (rTMS) on symptoms in obsessive compulsive disorder. A randomized, double blind, sham controlled study. Neuro Endocrinol Lett. 2006;27(3):327-32.

BACKGROUND: The goal of our study is to assess whether transcranial magnetic stimulation (rTMS) would facilitate the effect of antidepressant in OCD patients. METHOD: The aim of the randomized, double-blind, sham controlled study was to compare the 2 and 4 week efficacy of the 10 sessions rTMS with sham rTMS in serotonin reuptake inhibitor resistant OCD patient. Thirty three right-handed patients were randomly assigned to either active rTMS or to sham rTMS. Active rTMS with the frequency of 1 Hz at 110% of motor threshold (MT) was administered over the left dorsolateral prefrontal cortex. The same time schedule was used for sham administration. Thirty patients finished the study, three patients' dropped out at the beginning. Psychopathology was assessed by CGI, HAMA, Y-BOCS and BAI before the treatment, immediately after the experimental treatment, and 2 weeks after the experimental treatment by an independent reviewer. RESULTS: Both groups improved during the study period but the treatment effect did not differ between them in any of the instruments. CONCLUSION: Low frequency rTMS administered over the left dorso-lateral pre-

frontal cortex during 10 daily sessions did not differ from sham rTMS in facilitating the effect of serotonin reuptake inhibitors in OCD patients.

Okun MS, Mann G, et al. Deep brain stimulation in the internal capsule and nucleus accumbens region: responses observed during active and sham programming. J Neurol Neurosurg Psychiatry. 2007;78(3):310-4.

BACKGROUND: Recently, anterior limb of the internal capsule and nucleus accumbens deep brain stimulation (DBS) has been used in the treatment of medication-refractory obsessive-compulsive disorder (OCD). This region has been previously explored with lesion therapy, but with the advent of DBS there exists the possibility of monitoring the acute and chronic effects of electrical stimulation. The stimulation-induced benefits and side effects can be reversibly and blindly applied to a variety of locations in this region. OBJECTIVE: To explore the acute effects of DBS in the anterior limb of the internal capsule and nucleus accumbens region. METHODS: Ten total DBS leads in five patients with chronic and severe treatment-refractory OCD were tested. Patients were examined 30 days after DBS placement and received either "sham" testing or actual testing of the acute effects of DBS (the alternative condition tested 30 days later). RESULTS: Pooled responses were reviewed for comparability of distribution using standard descriptive methods, and relationships between the variables of interest were sought using chi2 analysis. A total of 845 stimulation trials across the five patients were recorded and pooled. Of these 16% were elicited from sham stimulation and 17% from placebo (0 V stimulation). A comparison of active to sham trials showed that sham stimulation was not associated with significant side effects or responses from patients. Non-mood-related responses were found to be significantly associated with the ventral lead contacts (0 and 1) ($p = 0.001$). Responses such as taste, smell and smile were strongly associated with the most ventral lead positions. Similarly, physiological responses--for example, autonomic changes, increased breathing rate, sweating, nausea, cold sensation, heat sensation, fear, panic and panic episodes--were significantly associated with ventral stimulation ($p = 0.001$). Fear and panic responses appeared clustered around the most ventral electrode (0). Acute stimulation resulted in either improved or worsened mood responses in both the dorsal and ventral regions of the anterior limb of the internal capsule. CONCLUSION: The acute effects of DBS in the region of the anterior limb of the internal capsule and nucleus accumbens, particularly when obtained in a blinded fashion, provide a unique opportunity to localise brain regions and explore circuitry.

Sachdev PS, Loo CK, et al. Repetitive transcranial magnetic stimulation for the treatment of obsessive compulsive disorder: a double-blind controlled investigation. Psychol Med. 2007;37(11):1645-9.

BACKGROUND: To determine the efficacy and tolerability of repetitive transcranial magnetic stimulation (rTMS) as a treatment for obsessive compulsive disorder (OCD) in a double-blind placebo-controlled study. METHOD: Subjects with treatment-resistant OCD were randomized to rTMS ($n = 10$) or sham rTMS ($n = 8$) for 10 sessions of daily stimulation over the left dorsolateral prefrontal cortex (DLPFC), with subjects and raters being blind to the treatment. Subjects were offered an open extension of up to 20 sessions of rTMS. RESULTS: The two groups did not differ on change in Yale-Brown Obsessive Compulsive Scale (YBOCS) or Maudsley Obsessive-Compulsive Inventory scores over 10 sessions, with or without correction for depression ratings. Over 20 sessions, there was a significant reduction in total YBOCS scores, but not after controlling for depression. rTMS over 20 sessions was well tolerated. CONCLUSION: Two weeks of rTMS over the left DLPFC is ineffective for treatment-resistant OCD.

Mallet L, Polosan M, et al. Subthalamic nucleus stimulation in severe obsessive-compulsive disorder. N Engl J Med. 2008;359(20):2121-34.

BACKGROUND: Severe, refractory obsessive-compulsive disorder (OCD) is a disabling condition. Stimulation of the subthalamic nucleus, a procedure that is already validated for the treatment of movement disorders, has been proposed as a therapeutic option. METHODS: In this 10-month, crossover, double-blind, multicenter study assessing the efficacy and safety of stimulation of the subthalamic nucleus, we randomly assigned eight patients with highly refractory OCD to undergo active stimulation of the subthalamic nucleus followed by sham stimulation and eight to undergo sham stimulation followed by active stimulation. The primary outcome measure was the severity of OCD, as assessed by the Yale-Brown Obsessive Compulsive Scale (Y-BOCS), at the end of two 3-month periods. General psychopathologic findings, functioning, and tolerance were assessed with the use of standardized psychiatric scales, the Global Assessment of Functioning (GAF) scale, and neuropsychological tests. RESULTS: After active stimulation of the subthalamic nucleus, the Y-BOCS score (on a scale from 0 to 40, with lower scores indicating less severe symptoms) was significantly

lower than the score after sham stimulation (mean [+/-SD], 19+/-8 vs. 28+/-7; P=0.01), and the GAF score (on a scale from 1 to 90, with higher scores indicating higher levels of functioning) was significantly higher (56+/-14 vs. 43+/-8, P=0.005). The ratings of neuropsychological measures, depression, and anxiety were not modified by stimulation. There were 15 serious adverse events overall, including 1 intracerebral hemorrhage and 2 infections; there were also 23 nonserious adverse events. CONCLUSIONS: These preliminary findings suggest that stimulation of the subthalamic nucleus may reduce the symptoms of severe forms of OCD but is associated with a substantial risk of serious adverse events. (ClinicalTrials.gov number, NCT00169377.).

Kang JI, Kim CH, et al. A randomized controlled study of sequentially applied repetitive transcranial magnetic stimulation in obsessive-compulsive disorder. J Clin Psychiatry. 2009;70(12):1645-51.

OBJECTIVE: The present study investigated possible therapeutic effects and safety of sequentially combined low-frequency repetitive transcranial magnetic stimulation (rTMS) to the right dorsolateral prefrontal cortex and supplementary motor area in patients with treatment-resistant obsessive-compulsive disorder. METHOD: Between February 2007 and January 2008, we carried out a study with a rater-blinded, sham-controlled design in which 20 patients with treatment-resistant obsessive-compulsive disorder, confirmed by a psychiatrist after use of the Structured Clinical Interview for DSM-IV Axis I Disorders-Clinician Version, were randomly assigned to either active rTMS (n = 10) or sham treatment (n = 10). Over 10 days, rTMS of 1 Hz was given at 110% of the motor threshold for 20 minutes over the right dorsolateral prefrontal cortex and sequentially at 1 Hz at 100% of the motor threshold for 20 minutes over the supplementary motor area. The primary outcome measure was the Yale-Brown Obsessive Compulsive Scale (YBOCS) score. RESULTS: For the between-group analyses, there were no significant differences over 4 weeks between the active and sham groups on the YBOCS (F = 0.01, P = .92) and the Montgomery-Asberg Depression Rating Scale (MADRS; F = 0.39, P = .54). In repeated-measures analyses on all subjects, there was a significant effect of time on the YBOCS (F = 5.48, P = .009) and the MADRS (F = 6.55, P = .004). There were no significant group-by-time interactions for the YBOCS (F = 0.03, P = .94) or the MADRS (F = 0.09, P = .67). CONCLUSIONS: These findings suggest that 10 sessions of sequential rTMS of the right dorsolateral prefrontal cortex and the supplementary motor area at low frequency had no therapeutic effect on obsessive-compulsive symptoms. However, rTMS was a safe method of treatment, and there was no significant change in cognitive function after rTMS. Further controlled studies using a more sophisticated sham system in larger samples are required to confirm the effect of rTMS in obsessive-compulsive disorder. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT00932204.

Denys D, Mantione M, et al. (2010) Deep brain stimulation of the nucleus accumbens for treatment-refractory obsessive-compulsive disorder. Archives of general psychiatry. 2010;67:1061-8. DOI: 10.1001/archgenpsychiatry.2010.122.

CONTEXT: Obsessive-compulsive disorder (OCD) is a chronic psychiatric disorder that affects 2% of the general population. Even when the best available treatments are applied, approximately 10% of patients remain severely afflicted and run a long-term deteriorating course of OCD. OBJECTIVE: To determine whether bilateral deep brain stimulation of the nucleus accumbens is an effective and safe treatment for treatment-refractory OCD. DESIGN: The study consisted of an open 8-month treatment phase, followed by a double-blind crossover phase with randomly assigned 2-week periods of active or sham stimulation, ending with an open 12-month maintenance phase. SETTING: Academic research. Patients Sixteen patients (age range, 18-65 years) with OCD according to DSM-IV criteria meeting stringent criteria for refractoriness to treatment were included in the study. INTERVENTIONS: Treatment with bilateral deep brain stimulation of the nucleus accumbens. MAIN OUTCOME MEASURES: Primary efficacy was assessed by score change from baseline on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS). Responders were defined by a score decrease of at least 35% on the Y-BOCS. RESULTS: In the open phase, the mean (SD) Y-BOCS score decreased by 46%, from 33.7 (3.6) at baseline to 18.0 (11.4) after 8 months (P < .001). Nine of 16 patients were responders, with a mean (SD) Y-BOCS score decrease of 23.7 (7.0), or 72%. In the double-blind, sham-controlled phase (n = 14), the mean (SD) Y-BOCS score difference between active and sham stimulation was 8.3 (2.3), or 25% (P = .004). Depression and anxiety decreased significantly. Except for mild forgetfulness and word-finding problems, no permanent adverse events were reported. CONCLUSION: Bilateral deep brain stimulation of the nucleus accumbens may be an effective and safe treatment for treatment-refractory OCD. CLINICAL TRIAL REGISTRATION: isrctn.org Identifier: ISRCTN23255677.

Mantovani A, Simpson HB, et al. Randomized sham-controlled trial of repetitive transcranial magnetic stimulation in treatment-resistant obsessive-compulsive disorder. Int J Neuropsychopharmacol. 2010;13(2):217-27.

In open trials, 1-Hz repetitive transcranial magnetic stimulation (rTMS) to the supplementary motor area (SMA) improved symptoms and normalized cortical hyper-excitability of patients with obsessive-compulsive disorder (OCD). Here we present the results of a randomized sham-controlled double-blind study. Medication-resistant OCD patients (n=21) were assigned 4 wk either active or sham rTMS to the SMA bilaterally. rTMS parameters consisted of 1200 pulses/d, at 1 Hz and 100% of motor threshold (MT). Eighteen patients completed the study. Response to treatment was defined as a > or = 25% decrease on the Yale-Brown Obsessive Compulsive Scale (YBOCS). Non-responders to sham and responders to active or sham rTMS were offered four additional weeks of open active rTMS. After 4 wk, the response rate in the completer sample was 67% (6/9) with active and 22% (2/9) with sham rTMS. At 4 wk, patients receiving active rTMS showed on average a 25% reduction in the YBOCS compared to a 12% reduction in those receiving sham. In those who received 8-wk active rTMS, OCD symptoms improved from 28.2+/-5.8 to 14.5+/-3.6. In patients randomized to active rTMS, MT measures on the right hemisphere increased significantly over time. At the end of 4-wk rTMS the abnormal hemispheric laterality found in the group randomized to active rTMS normalized. The results of the first randomized sham-controlled trial of SMA stimulation in the treatment of resistant OCD support further investigation into the potential therapeutic applications of rTMS in this disabling condition.

Sarkhel S, Sinha VK, et al. Adjunctive high-frequency right prefrontal repetitive transcranial magnetic stimulation (rTMS) was not effective in obsessive-compulsive disorder but improved secondary depression. J Anxiety Disord. 2010;24(5):535-9.

BACKGROUND: There is preliminary evidence that repetitive transcranial magnetic stimulation (rTMS) may be useful in obsessive-compulsive disorder (OCD) patients. METHODS: Our objective was to examine efficacy of adjunctive right prefrontal high-frequency (rapid) rTMS treatment in OCD patients. 42 patients with OCD were randomly assigned to 10 sessions of add-on high-frequency right prefrontal active rTMS (10Hz, 110% of motor threshold, 4s per train, 20 trains per session) or sham stimulation. They were rated on Yale Brown Obsessive Compulsive Scale (YBOCS), Hamilton Rating Scale for Depression (HAM-D), Hamilton Rating Scale for Anxiety (HAM-A) and Clinical Global Impression-Severity of Illness (CGI-S) at baseline, day 14 and day 28. The dose of antiobsessive drug was kept constant throughout the period of assessment. RESULTS: For YBOCS scores, repeated measures ANOVA showed significant main effect of treatment, but no effect of treatment over time (Pillai's Trace F=1.39, p=.262). However, significant effect of treatment over time as shown by interaction effect for both HAM-D (Pillai's Trace F=3.67, p=.035, eta(2)=.158) and HAM-A scores (Pillai's Trace F=5.22, p=.01, eta(2)=.211) were seen. CONCLUSION: Adjunctive high-frequency right prefrontal rTMS does not have any significant effect in the treatment of OCD. However, it is modestly effective in the treatment of comorbid depressive symptoms in patients with OCD.

Mansur CG, Myczkowki ML, et al. Placebo effect after prefrontal magnetic stimulation in the treatment of resistant obsessive-compulsive disorder: a randomized controlled trial. The international journal of neuropsychopharmacology / official scientific journal of the Collegium Internationale Neuropsychopharmacologicum (CINP). 2011;14:1389-97. DOI: 10.1017/S1461145711000575.

Many patients with obsessive-compulsive disorder (OCD) do not achieve satisfactory symptom improvement with conventional treatments. Here, we evaluate the efficacy of repetitive transcranial magnetic stimulation (rTMS) applied over the right dorsolateral prefrontal cortex (rDLPFC) in patients with treatment-resistant OCD. This was a double-blind randomized trial involving 30 treatment-resistant OCD outpatients, allocated to have either sham or active high-frequency rTMS (over the rDLPFC) added to their treatment regimens for 6 wk, with 6 wk of follow-up. Active rTMS consisted of 30 applications (figure-of-eight coil; 10 Hz at 110% of motor threshold; 1 session/d; 40 trains/session; 5 s/train; 25-s intertrain interval). At weeks 0, 2, 6, 8, and 12, we applied the Yale-Brown Obsessive-Compulsive Scale (YBOCS), Clinical Global Impression (CGI) scale, 14-item Hamilton Anxiety Rating Scale (HAMA-14), 17-item Hamilton Depression Rating Scale (HAMD-17), and 36-item Short-form Health Survey. The primary outcome measure was a positive response (? 30% improvement in YBOCS score, together with a 'much improved' or 'very much improved' CGI - Improvement scale rating). One patient in each group showed a positive response (p=1.00). For YBOCS score, there was significant effect of time (F=7.33, p=0.002) but no significant group effect or group×time interaction. In treatment-resistant OCD, active rTMS over the rDLPFC does not appear to be superior to sham rTMS in relieving obsessive-compulsive symptoms, reducing clinical severity, or improving treatment response, although there is evidence of a placebo effect.

Oliveira Gomes PV, Brasil-Neto JP, et al. A randomized, double-blind trial of repetitive transcranial magnetic stimulation in obsessive-compulsive disorder with three-month follow-up. The Journal of Neuropsychiatry and Clinical Neurosciences. 2012;24(4):437-43.

Recent findings indicate that the motor and premotor cortices are hyperexcitable in obsessive-compulsive disorder (OCD). The authors have performed the first randomized, double-blind clinical trial of repetitive transcranial magnetic stimulation (rTMS) in OCD, with a 3-month follow-up. OCD patients (N = 22) were assigned to either 2 weeks of active or sham rTMS to the supplementary motor area bilaterally. After 14 weeks, the response rate was 4 1% (7/12) with active and 10% (1/10) with sham treatment. At 14 weeks, patients receiving active rTMS showed, on average, a 35% reduction on the Y-BOCS, as compared with a 6.2% reduction in those receiving sham treatment. (PsycINFO Database Record (c) 2013 APA, all rights reserved) (journal abstract).

Lopes AC, Greenberg BD, et al. Gamma ventral capsulotomy for obsessive-compulsive disorder: a randomized clinical trial. JAMA Psychiatry. 2014;71(9):1066-76.

IMPORTANCE: Select cases of intractable obsessive-compulsive disorder (OCD) have undergone neurosurgical ablation for more than half a century. However, to our knowledge, there have been no randomized clinical trials of such procedures for the treatment of any psychiatric disorder. OBJECTIVE: To determine the efficacy and safety of a radiosurgery (gamma ventral capsulotomy [GVC]) for intractable OCD. DESIGN, SETTING, AND PARTICIPANTS: In a double-blind, placebo-controlled, randomized clinical trial, 16 patients with intractable OCD were randomized to active (n = 8) or sham (n = 8) GVC. Blinding was maintained for 12 months. After unblinding, sham-group patients were offered active GVC. INTERVENTIONS: Patients randomized to active GVC had 2 distinct isocenters on each side irradiated at the ventral border of the anterior limb of the internal capsule. The patients randomized to sham GVC received simulated radiosurgery using the same equipment. MAIN OUTCOMES AND MEASURES: Scores on the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) and the Clinical Global Impression-Improvement (CGI-I) Scale. Response was defined as a 35% or greater reduction in Y-BOCS severity and "improved" or "much improved" CGI-I ratings. RESULTS: Three of 8 patients randomized to active treatment responded at 12 months, while none of the 8 sham-GVC patients responded (absolute risk reduction, 0.375; 95% CI, 0.04-0.71). At 12 months, OCD symptom improvement was significantly higher in the active-GVC group than in the sham group (Y-BOCS, P = .046; Dimensional Y-BOCS, P = .01). At 54 months, 2 additional patients in the active group had become responders. Of the 4 sham-GVC patients who later received active GVC, 2 responded by post-GVC month 12. The most serious adverse event was an asymptomatic radiation-induced cyst in 1 patient. CONCLUSIONS AND RELEVANCE: Gamma ventral capsulotomy benefitted patients with otherwise intractable OCD and thus appears to be an alternative to deep-brain stimulation in selected cases. Given the risks inherent in any psychiatric neurosurgery, such procedures should be conducted at specialized centers. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT01004302.

Ma X, Huang Y, et al. A randomized double-blinded sham-controlled trial of? electroencephalogram-guided transcranial magnetic stimulation for obsessive-compulsive disorder. Chinese medical journal. 2014;127:601-6.

BACKGROUND: Obsessive-compulsive disorder (OCD) is a highly prevalent and devastating psychiatric condition. Repetitive transcranial magnetic stimulation (rTMS) is a potential and non-invasive treatment for OCD. Diverse efficacies of rTMS have been reported in different locations or frequencies of the stimulation. The main objective of this study was to assess the treatment effect for OCD with alpha electroencephalogram (?EEG)-guided TMS over dorsal lateral prefrontal cortex bilaterally. METHODS: There were 25 OCD patients in the? TMS treatment group and 21 OCD patients in the sham control group. Each subject received 10 daily treatment sessions (5 days a week). The ?TMS group had significant reduction in scores of Yale-Brown Obsessive Compulsive Scale and Hamilton Rating Scale for Anxiety (HAMA) compared with the control group at the end of 2-week treatment and 1-week follow-up. Analysis of variance with repeated measures was used to test the effects between the two groups. RESULTS: Significant difference in scores of obsession and HAMA were found between the two groups after treatment. No significant difference in scores of Hamilton Rating Scale for Depression was found between the two groups after the treatment, but statistical significance was shown at the end of 1-week follow-up. CONCLUSIONS: ?EEG-guided TMS may be an effective treatment for OCD and related anxiety. Delayed response to ?TMS in depression suggests that it might be secondary to the improvement of primary response in OCD and anxiety.

Nauczyciel C, Jeune F, et al. Repetitive transcranial magnetic stimulation over the orbitofrontal cortex for obsessive-compulsive disorder: a double-blind, crossover study. Translational psychiatry. 2014;4:e436. DOI: 10.1038/tp.2014.62.

This pilot study was designed to assess the efficacy of low-frequency repetitive transcranial magnetic stimulation (rTMS) over the right orbitofrontal cortex (OFC) by means of a double-cone coil in patients suffering from obsessive-compulsive disorder. We hypothesized that low-frequency stimulation of the OFC would lead to a reduction in clinical symptoms, as measured on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS). A randomized, double-blind, crossover design was implemented with two 1-week treatment periods (active stimulation versus sham stimulation) separated by a 1-month washout period. Concomitantly, a subgroup of patients underwent a positron emission tomography (PET) scan after each stimulation sequence. Statistical analyses compared the Y-BOCS scores at the end of each period. At day 7, we observed a significant decrease from baseline in the Y-BOCS scores, after both active (P<0.01) and sham stimulation (P=0.02). This decrease tended to be larger after active stimulation than after sham stimulation: -6 (-29, 0) points versus -2 (-20, 4) points (P=0.07). Active versus sham PET scan contrasts showed that stimulation was related to a bilateral decrease in the metabolism of the OFC. The OFC should definitely be regarded as a key neuroanatomical target for rTMS, as it is easier to reach than either the striatum or the subthalamic nucleus, structures favored in neurosurgical approaches.

Tsai HC, Chang CH, et al. Acute stimulation effect of the ventral capsule/ventral striatum in patients with refractory obsessive–compulsive disorder—A double-blinded trial. Neuropsychiatric Disease and Treatment. 2014;10.

Objective: Deep-brain stimulation (DBS) for treating refractory obsessive–compulsive disorder (OCD) has shown positive results in small clinical trials. Ventral capsule/ventral striatum (VC/VS) is one of the promising targets; however, whether or not acute stimulation test can provide substantial information for chronic stimulation is not yet known. We evaluated postoperative test stimulation and examined the relationship of acute simulation-induced smile/laughter and 15-month clinical outcome. Methods: Four adult patients with refractory OCD were implanted with Model 3387 leads bilaterally in an area of VC/VS. Postoperative test stimulation was performed at least 2 weeks after surgery. We performed double-blinded postoperative test stimulation with different contact and voltage. The relationship of stimulation-induced smile/laughter and chronic response was examined. Results: Patients presented smile, laughter, euphoria, increased heart rate, increased blood pressure, smell, chest vibration, dizziness, nausea, heat, or increased sexual drive during acute stimulation. We found that the higher the percentage of smile/laughter (34.3%, 31.3%, 56.3%, and 12.5% for four cases), the greater the reduction in the Yale-Brown Obsessive Compulsive Scale (30.6%, 38.9%, 58.8%, and 7.7% respectively at 15-month DBS). Conclusion: This study showed that acute DBS of the VC/VS might cause mood change, cardiovascular, sensory, or motor effects. These effects were transient or habituated over six months. We suggest stimulation-induced smile/laughter may be a possible predictor for long-term DBS outcome. Larger studies, genetic studies, and imaging studies are needed to evaluate the effects of different parameters and possible predictors in the treatment of OCD. (PsycINFO Database Record (c) 2014 APA, all rights reserved)(journal abstract).

Haghighi M, Shayganfard M, et al. Repetitive Transcranial Magnetic Stimulation (rTMS) improves symptoms and reduces clinical illness in patients suffering from OCD: Results from a single-blind, randomized clinical trial with sham cross-over condition. Journal of Psychiatric Research. 2015;68:238-44.

Objectives: Both psychotherapeutic and psychopharmacological methods are used in the treatment of patients suffering from obsessive-compulsive disorders (OCD), and both with encouraging but also mixed results. Here, we tested the hypothesis that repetitive Transcranial Magnetic Stimulation (rTMS) improves symptoms and reduces illness severity in patients suffering from treatment-resistant OCD. Methods: A total of 21 patients (57% females; mean age: M = 35.8 years) suffering from treatment-resistant OCD were randomly assigned either to an rTMS-first-sham-second, or a sham-first-rTMS-second condition. Treatment sessions lasted for 4 weeks with five sessions per week, each of about 50 min duration. Symptoms were assessed via both self- and expert-ratings. Results: Both self- and expert-reported symptom severity reduced in the rTMS condition as compared to the sham condition. Full- and partial responses were observed in the rTMS-condition, but not in the sham-condition. Conclusions: The pattern of results from this single-blind, sham- and cross-over design suggests that rTMS is a successful intervention for patients suffering from treatment-resistant OCD. (PsycINFO Database Record (c) 2015 APA, all rights reserved) (journal abstract).

5.3.7. Comparación de estrategias de potenciación (5 - 1996-2013)

Ravizza L, Barzega G, et al. Therapeutic effect and safety of adjunctive risperidone in refractory obsessive-compulsive disorder (OCD). Psychopharmacol Bull. 1996;32(4):677-82.

It has been well established that more than 40 percent of patients with obsessive-compulsive disorder (OCD) do not improve after an adequate trial with serotonin uptake inhibitors (SUIs). The first purpose of this trial was to compare the short-term efficacy and safety of two different strategies in a sample of treatment-refractory OCD patients: dose increase of the ongoing treatment versus the addition of another SUI. The second purpose was to investigate the short-term efficacy and safety of adjunctive risperidone in SUI-refractory OCD patients. Thirty-three OCD patients who were unimproved after a short-term treatment with clomipramine (150 mg/day) were admitted to the study. In the first part of the study, the dose increase of clomipramine was compared with sertraline addition, in an open-label manner. The addition of sertraline to the ongoing treatment appeared to be more effective and tolerable than the clomipramine dose increase. Seven (50%) of the 14 patients who were considered nonresponders after the first part of the study, showed good clinical improvement and good tolerability after risperidone augmentation. These results suggest that risperidone addition to ongoing SUIs may be useful in augmenting pharmacologic response in OCD.

Storch EA, Merlo LJ, et al. D-cycloserine does not enhance exposure-response prevention therapy in obsessive-compulsive disorder. Int Clin Psychopharmacol. 2007;22(4):230-7.

Obsessive-compulsive disorder is a common, chronic, and oftentimes disabling disorder. The only established first-line treatments for obsessive-compulsive disorder are exposure and response prevention therapy and the serotonin reuptake inhibitors. Many patients do not experience complete symptom resolution with either modality and require augmentation approaches. Recent animal and clinical data suggest that D-cycloserine, a partial agonist that acts at the strychnine-insensitive glycine-recognition site of the N-methyl-D-aspartate receptor complex, may enhance extinction learning that occurs in exposure-based psychotherapies. Given this, this study examined if D-cycloserine (250 mg) enhances the overall efficacy and rate of change of exposure and response prevention therapy for adult obsessive-compulsive disorder. Participants were 24 adults meeting Diagnostic and Statistical Manual of Mental Disorders-IV criteria for obsessive-compulsive disorder. The study design was a randomized, double-blinded, placebo-controlled augmentation trial examining exposure and response prevention therapy+D-cycloserine versus exposure and response prevention therapy+placebo. All patients received 12 weekly sessions of exposure and response prevention treatment. The first session involved building a ritual hierarchy and providing psychoeducation about obsessive-compulsive disorder. The second session involved a practice exposure. Sessions 3-12 involved exposure and response prevention exercises. D-cycloserine or placebo (250 mg) was taken 4 h before every session. No significant group differences were found across outcome variables. The rate of improvement did not differ between groups. The present results fail to support the use of D-cycloserine with exposure and response prevention therapy for adult obsessive-compulsive disorder. As this study is the first to explore this question and a number of methodological issues must be considered when interpreting the findings, the conclusions that may be drawn from our results are limited.

Diniz JB, Shavitt RG, et al. Quetiapine versus clomipramine in the augmentation of selective serotonin reuptake inhibitors for the treatment of obsessive-compulsive disorder: a randomized, open-label trial. J Psychopharmacol. 2010;24(3):297-307.

After 12 weeks of selective serotonin reuptake inhibitor (SSRI) monotherapy with inadequate response, 10 patients received clomipramine and 11 received quetiapine as augmentation agents of the SSRI. The primary outcome measure was the difference between initial and final scores of the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), rated in a blinded fashion, and the score of clinical global improvement (CGI-I). Statistical analyses were performed using nonparametric tests to evaluate treatment efficacy and the difference between treatment groups. Percentile plots were constructed with YBOCS scores from the clomipramine and quetiapine groups. Considering response a >or=35% reduction in the initial Y-BOCS score plus a rating of 'much improved' or 'very much improved' on CGI-I, four of eleven quetiapine patients and one out of ten clomipramine patients were classified as responders. The mean final Y-BOCS score was significantly lower than baseline in the quetiapine augmentation group (P = 0.023), but not in the clomipramine augmentation group (P = 0.503). The difference between groups showed a trend towards significance only at week 4, the mean Y-BOCS score being lower for those receiving quetiapine (P = 0.052). A difference between groups was also observed at week 4 according to percentile plots. These results corroborate previous findings of quetiapine augmentation efficacy in obsessive-compulsive disorder (OCD). Clomipramine

augmentation did not produce a significant reduction in Y-BOCS scores. Higher target maximum dosages might have yielded different results.

Van Balkom AJ, Emmelkamp PM, et al. Cognitive therapy versus fluvoxamine as a second-step treatment in obsessive-compulsive disorder nonresponsive to first-step behavior therapy. Psychother Psychosom. 2012;81(6):366-74.

BACKGROUND: To compare the effectiveness of second-step treatment with cognitive therapy (CT) versus fluvoxamine in patients with obsessive-compulsive disorder (OCD) who are nonresponsive to exposure in vivo with response prevention (ERP). METHODS: A 12-week randomized controlled trial at an outpatient clinic in the Netherlands comparing CT with fluvoxamine in OCD. Of 118 subjects with OCD treated with 12 weeks of ERP, 48 appeared to be nonresponders (Y-BOCS improvement score of less than one third). These nonresponders were randomized to CT (n = 22) or fluvoxamine (n = 26). The main outcome measure was the Y-BOCS severity scale. Statistical analyses were conducted in the intention-to-treat sample (n = 45) on an 'as randomized basis' and in the per-protocol sample (n = 30). Due to selective dropout in the fluvoxamine group, two additional sensitivity analyses were performed. RESULTS: Complete data could be obtained from 45 subjects (94%) after 12 weeks. Fifty percent of the patients refused fluvoxamine after randomization compared to 13% who refused CT [chi(2)(1) = 7.10; p = 0.01]. CT as a second-step treatment did not appear to be effective in this sample of nonresponders. Fluvoxamine was significantly superior to CT in the intention-to-treat sample, in the per-protocol sample and in the two separately defined samples in which the sensitivity analyses were performed. CONCLUSIONS: OCD patients who are nonresponsive to ERP may benefit more from a switch to treatment with an antidepressant instead of switching to CT. In clinical practice, it may be important to motivate this subgroup of patients to undergo psychopharmacological treatment, as this may improve their outcome considerably.

Simpson HB, Foa EB, et al. Cognitive-behavioral therapy vs risperidone for augmenting serotonin reuptake inhibitors in obsessive-compulsive disorder: a randomized clinical trial. JAMA psychiatry. 2013;70:1190-9. DOI: 10.1001/jamapsychiatry.2013.1932.

IMPORTANCE: Obsessive-compulsive disorder (OCD) is one of the world's most disabling illnesses according to the World Health Organization. Serotonin reuptake inhibitors (SRIs) are the only medications approved by the Food and Drug Administration to treat OCD, but few patients achieve minimal symptoms from an SRI alone. In such cases, practice guidelines recommend adding antipsychotics or cognitive-behavioral therapy consisting of exposure and ritual prevention (EX/RP). OBJECTIVE: To compare the effects of these 2 SRI augmentation strategies vs pill placebo for the first time, to our knowledge, in adults with OCD. DESIGN, SETTING, AND PARTICIPANTS: A randomized clinical trial (conducted January 2007-August 2012) at 2 academic outpatient research clinics that specialize in OCD and anxiety disorders. Patients (aged 18-70 years) were eligible if they had OCD of at least moderate severity despite a therapeutic SRI dose for at least 12 weeks prior to entry. Of 163 who were eligible, 100 were randomized (risperidone, n?=?40; EX/RP, n?=?40; and placebo, n?=?20), and 86 completed the trial. INTERVENTIONS: While continuing their SRI at the same dose, patients were randomized to the addition of 8 weeks of risperidone (up to 4 mg/d), EX/RP (17 sessions delivered twice weekly), or pill placebo. Independent assessments were conducted every 4 weeks. MAIN OUTCOME AND MEASURE: The Yale-Brown Obsessive Compulsive Scale (Y-BOCS) to measure OCD severity. RESULTS: Patients randomized to EX/RP had significantly greater reduction in week 8 Y-BOCS scores based on mixed-effects models (vs risperidone: mean [SE], -9.72 [1.38]; P?<?.001 vs placebo: mean [SE], -10.10 [1.68]; P?<?.001). Patients receiving risperidone did not significantly differ from those receiving placebo (mean [SE], -0.38 [1.72]; P?=?.83). More patients receiving EX/RP responded (Y-BOCS score decrease ?25%: 80% for EX/RP, 23% for risperidone, and 15% for placebo; P?<?.001). More patients receiving EX/RP achieved minimal symptoms (Y-BOCS score ?12: 43% for EX/RP, 13% for risperidone, and 5% for placebo; P?=?.001). Adding EX/RP was also superior to risperidone and placebo in improving insight, functioning, and quality of life. CONCLUSIONS AND RELEVANCE: Adding EX/RP to SRIs was superior to both risperidone and pill placebo. Patients with OCD receiving SRIs who continue to have clinically significant symptoms should be offered EX/RP before antipsychotics given its superior efficacy and less negative adverse effect profile. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT00389493.

5.3.8. Efecto a plazo de la potenciación (1 - 2013)

Foa EB, Simpson HB, et al. Six-month follow-up of a randomized controlled trial augmenting serotonin reuptake inhibitor treatment with exposure and ritual prevention for obsessive-compulsive disorder. J Clin Psychiatry. 2013;74(5):464-9.

OBJECTIVE: This article describes the long-term effects of augmenting serotonin reuptake inhibitors (SRIs) with exposure and ritual prevention or stress management training in patients with DSM-IV obsessive-compulsive disorder (OCD). METHOD: Between November 2000 and November 2006, 111 OCD patients from 2 academic outpatient centers with partial SRI response were randomized to the addition of exposure and ritual prevention or stress management training, delivered twice weekly for 8 weeks (acute phase); 108 began treatment. Responders (38 of 52 in the exposure and ritual prevention condition, 11 of 52 in the stress management training condition) entered a 24-week maintenance phase. The Yale-Brown Obsessive Compulsive Scale (YBOCS) was the primary outcome measure. RESULTS: After 24 weeks, patients randomized to and receiving exposure and ritual prevention versus stress management training had significantly better outcomes (mean YBOCS scores of 14.69 and 21.37, respectively; t = 2.88, P = .005), higher response rates (decrease in YBOCS scores >/= 25%: 40.7% vs 9.3%, Fisher exact test P < .001), and higher rates of excellent response (YBOCS score </= 12: 24.1% vs 5.6%, Fisher exact test P = .01). During the maintenance phase, the slope of change in YBOCS scores was not significant in either condition (all P values >/= .55), with no difference between exposure and ritual prevention and stress management training (P > .74). Better outcome was associated with baseline variables: lower YBOCS scores, higher quality of life, fewer comorbid Axis I diagnoses, and male sex. CONCLUSIONS: Augmenting SRIs with exposure and ritual prevention versus stress management training leads to better outcome after acute treatment and 24 weeks later. Maintenance outcome, however, was primarily a function of OCD severity at entrance. Greater improvement during the acute phase influences how well patients maintain their gains, regardless of treatment condition.

5.4. Cambio (incluye cambio a i.v.) (3 – 1998-2004)

Fallon BA, Liebowitz MR, et al. Intravenous clomipramine for obsessive-compulsive disorder refractory to oral clomipramine: a placebo-controlled study. Arch Gen Psychiatry. 1998;55(10):918-24.

BACKGROUND: Uncontrolled reports suggest that intravenous clomipramine hydrochloride may be effective for patients with obsessive-compulsive disorder (OCD) who are nonresponsive to oral clomipramine. METHODS: Fifty-four patients with oral clomipramine-refractory OCD were randomized to receive 14 infusions of either placebo or clomipramine hydrochloride, starting at 25 mg/d and increasing to 250 mg/d. Ratings were conducted double-blind after infusion 14 among 54 patients, single-blind 1 week later among 39 patients, and nonblind 1 month later among 31 patients. Response was based on a Clinical Global Impressions rating of at least "much improved." RESULTS: Six (21%) of 29 patients randomized to receive intravenous (i.v.) clomipramine vs 0 of 25 patients given i.v. placebo were responders after 14 infusions (df = 1, P<.02). Dimensional ratings after infusion 14 revealed significant (P = .007) improvement on the National Institute of Mental Health-Obsessive-Compulsive Scale and the Clinical Global Impressions Scale (P = .03), but not the Yale-Brown Obsessive Compulsive Scale. One week later, all dimensional measures of OCD showed significant improvement. At 1 week post-i.v., 9 (43%) of 21 patients initially randomized to i.v. clomipramine and treated subsequently with oral clomipramine were responders, whereas 0 of 18 patients initially randomized to receive i.v. placebo and treated subsequently with several days of open-label i.v. clomipramine responded (df = 1, P<.002). Of the 31 patients assessed 1 month after i.v. infusion (treatment not controlled), 18 (58.1%) were responders. Intravenous clomipramine treatment was safe with no serious adverse consequences. CONCLUSIONS: Intravenous clomipramine is more effective than i.v. placebo for patients with OCD with a history of inadequate response or intolerance to oral clomipramine. Further study of this promising treatment for refractory OCD is needed.

Mathew SJ, Coplan JD, et al. Neuroendocrine predictors of response to intravenous clomipramine therapy for refractory obsessive-compulsive disorder. Depress Anxiety. 2001;14(4):199-208.

The current study examines the neuroendocrine response to intravenous clomipramine (IV CMI) in oral CMI-resistant obsessive-compulsive disorder (OCD) patients on day 1 and day 14 of treatment to identify predictors of response. Forty-four OCD patients with an inadequate response or poorly tolerant to oral CMI were begun at 25 mg IV CMI, increasing to 250 mg by day 10, and continuing on that dose to day 14. On day 1, plasma levels of prolactin (PRL), growth hormone (GH), and cortisol were obtained immediately before the 25 mg IV infusion, and at five 30-minute time points after the

infusion. On day 14, hormonal samples were obtained in a similar fashion. Response was assessed by the Clinical Global Impressions (CGI). Low PRL(MAX) to IV CMI and low cortisol levels overall on day 1 were both significantly associated with clinical response at day 14. An overall increase in growth hormone (GH) secretion during the day 14 testing was associated with positive response. A pronounced PRL response to IV CMI on day 14 was exhibited by the nonresponders, whereas a smaller and later but significant increase in PRL was noted in the responders. The findings suggest that in this sample of oral CMI-resistant patients with OCD, neuroendocrine measures derived from pharmacological challenge with IV CMI are capable of distinguishing IV CMI treatment responders from nonresponders. The limitations of IV CMI as a specific probe of serotonin function are discussed.

Denys D, Megen HJ, et al. A double-blind switch study of paroxetine and venlafaxine in obsessive-compulsive disorder. The Journal of clinical psychiatry. 2004;65:37-43.

BACKGROUND: The treatment guidelines for obsessive-compulsive disorder (OCD) propose to switch serotonin reuptake inhibitors (SRIs) in case of refractoriness. However, no controlled research has been published yet that prospectively examined the effects of changing SRIs. This article describes the first double-blind switch study of 2 SRIs in patients with OCD. METHOD: 150 patients with primary OCD, according to DSM-IV criteria, were randomly assigned in a 12-week, double-blind trial to receive dosages titrated upward to 300 mg/day of venlafaxine (N = 75) or 60 mg/day of paroxetine (N = 75). Primary efficacy was assessed by the change from baseline on the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), and nonresponse was defined as less than 25% reduction on the Y-BOCS. After a 4-week tapering phase, 43 nonresponders were switched to 12 additional weeks of the alternate antidepressant, of which 16 patients received venlafaxine and 27 received paroxetine. RESULTS: Eighteen of 43 patients benefited from a switch to the alternate SRI with a mean +/- SD decrease of at least 25% on the Y-BOCS. At the end of 12 weeks, responder rates were 56% for paroxetine (15/27) and 19% for venlafaxine (3/16). An intent-to-treat, last-observation-carried-forward analysis demonstrated a mean decrease on the Y-BOCS of 1.8 +/- 3.5 in the venlafaxine group and 6.5 +/- 7.1 in the paroxetine group. After 2 consecutive SRI trials, 109 of 150 patients (73%) achieved a Y-BOCS decrease of at least 25%. CONCLUSION: The results of the current study show that 42% of the nonresponders benefited from a crossover to the other SRI, and that paroxetine was more efficacious than venlafaxine in the treatment of nonresponders to a previous SRI trial. Switching SRIs in case of refractoriness may be considered a useful strategy for patients with OCD.

REVISIONES SISTEMÁTICAS

ÍNDICE

TRATAMIENTO FARMACOLÓGICO DEL TRASTORNO OBSESIVO COMPULSIVO (TOC) EN ADULTOS

1. TRATAMIENTO AGUDO

1.1. Psicofarmacológico versus psicoterapia versus combinado

Christensen H, Hadzi-Pavlovic D, et al. Behavior therapy and tricyclic medication in the treatment of obsessive-compulsive disorder: A quantitative review. Journal of Consulting and Clinical Psychology. 1987;55(5):701-11.

A meta-analysis was used to integrate the research literature on the treatment of obsessive-compulsive disorder. Antidepressants, such as clomipramine, and behavior therapy have produced appreciable changes in obsessive-compulsive and depressive symptoms. Patients with obsessions who did not suffer from compulsions have responded less to treatment. No follow-up data have been available for clomipramine, but the benefits of behavior therapy have been shown to be stable at follow-up. Ratings of improvement by assessors have been higher than ratings made by patients. The effects of tricyclic medication and exposure therapies have not significantly differed, but both have proven significantly superior to nonspecific treatment programs. There is a need for a large, randomized comparison of clomipramine and exposure that includes adequate follow-up of subjects after treatment has concluded. (PsycINFO Database Record (c) 2012 APA, all rights reserved)

Cox BJ, Swinson RP, et al. Clomipramine, fluoxetine, and behavior therapy in the treatment of obsessive-compulsive disorder: a meta-analysis. J Behav Ther Exp Psychiatry. 1993;24(2):149-53.

The most common effective treatments for obsessive-compulsive disorder include clomipramine, fluoxetine, and exposure-based behavior therapy. A meta-analysis was conducted on the results from 25 appropriate treatment studies (1975-1991). All three treatments were significantly effective for most of the outcome variables (overall severity, anxiety, depression). Exposure was not significantly effective for reducing depressed mood. More treatment outcome studies are needed before a clearly superior treatment or combination of treatments can be statistically determined.

Van Blakom AJLM, van Oppen P, et al. A meta-analysis on the treatment of obsessive compulsive disorder: A comparison of antidepressants, behavior, and cognitive therapy. Clinical Psychology Review. 1994;14(5):359-81.

Conducted a meta-analysis to integrate treatment results from outcome research on the efficacy of antidepressants, behavior therapy (BT), cognitive therapy, and the combination of these methods in obsessive compulsive disorder. The effect sizes for self-rated obsessive compulsive symptoms (OCSs) were significantly smaller than for assessor-ratings. On self- and assessor-rated OCSs, the serotonergic antidepressants (SAs) clomipramine, fluoxetine, and fluvoxamine; BT; and the combination of SAs with BT were significantly more effective than placebo. Although scarce, follow-up data from 3 mo to 6 yrs indicated that the short-term treatment effects remain stable. On self-ratings, BT was significantly more effective than SAs. The combination treatment tended to be more effective than SAs. On assessor ratings, however, no difference could be shown between these 3 treatments. (PsycINFO Database Record (c) 2013 APA, all rights reserved).

Abramowitz JS. Effectiveness of psychological and pharmacological treatments for obsessive-compulsive disorder: a quantitative review. J Consult Clin Psychol. 1997;65(1):44-52.

Quantitative review of the controlled treatment outcome literature for obsessive-compulsive disorder (OCD) showed that exposure with response prevention was highly effective in reducing OCD symptoms. Cognitive approaches were also found to be at least as effective as exposure procedures. It appears that both cognitive and exposure interventions involve some overlapping procedures and capitalize on similar mechanisms of change. Serotonergic medication, particularly clomipramine, also substantially reduced OCD symptoms. However, clomipramine may not be particularly superior to other serotonergic medication. The relationship between side effects and effect size in medication trials was explored.

Foa EB, Franklin ME, et al. Context in the clinic: how well do cognitive-behavioral therapies and medications work in combination? Biol Psychiatry. 2002;52(10):987-97.

Cognitive-behavioral therapy (CBT) and pharmacotherapy demonstrate efficacy across the anxiety disorders, but recognition of their limitations has sparked interest in combining modalities to maximize benefit. This article reviews the empirical literature to examine whether combining treatments influences efficacy of either monotherapy. We conducted a comprehensive literature search of published randomized trials that compared combined treatment with pharmacologic or CBT monother-

apies. Ten studies that met our inclusion criteria were reviewed in detail, and within-subjects effect sizes were calculated to compare treatment conditions within and across studies. At posttreatment and follow-up, effect size and percentage responder data failed to clearly demonstrate an advantage or disadvantage of combined treatment over CBT alone for obsessive-compulsive disorder, social phobia, and generalized anxiety disorder. Some advantage of combined treatment over pharmacotherapy alone emerged from the few studies that allowed for such a direct comparison. In contrast, combined treatment for panic disorder seems to provide an advantage over CBT alone at posttreatment, but is associated with greater relapse after treatment discontinuation. The advantage of combined treatment may vary across the anxiety disorders. The potential differences in usefulness of combined treatment are discussed, directions for future research are suggested, and implications for clinical practice are considered.

Meca JS, Conesa AG, et al. El tratamiento psicológico del trastorno obsesivo-compulsivo en Europa: Un estudio meta-analítico. Psicología Conductual Revista Internacional de Psicología Clínica de la Salud. 2003;11(2):213-37.

This article discusses the results of a meta-analysis of the effectiveness of psychological treatment, by itself or in combination with drugs, of the obsessive-compulsive disorder. Twenty-three European articles meeting the selection criteria were included, offering a total of 43 independent studies. Standardized mean difference was calculated between the pretest and postest means. The global mean effect size, d+ = 1.443, showed a clear efficacy for reducing obsessions and compulsions as well as symptoms of depression, anxiety, and social adjustment, although the latter was reduced to a lesser extent. The most effective treatments consisted of combining exposition and response prevention techniques or cognitive restructuring with antidepressants (d+ = 2.044 and d+ = 2.953, respectively), such as clomipramine or fluvoxamine. A predictive model of the efficacy is proposed as a function of the different treatments and the methodological quality of studies. Finally, the practical, clinical, and research implications of the results are discussed. (PsycINFO Database Record (c) 2013 APA, all rights reserved) (journal abstract).

Eddy KT, Dutra l, et al. A multidimensional meta-analysis of psychotherapy and pharmacotherapy for obsessive-compulsive disorder. Clin Psychol Rev. 2004;24(8):1011-30.

A number of qualitative and meta-analytic reviews point to the efficacy of psychotherapeutic and pharmacological interventions for obsessive-compulsive disorder (OCD). In this article, we report a multidimensional meta-analysis of psychological and pharmacological treatment studies for OCD published between 1980 and 2001, examining a range of variables not previously meta-analyzed, including exclusion rates and exclusion criteria, percent of patients improved or recovered post-treatment, mean post-treatment symptomatology, and long-term outcome. These additional metrics provide a more nuanced view of the strengths and limitations of the existing data and their implications for clinical practice. Behavioral and cognitive-behavioral therapy, and a range of pharmacological interventions, lead to substantial improvement for the average patient, with individual psychotherapies and clomipramine and other Serotonin reuptake inhibitors faring best across multiple metrics. However, OCD symptoms persist at moderate levels even following adequate treatment course, and no replicable data are available on maintenance of gains for either form of treatment at 1 year or beyond. Future research should track recruitment and exclusion of study participants, include more comorbid patients, and focus on longer-term follow-up using multiple indices of outcome. More research on combined pharmacological and psychotherapeutic interventions is also indicated.

Gava I, Barbui C, et al. Psychological treatments versus treatment as usual for obsessive compulsive disorder (OCD). Cochrane Database Syst Rev. 2007;(2):Cd005333.

BACKGROUND: Obsessive compulsive disorder (OCD) is a chronic anxiety disorder associated with significant morbidity, social impairment and lower quality of life. Psychological treatments are a frequently used approach for OCD. OBJECTIVES: To perform a systematic review of randomised trials of psychological treatments for obsessive compulsive disorder in comparison with treatment as usual. SEARCH STRATEGY: We conducted an electronic search of CCDANCTR-Studies (31/10/2006), and other databases. We searched reference lists, and contacted experts in the field. SELECTION CRITERIA: Published and unpublished randomised trials of psychological treatments versus treatment as usual for adults with a diagnosis of OCD DATA COLLECTION AND ANALYSIS: Two review authors worked independently throughout the selection of trials and data extraction. Findings were compared and disagreements were discussed with a third review author. Full data extraction, using a standardised data extraction sheet, was performed on all studies included in the review. Results were synthesised using Review Manager software. For dichotomous data, odds ratios were calculated. For continuous data, effect sizes were obtained and the standardised mean

difference, with 95% confidence intervals, was calculated. Fixed and random effects models were used to pool the data. Reasons for heterogeneity in studies were explored and sensitivity analyses were performed by excluding trials of lower quality. MAIN RESULTS: Eight studies (11 study comparisons) were identified, all of which compared cognitive and/or behavioural treatments versus treatment as usual control groups. Seven studies (ten comparisons) had usable data for meta-analyses. These studies demonstrated that patients receiving any variant of cognitive behavioural treatment exhibited significantly fewer symptoms post-treatment than those receiving treatment as usual (SMD -1.24, 95% CI -1.61 to -0.87, I(2) test for heterogeneity 33.4%). Different types of cognitive and/or behavioural treatments showed similar differences in effect when compared with treatment as usual. The overall treatment effect appeared to be influenced by differences in baseline severity. AUTHORS' CONCLUSIONS: The findings of this review suggest that psychological treatments derived from cognitive behavioural models are an effective treatment for adult patients with obsessive compulsive disorder. Larger high quality randomised controlled trials involving longer follow up periods are needed, to further test cognitive behavioural treatments, and other psychological approaches, in comparison to each other and control conditions. Future trials should examine the predictors of response to each treatment, and also conduct cost-effectiveness evaluations.

Jonsson H, Hougaard E. Group cognitive behavioural therapy for obsessive-compulsive disorder: a systematic review and meta-analysis. Acta Psychiatr Scand. 2009;119(2):98-106.

OBJECTIVE: Behaviour therapy with exposure and response prevention (ERP) or cognitive behavioural therapy (CBT) including ERP are considered the psychological treatments of choice for obsessive-compulsive disorder (OCD), but group CBT/ERP has received relatively little research attention in the treatment of OCD. The aim of this study was to provide a meta-analysis of the effectiveness of group CBT/ERP for OCD. METHOD: A systematic literature search was conducted and studies were meta-analysed by means of the Cochrane Review Manager Program with measures of i) pre- to post-effect sizes (ES) and ii) between-group ES in comparison with different control conditions. Outcome was primarily measured on the Y-BOCS and ES was calculated in the form of Cohens d. RESULTS: Thirteen trials were included in the meta-analysis. The overall pre-post-ES of these trials of 1.18 and a between-group ES of 1.12 compared with waiting list control in three randomized controlled studies indicate that group CBT/ERP is an effective treatment for OCD. Group CBT achieved better results than pharmacological treatment in two studies. One study found no significant differences between individual and group CBT. CONCLUSION: Group CBT is an effective treatment for OCD, but more studies are needed to compare the effectiveness of group and individual treatment formats.

Podea D, Suciu R, et al. An update on the cognitive behavior therapy of obsessive compulsive disorder in adults. Journal of Cognitive and Behavioral Psychotherapies. 2009;9(2):221-33.

Obsessive-compulsive disorder (OCD) is a chronic anxiety disorder with an estimated lifetime prevalence in adults of 2–3 %. Our aim is to provide an overview of the development of effective psychological treatments for OCD, together with a systematic literature review of the latest research in the field. An extensive literature search was performed to identify relevant articles in several databases including MEDLINE, PUBMED and PsycINFO, using the following keywords: obsessive–compulsive disorder, cognitive-behavioural therapy, exposure, response prevention, cognitive therapy. Controlled trials have demonstrated that cognitive- behavioral therapy (CBT) is an effective treatment for OCD. CBT is at least as effective as medication and shows good benefits at follow up. Nevertheless, more studies are still needed, mainly focusing on long-term follow-up, group-treatment and the combined use of CBT with SSRIs. A prefrontal cortico-striato-thalamic brain system is involved in the mediation of OCD symptoms. Recent research has demonstrated that CBT for OCD can systematically modify cerebral metabolic activity in this cortico-subcortical circuit in a manner which is significantly related to clinical outcome. (PsycINFO Database Record (c) 2014 APA, all rights reserved) (journal abstract).

Huang FF, Li ZJ, et al. Cognitive behavioral therapy combined with pharmacotherapy for obsessive compulsive disorder: A meta-analysis. Chinese Mental Health Journal. 2013;27(9):643-9.

Objective: To evaluate the efficacy of pharmacotherapy combined with cognitive behavioral therapy (CBT) in the treatment of obsessive compulsive disorder (CCD) with meta-analysis of data came from randomized controlled trials (RCTs) and to help choose suitable treatment plan in clinic. Methods: The databases of Pubmed, Embase and Central were searched to collect efficacy data of pharmacotherapy combined with CBT versus either alone in RCTs, the mean difference was used as effect size and the measured data of Yale-Brown Obsessive Compulsive Scale (Y-BOCS) were extracted from each study to conduct a meta-analysis with RevMan5. Results: Seven studies were involved in

the meta-analysis, including 468 patients with OCD. There was no heterogeneity between 3 sets of data which compared the efficacy of combined therapy and pharmacotherapy alone after excluding 1 set of data which possibly caused the heterogeneity (Q = 0.48, P > 0.1) and combined therapy was superior to pharmacotherapy alone in improving obsessive compulsive symptom (MD = 6.46, Z = 5.03, P ≤ 0.05). There was no heterogeneity between 7 sets of data which compared the efficacy of combined therapy and CBT alone (Q = 9.08, P > 0.1) and combined therapy was not superior to CBT alone in improving obsessive compulsive symptom (MD = 0.87, Z = 1.22, P > 0.05). Conclusion: It suggests that pharmacotherapy combined with CBT may be superior to pharmacotherapy alone but be comparable to CBT alone in improving obsessive compulsive symptom and further study is necessary. (PsycINFO Database Record (c) 2014 APA, all rights reserved) (journal abstract).

Romanelli RJ, Wu FM, et al. Behavioral therapy and serotonin reuptake inhibitor pharmacotherapy in the treatment of obsessive-compulsive disorder: a systematic review and meta-analysis of head-to-head randomized controlled trials. Depress Anxiety. 2014;31(8):641-52.

BACKGROUND: Effective treatments for obsessive-compulsive disorder (OCD) include behavioral therapy (exposure and response/ritual prevention and cognitive behavioral therapy) and serotonin-reuptake inhibitors (SRIs); however, the relative efficacy of these treatments is not well established. We sought to review evidence from head-to-head randomized-controlled trials (RCTs) of behavioral therapy and SRIs in the treatment of OCD. METHODS: A systematic search of multiple databases was conducted from first available date to June 30, 2012, for RCTs in the treatment of OCD among outpatients, comparing behavioral therapy and SRIs, alone or combined. Two independent reviewers evaluated studies for eligibility and risk of bias. The main outcome measure was posttreatment mean Yale-Brown Obsessive-Compulsive Scale (YBOCS) score. RESULTS: We identified 2,186 unique articles. Fifteen articles were included, describing 13 RCTs. Pooled standardized mean difference (SMD; 95% confidence intervals) in YBOCS score significantly favored behavioral therapy over SRIs (0.37; 0.10, 0.64; P = .007), but not in a subset of trials that used selective SRIs (0.22; -0.02, 0.47; P = .070). Within individual trials, effect sizes significantly favored the combination of behavioral therapy plus an SRI over an SRI, but not behavioral therapy, alone. CONCLUSIONS: This review provides evidence that, among outpatients with OCD, behavioral therapy is more effective than SRIs, overall, but not selective SRIs. Furthermore, the combination of behavioral therapy plus an SRI is more effective than an SRI alone. These data may be used to inform the development of evidence-based treatment guidelines; however, more studies are also needed to further evaluate the relative efficacy of these interventions.

Öst **LG, Havnen A, et al. Cognitive behavioral treatments of obsessive–compulsive disorder. A systematic review and meta-analysis of studies published 1993–2014. Clinical Psychology Review. 2015;40:156-69.**

Obsessive–compulsive disorder is ranked by the WHO as among the 10 most debilitating disorders and tends to be chronic without adequate treatment. The only psychological treatment that has been found effective is cognitive behavior therapy (CBT). This meta-analysis includes all RCTs (N=37) of CBT for OCD using the interview-based Yale–Brown Obsessive Compulsive Scale, published 1993 to 2014. The effect sizes for comparisons of CBT with waiting-list (1.31), and placebo conditions (1.33) were very large, whereas those for comparisons between individual and group treatment (0.17), and exposure and response prevention vs. cognitive therapy (0.07) were small and non–significant. CBT was significantly better than antidepressant medication (0.55), but the combination of CBT and medication was not significantly better than CBT plus placebo (0.25). The RCTs have a number of methodological problems and recommendations for improving the methodological rigor are discussed as well as clinical implications of the findings. (PsycINFO Database Record (c) 2015 APA, all rights reserved) (journal abstract).

Öst **LG, Havnen A, et al. Cognitive behavioral treatments of obsessive–compulsive disorder. A systematic review and meta-analysis of studies published 1993–2014. Clinical Psychology Review. 2015;40:156-69.**

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number of methodological problems and recommendations for improving the methodological rigor are discussed as well as clinical implications of the findings. (PsycINFO Database Record (c) 2015 APA, all rights reserved) (journal abstract).

1.2. Eficacia, tolerabilidad y seguridad de los tratamientos psicofarmacológicos en monoterapia

Piccinelli M, Pini S, et al. Efficacy of drug treatment in obsessive-compulsive disorder. A meta-analytic review. Br J Psychiatry. 1995;166(4):424-43.

BACKGROUND: A review of the efficacy of antidepressant drug treatment in patients with obsessive-compulsive disorder (OCD), using a meta-analytic approach. METHOD: Randomised double-blind clinical trials of antidepressant drugs, carried out among patients with OCD and published in peer-reviewed journals between 1975 and May 1994, were selected together with three studies currently in press. Forty-seven trials were located by searching the Medline and Excerpta Medica-Psychiatry data bases, scanning psychiatric and psychopharmacological journals, consulting recent published reviews and bibliographies, contacting pharmaceutical companies and through cross-references. Hedges' g was computed in pooled data at the conclusion of treatment under double-blind conditions or at the latest reported point of time during this treatment period. For each trial, effect sizes were computed for all available outcome measures of the following dependent variables: obsessive-compulsive symptoms considered together; obsessions; compulsions; depression; anxiety; global clinical improvement; psychosocial adjustment; and physical symptoms. RESULTS: Clomipramine was superior to placebo in reducing both obsessive-compulsive symptoms considered together (g = 1.31; 95% CI = 1.15 to 1.47) as well as obsessions (g = 0.89, 95% CI = 0.36 to 1.42) and compulsions (g = 0.79; 95% CI = 0.34 to 1.24) taken separately. Also, selective serotonin re-uptake inhibitors (SSRIs) as a class were superior to placebo, weighted mean g being respectively 0.47 (95% CI = 0.33 to 0.61), 0.54 (95% CI = 0.34 to 0.74) and 0.52 (95% CI = 0.34 to 0.70) for obsessive-compulsive symptoms considered together, and obsessions and compulsions taken separately. Although on Y-BOCS the increase in improvement rate over placebo was 61.3%, 28.5%, 28.2% and 21.6% for clomipramine, fluoxetine, fluvoxamine, and sertraline respectively, the trials testing clomipramine against fluoxetine and fluvoxamine showed similar therapeutic efficacy between these drugs. Finally, both clomipramine and fluvoxamine proved superior to antidepressant drugs with no selective serotonergic properties. CONCLUSION: Antidepressant drugs are effective in the short-term treatment of patients suffering from OCD; although the increase in improvement rate over placebo was greater for clomipramine than for SSRIs, direct comparison between these drugs showed that they had similar therapeutic efficacy on obsessive-compulsive symptoms; clomipramine and fluvoxamine had greater therapeutic efficacy than antidepressant drugs with no selective serotonergic properties; concomitant high levels of depression at the outset did not seem necessary for clomipramine and for SSRIs to improve obsessive-compulsive symptoms.

Stein DJ, Spadaccini E, et al. Meta-analysis of pharmacotherapy trials for obsessive-compulsive disorder. Int Clin Psychopharmacol. 1995;10(1):11-8.

Since the discovery that clomipramine was effective in the treatment of obsessive-compulsive disorder (OCD), trials of several different medications for OCD have been published. The question of which agent, if any, is the medication of choice in OCD is of real clinical concern. Published clinical trials were collected using computerized search on MedLine and PsychLit. Trials that met predetermined criteria were included in a meta-analysis. Analyses of variance were used to compare the specific effect sizes of different medications in OCD. In placebo-controlled trials, serotonin reuptake inhibitor (SRI) type had a significant effect on medication effect size, with clomipramine more effective than fluoxetine. Although this finding did not alter when trials were restricted to those with large numbers of subjects (n > 50), the analysis was based on a very limited number of studies. The fact that so few placebo-controlled studies have been done in OCD compromises the findings of this meta-analysis. It would be premature to extrapolate the results to clinical practice, where clomipramine and certain selective SRIs are currently and justifiably used as first-line agents. Nevertheless, the current study supports previous work suggesting that increased serotonergic specificity is not necessarily correlated with greater efficacy in the treatment of OCD. Further head-to-head comparison studies are necessary to confirm or refute this preliminary impression.

Greist JH, Jefferson JW, et al. Efficacy and tolerability of serotonin transport inhibitors in obsessive-compulsive disorder. A meta-analysis. Arch Gen Psychiatry. 1995;52(1):53-60.

BACKGROUND: Questions have been raised regarding the relative efficacy and tolerability of the different serotonin transport inhibitors in the treatment of obsessive-compulsive disorder. We compared the results from four large multicenter placebo-controlled trials of the serotonin transport

inhibitors clomipramine hydrochloride (N = 520), fluoxetine hydrochloride (N = 355), fluvoxamine maleate (N = 320), and sertraline hydrochloride (N = 325) for the treatment of obsessive-compulsive disorder. METHODS: Effect size was calculated by subtracting the end-point drug treatment mean change from the end-point placebo mean change and dividing by the end-point pooled change standard deviation. A test for overall differences between effect sizes was conducted, followed by all possible pairwise comparisons. The Yale-Brown Obsessive Compulsive Scale was the primary outcome measure for all four studies. RESULTS: All four agents were significantly more effective than placebo, with clomipramine significantly more effective than the other three treatments, which did not differ in effect size. A significantly greater percentage of patients treated with clomipramine were rated much or very much improved than were patients treated with fluoxetine, fluvoxamine, or sertraline. CONCLUSION: While the results of this meta-analysis support the superiority of clomipramine, head-to-head, double-blind comparisons of these compounds would be the best test of comparative efficacy and tolerability.

Ackerman D, Greenland S. Multivariate meta-analysis of controlled drug studies for obsessive-compulsive disorder. Journal of Clinical Psychopharmacology. 2002;22(3):309-17.

Used metaregression to identify sources of heterogeneity in placebo-controlled trials of clomipramine, fluvoxamine, sertraline, and paroxetine with obsessive-compulsive disorder (OCD). 25 randomized, double-blind, parallel trials published between 1989 and 1999 were analyzed. Such patient characteristics as age, gender, age of obsessive-compulsive disorder (OCD) onset, and baseline severity of OCD and depression, and such study characteristics as exclusion or inclusion criteria, length of single-blind pre-randomization period, length of trial, number of subjects, and publication year were evaluated. Considerable heterogeneity was found across studies that was associated, in part, with publication year, length of single-blind pre-randomization period, length of trial, and severity of patients' OCD. The apparent superiority of clomipramine persisted after controlling for these factors. Results confirm previous reports that placebo response is higher in more recent studies. It is concluded that meta-analyses can help characterize responders and nonresponders. The authors urge investigators to provide summaries of patient characteristics, especially baseline severity, age at onset, and duration of OCD, by patients' response. (PsycINFO Database Record (c) 2012 APA, all rights reserved).

Geller DA, Biederman J, et al. Which SSRI? A meta-analysis of pharmacotherapy trials in pediatric obsessive-compulsive disorder. Am J Psychiatry. 2003;160(11):1919-28.

OBJECTIVE: The authors conducted a meta-analysis of published randomized, controlled medication trials in children and adolescents with obsessive-compulsive disorder (OCD) to assess evidence for differential efficacy based on type of drug, study design, and outcome measure. METHOD: A systematic literature search was performed for articles pertaining to the pharmacological treatment of pediatric and/or adolescent OCD. All baseline, posttreatment, and change scores with standard deviations reported in each study were included in the analyses. Effect sizes for dependent measures were expressed as standardized mean differences. The analysis included data on efficacy for four selective serotonin reuptake inhibitors (SSRIs) (paroxetine, fluoxetine, fluvoxamine, and sertraline) and clomipramine, four study designs, four dependent outcome measures, and two types of outcome scores (change and posttreatment scores). Multivariate regression was performed to assess the degree to which the effect sizes varied with the methodological features of each study. RESULTS: Twelve studies with a total of 1,044 participants met all inclusion criteria for the analysis. The pooled standardized mean difference for the results of all studies was 0.46 and showed a highly significant difference between drug and placebo treatment. Only one of the four outcome measures evaluated was not sensitive to change with treatment. A multivariate regression analysis of drug effect with other variables controlled showed that clomipramine was significantly superior to each of the SSRIs but that the SSRIs were comparably effective. CONCLUSIONS: Although highly significant, the overall effect sizes for medication were modest. Similarities and differences between the variables studied that emerged in the meta-analysis may have implications for both clinical care and future research.

Dell'Osso B, Nestadt G, et al. Serotonin-norepinephrine reuptake inhibitors in the treatment of obsessive-compulsive disorder: A critical review. J Clin Psychiatry. 2006;67(4):600-10.

OBJECTIVE: To critically review the antiobsessional properties of serotonin-norepinephrine reuptake inhibitors (SNRIs) (venlafaxine and clomipramine) in the treatment of obsessive-compulsive disorder (OCD) as an alternative to selective serotonin reuptake inhibitors (SSRIs), which are currently considered the first-line treatment of OCD. DATA SOURCES: A MEDLINE search was performed to identify clinical trials with the SNRIs venlafaxine and clomipramine published from 1996

to 2004 (keywords: SNRIs, venlafaxine, duloxetine, and clomipramine, each matched individually with the term OCD), focusing on the best-designed studies for inclusion. DATA SYNTHESIS: Much of the literature about SNRIs in OCD supports the efficacy of these compounds in the treatment of OCD. However, double-blind, placebo-controlled studies with venlafaxine are lacking, and the most relevant studies consist of active comparison trials between SNRIs and SSRIs. In these studies, SNRIs seem to be as effective as SSRIs in OCD; SNRIs might be preferred for patients with certain types of treatment-resistant OCD or those with particular comorbid conditions. A large number of placebo-controlled and active comparison trials with clomipramine document efficacy in OCD, and meta-analytic studies suggest a small superiority over SSRIs. Compared with clomipramine, the SNRI venlafaxine showed fewer side effects and better tolerability. CONCLUSION: The SNRIs may represent a valid alternative to the SSRIs, particularly in specific cases. Double-blind, placebo-controlled studies are, however, needed to confirm the positive findings reported by several studies with venlafaxine.

Soomro GM, Altman D, et al. Selective serotonin re-uptake inhibitors (SSRIs) versus placebo for obsessive compulsive disorder (OCD). Cochrane Database Syst Rev. 2008;(1):CD001765.

BACKGROUND: Obsessive compulsive disorder is a common and disabling disorder. A significant proportion of patients manifest a chronic course. Individual randomised controlled trials (RCTs) have shown that selective serotonin re-uptake inhibitors (SSRIs) are effective in this condition. Previous systematic reviews or meta-analyses summarising the evidence are methodologically problematic or limited in the scope of their analysis. OBJECTIVES: To examine the efficacy and adverse effects of serotonin re-uptake inhibitors (SSRIs) versus placebo for obsessive compulsive disorder (OCD) in adults. SEARCH STRATEGY: CCDANCTR-Studies and CCDANCTR-References were searched on 12/11/2007. Reference lists were checked. Experts in the field were contacted. SELECTION CRITERIA: All RCTs and quasi-RCTs examining the efficacy of SSRIs compared with placebo for OCD in adults were eligible for inclusion. DATA COLLECTION AND ANALYSIS: Selection of studies and data extraction were carried out by two review authors independently, and quality assessment of studies was undertaken. Data analysis was conducted using Review Manager software. Summary measures were produced using the weighted mean difference (WMD) for continuous data and relative risk (RR) for dichotomous data, with 95% confidence intervals (CI). SSRIs were examined as an overall group of drugs, and as individual drugs. MAIN RESULTS: Seventeen studies were included in the review, involving 3097 participants. Based on all 17 studies, SSRIs as a group were more effective than placebo in reducing the symptoms of OCD between 6 and 13 weeks post-treatment, measured using the Yale-Brown Obsessive Compulsive Scale (YBOCS) (WMD -3.21, 95% CI -3.84 to -2.57). The WMD for individual SSRI drugs were similar and not statistically different. Based on 13 studies (2697 participants), SSRIs were more effective than placebo in achieving clinical response at post-treatment (RR 1.84, 95% CI 1.56 to 2.17). The pooled RR was shown to be similar between individual SSRI drugs. Although reported adverse effects data were more limited, with few exceptions, the overall and individual adverse effects for the different SSRIs were always worse than for placebo and, in the majority of cases, the difference was statistically significant. Nausea, headache and insomnia were always reported amongst the most common adverse effects in trials of each of the drugs. AUTHORS' CONCLUSIONS: SSRIs are more effective than placebo for OCD, at least in the short-term, although there are differences between the adverse effects of individual SSRI drugs. The longer term efficacy and tolerability of different SSRI drugs for OCD has yet to be established.

Choi YJ. Efficacy of treatments for patients with obsessive-compulsive disorder: A systematic review. Journal of the American Academy of Nurse Practitioners. 2009;21(4):207-13.

Purpose: This systematic review examines the efficacy of pharmacological therapy for obsessive-compulsive disorder (OCD), addressing two major issues: which treatment is most effective in treating the patient's symptoms and which is beneficial for maintaining remission. Data sources: Seven databases were used to acquire articles. The key words used to search for the relative topics published from 1996 to 2007 were "obsessive-compulsive disorder" and "Yale-Brown obsession-compulsion scale." Based on the inclusion and exclusion criteria, 25 studies were selected from 57 potentially relevant studies. Conclusions: The effects of treatment with clomipramine and selective serotonin reuptake inhibitors (SSRIs: fluvoxamine, sertraline, fluoxetine, citalopram, and escitalopram) proved to be similar, except for the lower adherence rate in case of clomipramine because of its side effects. An adequate drug trial involves administering an effective daily dose for a minimum of 8 weeks. An augmentation strategy proven effective for individuals refractory to monotherapy with SSRI treatment alone is the use of atypical antipsychotics (risperidone, olanzapine, and quetiapine). Implications for practice: Administration of fluvoxamine or sertraline to patients for an adequate duration is recommended as the first-line prescription for OCD, and augmentation therapy

with risperidone, olanzapine, or quetiapine is recommended for refractory OCD. (PsycINFO Database Record (c) 2013 APA, all rights reserved) (journal abstract).

Mukai T, Kishi T, et al. A meta-analysis of inositol for depression and anxiety disorders. Human Psychopharmacology: Clinical and Experimental. 2014;29(1):55-63.

Objective This study is a meta-analysis of inositol as a treatment for depression and anxiety disorders. Methods PubMed, Cochrane Library database, and PsycINFO were searched up to 14 August 2013. A systematic review and meta-analysis of double-blind, randomized, placebo-controlled trials (RCTs) were conducted comparing inositol for depressed or anxiety disorder patients. Results Seven RCTs in depression (two bipolar depression studies, one bipolar depression and major depressive disorder (MDD) study, two MDD studies, and two premenstrual dysphoric disorder (PMDD) studies) (n = 242) were identified. Four RCTs in anxiety disorders (two obsessive–compulsive disorder studies, one panic disorder study, and one posttraumatic stress disorder study) (n = 70) were also identified. There were no statistically significant effects of inositol on depressive, anxiety, and obsessive–compulsive symptoms and discontinuation (all-cause, side effects, and worsening psychiatric symptoms). However, inositol had marginally more responders in depression than placebo (p = 0.06), and inositol showed a trend towards superior efficacy for depressive symptoms in patients with PMDD (p = 0.07). Inositol marginally caused gastrointestinal upset compared with placebo (p = 0.06). Conclusions Our results suggest that inositol may be beneficial for depressed patients, especially those with PMDD. The main limitation of this report is that a small number of studies were included in this meta-analysis. Copyright © 2013 John Wiley & Sons, Ltd. (PsycINFO Database Record (c) 2014 APA, all rights reserved) (journal abstract).

Pizarro M, Fontenelle LF, et al. An updated review of antidepressants with marked serotonergic effects in obsessive-compulsive disorder. Expert Opin Pharmacother. 2014;15(10):1391-401.

INTRODUCTION: Since the recognition of the effectiveness of clomipramine in treating obsessive-compulsive disorder (OCD), a number of recent empirical studies have confirmed a key role of the serotonergic (5-HT) system in the pathophysiology of OCD. The current study presents a review of the existing double-blind studies testing 5-HT antidepressants in OCD. AREAS COVERED: A systematic review was performed to identify double-blind, placebo-controlled, randomized clinical trials investigating the efficacy of antidepressants with marked 5-HT effects [clomipramine, selective serotonin reuptake inhibitors (SSRIs), venlafaxine, desvenlafaxine, duloxetine, mirtazapine, agomelatine, vortioxetine and vilazodone] in the short-term treatment of OCD. The search provided 29 studies investigating eight different 5-HT antidepressants. While the findings show reliable efficacy of clomipramine and SSRIs in the treatment of OCD symptoms, no double-blind studies were identified investigating the efficacy of desvenlafaxine, duloxetine, mirtazapine, agomelatine, vortioxetine or vilazodone. EXPERT OPINION: While our results support the effectiveness of older antidepressants with marked 5-HT effects in OCD, it also suggests that newer agents should be tested more comprehensively.

Serata D, Kotzalidis GD, et al. Are 5-HT3 antagonists effective in obsessive-compulsive disorder? A systematic review of literature. Hum Psychopharmacol. 2015;30(2):70-84.

OBJECTIVE: The purpose of this literature database search-based review was to critically consider and evaluate the findings of literature focusing on efficacy and safety of 5-HT3 antagonists in the treatment of obsessive-compulsive disorder (OCD), so as to test whether preclinical data match clinical therapeutic trials. DESIGN: The PubMed database has been searched for papers on 5-HT3 antagonists and OCD in humans and for animal models of OCD and 5-HT3 receptors. RESULTS: Of the clinically tested 5-HT3 receptor antagonists, ondansetron has been used to treat OCD in five therapeutic studies, whereas granisetron only in one recent trial. Both showed some efficacy in open studies and superiority to placebo in double-blind studies, along with fair safety. No animal OCD model directly implicated 5-HT3 receptors. CONCLUSIONS: Overall, results indicate some utility, but the available literature is too scanty to allow for valid conclusions to be drawn. The mismatch between animal models of obsessive-compulsive disorder and clinical data with 5-HT3 antagonists needs more clinical data to ensure that it is not an artefact.

1.3. Relación dosis-respuesta de los tratamientos psicofarmacológicos (utilización de dosis elevadas)

Bloch MH, McGuire J, et al. Meta-analysis of the dose-response relationship of SSRI in obsessive-compulsive disorder. Mol Psychiatry. 2010;15(8):850-5.

We sought to determine differences in efficacy and tolerability between different doses of selective serotonin reuptake inhibitors in the treatment of obsessive-compulsive disorder (OCD) using

meta-analysis. We identified 9 studies involving 2268 subjects that were randomized, double-blind placebo-controlled clinical trials that compared multiple, fixed-doses of selective serotonin reuptake inhibitors (SSRIs) to each other and to placebo in the treatment of adults with OCD. Change in Y-BOCS score, proportion of treatment responders, and dropouts (all-cause and due to side-effects) were determined for each included study. Weighted mean difference was used to examine mean change in Y-BOCS score. Pooled absolute risk difference was used to examine dichotomous outcomes. Meta-analysis was performed using a fixed effects model in RevMan 4.2.8. We found that compared with either low or medium doses, higher doses of SSRIs were associated with improved treatment efficacy, using either Y-BOCS score or proportion of treatment responders as an outcome. Dose of SSRIs was not associated with the number of all-cause dropouts. Higher doses of SSRIs were associated with significantly higher proportion of dropouts due to side-effects. These results suggests that higher doses of SSRIs are associated with greater efficacy in the treatment of OCD. This SSRI efficacy pattern stands in contrast to other psychiatric disorders like Major Depressive Disorder. This greater treatment efficacy is somewhat counterbalanced by the greater side-effect burden with higher doses of SSRIs. At present, there are insufficient data to generalize these findings to children or adolescents with OCD.

1.4. Acelerar la respuesta (por ejemplo, gabapentina, mirtazapina)

No se han encontrado revisiones sistemáticas.

1.5. Otros tratamientos combinados

No se han encontrado revisiones sistemáticas.

2. INTERRUPCIÓN DEL TRATAMIENTO (DURACIÓN DEL TRATAMIENTO) Y TRATAMIENTO A LARGO PLAZO

Donovan MR, Glue P, et al. Comparative efficacy of antidepressants in preventing relapse in anxiety disorders - a meta-analysis. J Affect Disord. 2010;123(1-3):9-16.

BACKGROUND: We assessed the efficacy of continuation treatment with antidepressants in a meta-analysis of relapse prevention studies in the five principal anxiety disorders, to explore the benefit of continuation treatment in each disorder, and their relative efficacy across these disorders. METHOD: Double-blind placebo-controlled studies with relapse prevention designs in Panic Disorder, Generalized Anxiety Disorder, Social Phobia, Post-Traumatic Stress Disorder and Obsessive-Compulsive Disorder were identified in a systematic literature search. The primary efficacy comparison was relapse rates between active and placebo arms calculated as odds ratios (ORs) using Review Manager version 5.0. Relapse data were also used to calculate relative risk (RR), risk difference (RD) and number needed to treat (NNT). RESULTS: Twenty-two relapse prevention trials were identified for these 5 disorders. Continuation antidepressant treatment produced robust treatment effects for each disorder, however the magnitude varied by indication. The greatest treatment effect was noted for GAD (pooled OR 0.20), whereas the pooled ORs for PD and OCD were for almost 2-fold higher (0.35 and 0.38 respectively). RR, RD and NNT showed similar statistically significant trends. LIMITATIONS: This study cannot identify an optimal duration of therapy. This analysis only examined studies testing monoamine reuptake inhibiting antidepressants, and therefore these results might not be generalizable to other classes of antianxiety agents. CONCLUSIONS: This meta-analysis underscores the importance of continuation treatment following acute response in all 5 anxiety disorders, however the relative efficacy of continuation antidepressant treatment appears to vary by disorder.

Sharma E, Thennarasu K, et al. Long-term outcome of obsessive-compulsive disorder in adults: a meta-analysis. J Clin Psychiatry. 2014;75(9):1019-27.

OBJECTIVE: To study the long-term rate and predictors of remission in adults with obsessive-compulsive disorder (OCD), using meta-analysis. DATA SOURCES: The MEDLINE database was searched to May 2013 using the search terms obsessive-compulsive disorder, prospective, outcome study, clinical course, remission, prognosis, follow-up, and long-term and limits for language (English), species (humans), and age (adults). This was supplemented by manual bibliographic cross-referencing. STUDY SELECTION: English-language studies from peer-reviewed journals on adults with DSM-III-R, DSM-IV, DSM-IV-TR, ICD-9, or ICD-10 diagnosis of OCD followed up for >/= 1 year and treated with serotonin reuptake inhibitors and/or cognitive-behavioral therapy that re-

ported rate of remission (Yale-Brown Obsessive Compulsive Scale [YBOCS] score < 16 at longest follow-up) were included. DATA EXTRACTION: Data were gathered as numbers/means/percentages/categories on sample size, study design, follow-up duration, age at assessment, illness duration, age at illness onset, gender, marital status, inpatient/outpatient status, family history, baseline YBOCS score, comorbidities, and remission. RESULTS: Seventeen studies (pooled N = 1,265) fit the selection criteria and were used for the meta-analysis. The pooled sample had a mean follow-up duration 4.91 years and was predominantly male and outpatient and had onset of illness in the second decade, illness duration more than 10 years, and moderate-to-severe OCD. Pooled remission rate was 53% (95% CI, 42%-65%). Prospective studies showed higher pooled remission rate than retrospective studies (55% [95% CI, 45%-65%] vs 50% [95% CI, 27%-73%], P < .001). Indian studies showed higher pooled remission rate than others (71% [95% CI, 59%-83%] vs 48% [95% CI, 37%-59%], P < .001). Age at onset (t = -7.08, P = .019), illness duration (t = -8.13, P = .015), baseline YBOCS score (t = -6.81,P = .021), and male gender (t = -5.92, P = .027) had significant negative association with remission on meta-regression. CONCLUSION: A high long-term remission rate found in this meta-analysis is contrary to generally held beliefs about poor outcome of individuals with OCD. Multicenter, prospective, long-term studies should systematically examine course and outcome in larger samples, emphasizing symptomatic and functional recovery.

3. PREDICTORES DE RESPUESTA AL TRATAMIENTO FARMACOLÓGICO (síntomas especiales)

- Conductas de acumulación.
- Tics.
- Depresión.
- Bajo *insight*.
- Según subtipos.

Thiel N, Hertenstein E, et al. The effect of personality disorders on treatment outcomes in patients with obsessive-compulsive disorders. J Pers Disord. 2013;27(6):697-715.

The effect of comorbid personality disorders (PD) on treatment outcomes in obsessive-compulsive disorder (OCD) is unclear. The authors systematically review results from investigations of therapy outcomes in adult patients with OCD and a comorbid PD. PsycINFO and MEDLINE were searched for original articles. Twenty-three studies assessing PDs through interviews were selected. Cluster A PDs, particularly schizotypal PD, narcissistic PD, and the presence of two or more comorbid PDs, were associated with poorer treatment outcomes in patients with OCD. With regard to other PDs and clusters, the results are inconsistent or the sample sizes are too small to reach a conclusion. OCD patients with different comorbid PDs differ in their therapeutic response to treatment. To optimize the treatment of OCD, the predictive value of PDs on the treatment outcome should be further investigated, and treatment of Axis I and II comorbidity requires more attention.

Bloch MH, Bartley CA, et al. Meta-analysis: hoarding symptoms associated with poor treatment outcome in obsessive-compulsive disorder. Mol Psychiatry. 2014;19(9):1025-30.

DSM-5 recognizes hoarding disorder as distinct from obsessive-compulsive disorder (OCD), codifying a new consensus. Hoarding disorder was previously classified as a symptom of OCD and patients received treatments designed for OCD. We conducted a meta-analysis to determine whether OCD patients with hoarding symptoms responded differently to traditional OCD treatments compared with OCD patients without hoarding symptoms. An electronic search was conducted for eligible studies in PubMed. A trial was eligible for inclusion if it (1) was a randomized controlled trial, cohort or case-control study; (2) compared treatment response between OCD patients with and those without hoarding symptoms, or examined response to treatment between OCD symptom dimensions (which typically include hoarding) and (3) examined treatment response to pharmacotherapy, behavioral therapy or their combination. Our primary outcome was differential treatment response between OCD patients with and those without hoarding symptoms, expressed as an odds ratio (OR). Twenty-one studies involving 3039 total participants including 304 with hoarding symptoms were included. Patients with OCD and hoarding symptoms were significantly less likely to respond to traditional OCD treatments than OCD patients without hoarding symptoms (OR=0.50 (95% confidence interval 0.42-0.60), z=-7.5, P<0.0001). This finding was consistent across treatment modalities. OCD patients with hoarding symptoms represent a population in need of further treatment research. OCD patients with hoarding symptoms may benefit more from interventions specifically targeting their hoarding symptoms

4. TRATAMIENTO FARMACOLÓGICO EN POBLACIONES ESPECIALES

4.1. Ancianos

No hemos encontrado revisiones sistemáticas.

4.2. Embarazo y lactancia (NOTA: requiere búsqueda específica)

Ross LE, McLean LM. Anxiety disorders during pregnancy and the postpartum period: A systematic review. J Clin Psychiatry. 2006;67(8):1285-98.

OBJECTIVE: The postpartum period is recognized as a time of vulnerability to affective disorders, particularly postpartum depression. In contrast, the prevalence and clinical presentation of anxiety disorders during pregnancy and the postpartum period have received little research attention. In this article, we review the medical literature as it relates to the prevalence and clinical presentation of panic disorder, obsessive-compulsive disorder, posttraumatic stress disorder, and generalized anxiety disorder during pregnancy and the postpartum period. DATA SOURCES: MEDLINE (1966 to July 2005 week 1) and PsycInfo (1840 to July 2005 week 1) were searched using combinations of the following search terms: pregnancy, childbirth, postpartum, panic disorder, phobia, obsessive-compulsive disorder, posttraumatic stress disorder, and generalized anxiety disorder. STUDY SELECTION: All relevant papers published in English and reporting original data related to perinatal anxiety disorders were included. DATA EXTRACTION: Studies were examined for data related to the prevalence, presentation, predictors/risk factors, new onset, course, and treatment of anxiety disorders during pregnancy and the postpartum period. DATA SYNTHESIS: Anxiety disorders are common during the perinatal period, with reported rates of obsessive-compulsive disorder and generalized anxiety disorder being higher in postpartum women than in the general population. The perinatal context of anxiety disorders presents unique issues for detection and management. CONCLUSIONS: Future research is needed to estimate the prevalence of perinatal anxiety disorders more precisely, to identify potential implications of maternal anxiety disorders for maternal quality of life and child development, and to determine safe and effective treatment methods

Marchesi C, Ossola P, et al. Clinical management of perinatal anxiety disorders: A systematic review. Journal of Affective Disorders. 2016;190:543-50.

Background: In the last few decades, there has been a growing interest in anxiety disorders (AnxD) in the perinatal period. Although AnxD are diagnosed in 4–39% of pregnant women and in up to 16% of women after delivery, evidence on their clinical management is limited. Methods: A systematic review was conducted on pharmacological and non-pharmacological treatment of AnxD in the perinatal period. Relevant papers published from January 1st 2015 were identified searching the electronic databases MEDLINE, Embase, PsycINFO and the Cochrane Library. Results: 18 articles met inclusion criteria. Selected studies supported the use of cognitive-behavioural therapy (CBT) for obsessive–compulsive disorder (OCD), panic disorder (PD) and specific phobia both in pregnancy and postpartum. Selective serotonin reuptake inhibitors (SSRIs) led to significant OCD and PD improvement both in pregnancy and postpartum with no side effects for the babies. In the largest clinical sample to date, 65% of postpartum patients who entered the open-label trial of fluvoxamine (up to 300 mg/day) experienced a 30% or greater decrease in the total score of the Yale–Brown Obsessive– Compulsive Scale (Y-BOCS). During pregnancy, SSRIs and tricyclic antidepressants (TCAs) led to remission of panic symptoms and healthy outcomes for the babies. Limitations: Study design, mostly case reports, and enrolment of subjects mainly from outpatient specialty units might have limited community-wide generalisability. Conclusions: Keeping in mind the scantiness and heterogeneity of the available literature, the best interpretation of the available evidence appears to be that CBT should be the first treatment offered to pregnant and breastfeeding women with AnxD. However SSRIs can represent a first line treatment strategy, and not exclusively in cases where AnxD is refractory to CBT. (PsycINFO Database Record (c) 2016 APA, all rights reserved) (journal abstract).

4.3. Comorbilidades psiquiátricas

No hemos encontrado revisiones sistemáticas con TOC como diagnóstico primario.

5. TRATAMIENTO DEL TOC CON RESPUESTA PARCIAL O FALTA DE RESPUESTA

5.1. Optimización del tratamiento

No hemos encontrado revisiones sistemáticas.

5.2. Combinación (de dos antidepresivos)

No hemos encontrado revisiones sistemáticas.

5.3. Potenciación

5.3.1. Con psicoterapia

No hemos encontrado revisiones sistemáticas. Tal vez haya información en alguno de los metanálisis de psicoterapia.

5.3.2. Con antipsicóticos

Sareen J, Kirshner A, et al. Do antipsychotics ameliorate or exacerbate Obsessive Compulsive Disorder symptoms? A systematic review. J Affect Disord. 2004;82(2):167-74.

BACKGROUND: Paradoxically, some reports in the literature support the use of antipsychotics in the treatment of Obsessive Compulsive Disorder (OCD), while other reports suggest that antipsychotics can exacerbate OCD symptoms. To date, there is no published systematic review of the relationship between OCD symptoms and antipsychotic drugs. METHODS: A Medline and PsychInfo search (1980-2003) was conducted to collect published reports of the interactions between antipsychotics and OCD symptoms. RESULTS: In the treatment of refractory OCD, case series, open label trials and placebo-controlled trials were found suggesting efficacy of antipsychotic augmentation to ongoing antidepressant treatment. In the placebo-controlled trials with haloperidol, risperidone, olanzapine, and quetiapine, a significantly higher response rate (46-71%) was found for the antipsychotic groups, compared to no response for the placebo groups. Reports of exacerbation of OCD symptoms with the use of atypical antipsychotics were limited to individuals with a primary psychotic disorder. LIMITATIONS: Definition of response in most of these treatment studies was based on a modest reduction of OCD symptoms, and no studies were available on long-term efficacy. There were also no published reports that systematically evaluated the incidence of OCD symptoms associated with atypical antipsychotics. CONCLUSIONS: All antipsychotics mentioned above had short-term controlled evidence to support their use as augmenting agents in the treatment of refractory OCD. The suggested management of OCD induction/exacerbation due to atypical antipsychotics is to increase the dose of the atypical antipsychotic and/or add a selective serotonin reuptake inhibitor.

Bloch MH, Landeros-Weisenberger A, et al. A systematic review: antipsychotic augmentation with treatment refractory obsessive-compulsive disorder. Mol Psychiatry. 2006;11(7):622-32.

As many as half of obsessive-compulsive disorder (OCD) patients treated with an adequate trial of serotonin reuptake inhibitors (SRIs) fail to fully respond to treatment and continue to exhibit significant symptoms. Many studies have assessed the effectiveness of antipsychotic augmentation in SRI-refractory OCD. In this systematic review, we evaluate the efficacy of antipsychotic augmentation in treatment-refractory OCD. The electronic databases of PubMed, PsychINFO (1967-2005), Embase (1974-2000) and the Cochrane Central Register of Controlled Trials (CENTRAL, as of 2005, Issue 3) were searched for relevant double-blind trials using keywords 'antipsychotic agents' or 'neuroleptics' and 'obsessive-compulsive disorder'. Search results and analysis were limited to double-blind, randomized control trials involving the adult population. The proportion of subjects designated as treatment responders was defined by a greater than 35% reduction in Yale Brown Obsessive-Compulsive Scale (Y-BOCS) rating during the course of augmentation therapy. Nine studies involving 278 participants were included in the analysis. The meta-analysis of these studies demonstrated a significant absolute risk difference (ARD) in favor of antipsychotic augmentation of 0.22 (95% confidence interval (CI): 0.13, 0.31). The subgroup of OCD patients with comorbid tics have a particularly beneficial response to this intervention, ARD=0.43 (95% CI: 0.19, 0.68). There was also evidence suggesting OCD patients should be treated with at least 3 months of maximal-tolerated therapy of

an SRI before initiating antipsychotic augmentation owing to the high rate of treatment response to continued SRI monotherapy (25.6%). Antipsychotic augmentation in SRI-refractory OCD is indicated in patients who have been treated for at least 3 months of maximal-tolerated therapy of an SRI. Unfortunately, only one-third of treatment-refractory OCD patients show a meaningful treatment response to antipsychotic augmentation. There is sufficient evidence in the published literature, demonstrating the efficacy of haloperidol and risperidone, and evidence regarding the efficacy of quetiapine and olanzapine is inconclusive. Patients with comorbid tics are likely to have a differential benefit to antipsychotic augmentation.

Fineberg NA, Stein DJ, et al. Adjunctive quetiapine for serotonin reuptake inhibitor-resistant obsessive-compulsive disorder: a meta-analysis of randomized controlled treatment trials. Int Clin Psychopharmacol. 2006;21(6):337-43.

Small studies have shown positive effects from adding a variety of antipsychotic agents in patients with obsessive-compulsive disorder who are unresponsive to treatment with serotonin reuptake inhibitors. The evidence, however, is contradictory. This paper reports a meta-analysis of existing double-blind randomized placebo-controlled studies looking at the addition of the second-generation antipsychotic quetiapine in such cases. Three studies fulfilled the inclusion criteria. Altogether 102 individuals were subjected to analysis using Review Manager (4.2.7). The results showed evidence of efficacy for adjunctive quetiapine (<400 mg/day) on the primary efficacy criterion, measured as changes from baseline in total Yale-Brown Obsessive Compulsive Scale scores (P=0.008), the clinical significance of which was limited by between-study heterogeneity. The mechanism underlying the effect may involve serotonin and/or dopamine neurotransmission.

Skapinakis P, Papatheodorou T, et al. Antipsychotic augmentation of serotonergic antidepressants in treatment-resistant obsessive-compulsive disorder: a meta-analysis of the randomized controlled trials. Eur Neuropsychopharmacol. 2007;17(2):79-93.

This study aimed to determine the effectiveness of antipsychotic augmentation of serotonergic antidepressants in the management of treatment-resistant obsessive compulsive disorder by carrying out a meta-analysis of all randomized controlled trials. Studies selected through a literature search conducted in March 2006. Ten trials comparing antipsychotic drugs versus placebo met inclusion criteria (haloperidol [n=1], risperidone [n=3], olanzapine [n=2], quetiapine [n=4]). A total of 157 patients were randomized to study drug and 148 were randomized to placebo. Response occurred more often among patients randomized to antipsychotic drugs. The weighted combined response rate ratio by random effects meta-analysis was 3.31 (95% CI 1.40-7.84). Significant between studies heterogeneity was partly explained by the definition of refractoriness, the type and dose of the drug used and the inclusion or exclusion of patients with tic disorders. The study supports the use of antipsychotic drugs as an augmentation strategy but more and larger trials are needed.

Komossa K, Depping AM, et al. Second-generation antipsychotics for obsessive compulsive disorder. Cochrane Database Syst Rev. 2010;(12):Cd008141.

BACKGROUND: Obsessive compulsive disorder (OCD) is a psychiatric disorder which has been shown to affect 2 to 3.5% of people during their lifetimes. Inadequate response occurs in 40% to 60% of people that are prescribed first line pharmaceutical treatments (selective serotonin reuptake inhibitors (SSRIs)). To date not much is known about the efficacy and adverse effects of second-generation antipsychotic drugs (SGAs) in people suffering from OCD. OBJECTIVES: To evaluate the effects of SGAs (monotherapy or add on) compared with placebo or other forms of pharmaceutical treatment for people with OCD. SEARCH STRATEGY: The Cochrane Depression, Anxiety and Neurosis Group's controlled trial registers (CCDANCTR-Studies and CCDANCTR-References) were searched up to 21 July 2010. The author team ran complementary searches on ClinicalTrials.gov and contacted key authors and drug companies. SELECTION CRITERIA: We included double-blind randomised controlled trials (RCTs) comparing oral SGAs (monotherapy or add on) in adults with other forms of pharmaceutical treatment or placebo in people with primary OCD. DATA COLLECTION AND ANALYSIS: We extracted data independently. For dichotomous data we calculated the odds ratio (OR) and their 95% confidence intervals (CI) on an intention-to-treat basis based on a random-effects model. For continuous data, we calculated mean differences (MD), again based on a random-effects model. MAIN RESULTS: We included 11 RCTs with 396 participants on three SGAs. All trials investigated the effects of adding these SGAs to antidepressants (usually SSRIs). The duration of all trials was less than six months. Only 13% of the participants left the trials early. Most trials were limited in terms of quality aspects.Two trials examined olanzapine and found no difference in the primary outcome (response to treatment) and most other efficacy-related outcomes but it was associated with more weight gain than monotherapy with antidepressants.Quetiapine combined with

antidepressants was also not any more efficacious than placebo combined with antidepressants in terms of the primary outcome, but there was a significant superiority in the mean Yale-Brown Obsessive Compulsive Scale (Y-BOCS) score at endpoint (MD -2.28, 95% CI -4.05 to -0.52). There were also some beneficial effects of quetiapine in terms of anxiety or depressive symptoms.Risperidone was more efficacious than placebo in terms of the primary outcome (number of participants without a significant response) (OR 0.17, 95% CI 0.04 to 0.66) and in the reduction of anxiety and depression (MD -7.60, 95% CI -12.37 to -2.83). AUTHORS' CONCLUSIONS: The available data of the effects of olanzapine in OCD are too limited to draw any conclusions. There is some evidence that adding quetiapine or risperidone to antidepressants increases efficacy, but this must be weighed against less tolerability and limited data.

Maher AR, Maglione M, et al. Efficacy and comparative effectiveness of atypical antipsychotic medications for off-label uses in adults: a systematic review and meta-analysis. Jama. 2011;306(12):1359-69.

CONTEXT: Atypical antipsychotic medications are commonly used for off-label conditions such as agitation in dementia, anxiety, and obsessive-compulsive disorder. OBJECTIVE: To perform a systematic review on the efficacy and safety of atypical antipsychotic medications for use in conditions lacking approval for labeling and marketing by the US Food and Drug Administration. DATA SOURCES AND STUDY SELECTION: Relevant studies published in the English language were identified by searches of 6 databases (PubMed, EMBASE, CINAHL, PsycInfo, Cochrane DARE, and CENTRAL) from inception through May 2011. Controlled trials comparing an atypical antipsychotic medication (risperidone, olanzapine, quetiapine, aripiprazole, ziprasidone, asenapine, iloperidone, or paliperidone) with placebo, another atypical antipsychotic medication, or other pharmacotherapy for adult off-label conditions were included. Observational studies with sample sizes of greater than 1000 patients were included to assess adverse events. DATA EXTRACTION: Independent article review and study quality assessment by 2 investigators. DATA SYNTHESIS: Of 12 228 citations identified, 162 contributed data to the efficacy review. Among 14 placebo-controlled trials of elderly patients with dementia reporting a total global outcome score that includes symptoms such as psychosis, mood alterations, and aggression, small but statistically significant effects sizes ranging from 0.12 and 0.20 were observed for aripiprazole, olanzapine, and risperidone. For generalized anxiety disorder, a pooled analysis of 3 trials showed that quetiapine was associated with a 26% greater likelihood of a favorable response (defined as at least 50% improvement on the Hamilton Anxiety Scale) compared with placebo. For obsessive-compulsive disorder, risperidone was associated with a 3.9-fold greater likelihood of a favorable response (defined as a 25% improvement on the Yale-Brown Obsessive Compulsive Scale) compared with placebo. In elderly patients, adverse events included an increased risk of death (number needed to harm [NNH] = 87), stroke (NNH = 53 for risperidone), extrapyramidal symptoms (NNH = 10 for olanzapine; NNH = 20 for risperidone), and urinary tract symptoms (NNH range = 16-36). In nonelderly adults, adverse events included weight gain (particularly with olanzapine), fatigue, sedation, akathisia (for aripiprazole), and extrapyramidal symptoms. CONCLUSIONS: Benefits and harms vary among atypical antipsychotic medications for off-label use. For global behavioral symptom scores associated with dementia in elderly patients, small but statistically significant benefits were observed for aripiprazole, olanzapine, and risperidone. Quetiapine was associated with benefits in the treatment of generalized anxiety disorder, and risperidone was associated with benefits in the treatment of obsessive-compulsive disorder; however, adverse events were common.

Dold M, Aigner M, et al. Antipsychotic augmentation of serotonin reuptake inhibitors in treatment-resistant obsessive-compulsive disorder: a meta-analysis of double-blind, randomized, placebo-controlled trials. Int J Neuropsychopharmacol. 2013;16(3):557-74.

Because of the high number of patients with obsessive-compulsive disorder (OCD) not responding satisfactorily to initial monotherapy with serotonin reuptake inhibitors (SRIs), the evaluation of additional treatment options is highly relevant. To examine efficacy of add-on pharmacotherapy with antipsychotics, a systematic literature search was applied to identify all double-blind, randomized, placebo-controlled trials (DB-PC-RCTs) determining the efficacy of antipsychotic augmentation of SRIs in treatment-resistant OCD. The primary outcome of the pooled meta-analytic data analysis was response to the adjunctive antipsychotic treatment measured by both the rates of participants achieving response [defined as >/= 35% reduction in Yale-Brown Obsessive-Compulsive Scale (YBOCS)] and mean changes in YBOCS total score. Twelve DB-PC-RCTs investigating quetiapine (N = 5), risperidone (N = 3), olanzapine (N = 2), aripiprazole (N = 1) and haloperidol (N = 1) with a total of 394 subjects were included. Significantly more patients responded to augmentation with antipsychotics than with placebo [relative risk = 2.10, 95% confidence intervals (CI) 1.16-3.80]. Addition-

ally, the mean reduction of the YBOCS total score revealed an efficacy in favour of the antipsychotic medication [standardized mean difference (SMD) = 0.54, 95% CI 0.15-0.93]. Significant efficacy was identifiable only for risperidone, but not for quetiapine and olanzapine. The results regarding aripiprazole and haloperidol were inconsistent. Overall, about one-third of SRI-resistant OCD patients benefited from an augmentation strategy with antipsychotics. Based on the favourable risk:benefit ratio, risperidone can be considered as the agent of first choice and should be preferred to quetiapine and olanzapine. Further trials, mainly with higher antipsychotic doses, are required to optimize pharmacological treatment recommendations for SRI-refractory OCD.

Veale D, Miles S, et al. Atypical antipsychotic augmentation in SSRI treatment refractory obsessive-compulsive disorder: a systematic review and meta-analysis. BMC Psychiatry. 2014;14:317.

BACKGROUND: In 2006, the National Institute of Clinical and Health Excellence (NICE) guidelines for Obsessive Compulsive Disorder (OCD) recommended anti-psychotics as a class for SSRI treatment resistant OCD. The article aims to systematically review and conduct a meta-analysis on the clinical effectiveness of atypical anti-psychotics augmenting an SSRI. METHODS: Studies that were double-blind randomized controlled trials of an atypical antipsychotic against a placebo, for a minimum of 4 weeks, in adults with OCD, were included. Yale-Brown Obsessive Compulsive Scale (Y-BOCS) scores were the primary outcome measure. Inclusion criteria included Y-BOCS score of 16 or more and at least one adequate trial of a SSRI or clomipramine for at least 8 weeks prior to randomization. Data sources included Medline, Embase, PsycINFO, Cochrane Database of Systematic Reviews (CDSR), trial registries and pharmaceutical databases and manufacturers up to September 2013. Forest-plots were drawn to display differences between drug and placebo on the Y-BOCS. RESULTS: Two studies found aripiprazole to be effective in the short-term. There was a small effect-size for risperidone or anti-psychotics in general in the short-term. We found no evidence for the effectiveness of quetiapine or olanzapine in comparison to placebo. CONCLUSIONS: Risperidone and aripiprazole can be used cautiously at a low dose as an augmentation agent in non-responders to SSRIs and CBT but should be monitored at 4 weeks to determine efficacy.

5.3.3. Con estimulantes

No hemos encontrado revisiones sistemáticas.

5.3.4. Con moduladores glutamatérgicos (riluzol, topiramato, lamotrigina, N-acetilcisteína, etc.)

Oliver G, Dean O, et al. N-acetyl cysteine in the treatment of obsessive compulsive and related disorders: A systematic review. Clinical Psychopharmacology and Neuroscience. 2015;13(1):12-24.

Objective: Obsessive compulsive and related disorders are a collection of debilitating psychiatric disorders in which the role of glutamate dysfunction in the underpinning neurobiology is becoming well established. N-acetyl cysteine (NAC) is a glutamate modulator with promising therapeutic effect. This paper presents a systematic review of clinical trials and case reports exploring the use of NAC for these disorders. A further objective was to detail the methodology of current clinical trials being conducted in the area. Methods: PubMed, Web of Science and Cochrane Library Database were searched for human clinical trials or case reports investigating NAC in the treatment of obsessive compulsive disorder (OCD) or obsessive compulsive related disorders. Researchers with known involvement in NAC studies were contacted for any unpublished data. Results: Four clinical trials and five case reports/series were identified Study durations were commonly 12-weeks, using 2,400-3,000 mg/day of NAC. Overall, NAC demonstrates activity in reducing the severity of symptoms, with a good tolerability profile and minimal adverse effects Currently there are three ongoing randomized controlled trials using NAC for OCD (two adults and one pediatric), and one for excoriation. Conclusion: Encouraging results have been demonstrated from the few pilot studies that have been conducted. These results are detailed, in addition to a discussion of future potential research. (PsycINFO Database Record (c) 2015 APA, all rights reserved) (journal abstract).

5.3.5. Otros fármacos (por ejemplo, ondansetrón)

No hemos encontrado revisiones sistemáticas. Es posible que la revisión sistemática de antagonistas 5-HT3 incluya información.

5.3.6. Otras terapias físicas

Martin JL, Barbanoj MJ, et al. Transcranial magnetic stimulation for the treatment of obsessive-compulsive disorder. Cochrane Database Syst Rev. 2003;(3):Cd003387.

BACKGROUND: Transcranial magnetic stimulation (TMS) was introduced as a neurophysiological technique in 1985 when Anthony Barker and his team developed a compact machine that permitted non-invasive stimulation of the cerebral cortex (Barker 1985). Since its introduction, TMS has been used to evaluate the motor system, to study the function of several cerebral regions, and for the pathophysiology of several neuropsychiatric illnesses. In addition, it has been suggested that TMS might have therapeutic potential. Some controlled studies have evaluated the effects of repetitive TMS (rTMS) in patients with obsessive-compulsive disorder (OCD). Greenberg (Greenberg 1997) observed that a single session of right prefrontal cortex stimulation produced a significant decrease in compulsive urges in OCD patients lasting over eight hours. Other studies have reported transitory improvements in mood but there are no observations for changes in anxiety or obsessions. OBJECTIVES: To develop a systematic review on the clinical efficacy and safety of transcranial magnetic stimulation from randomised controlled trials in the treatment of obsessive-compulsive disorder. SEARCH STRATEGY: An electronic search was performed including the Cochrane Collaboration Depression, Anxiety and Neurosis Review Group trials register (last searched June, 2002), the Cochrane Controlled Trials Register (Issue 2, 2002), MEDLINE (1966-2002), EMBASE (1974-2002), PsycLIT (1980-2002), and bibliographies from reviewed articles. SELECTION CRITERIA: Randomised controlled trials assessing the therapeutic efficacy and safety of transcranial magnetic stimulation for obsessive-compulsive disorder. DATA COLLECTION AND ANALYSIS: All reviewers independently extracted the information and verified it by cross-checking. Disagreements were resolved through discussion. MAIN RESULTS: Three trials were included in the review and only two contained data in a suitable form for quantitative analysis. It was not possible to pool any results for a meta-analysis. No difference was seen between rTMS and sham TMS using the Yale-Brown Obsessive-Compulsive Scale or the Hamilton Depression Rating Scale for all time periods analysed. REVIEWER'S CONCLUSIONS: There are currently insufficient data from randomised controlled trials to draw any conclusions about the efficacy of transcranial magnetic stimulation in the treatment of obsessive-compulsive disorder.

Slotema CW, Blom JD, et al. Should we expand the toolbox of psychiatric treatment methods to include Repetitive Transcranial Magnetic Stimulation (rTMS)? A meta-analysis of the efficacy of rTMS in psychiatric disorders. J Clin Psychiatry. 2010;71(7):873-84.

OBJECTIVE: Repetitive transcranial magnetic stimulation (rTMS) is a safe treatment method with few side effects. However, efficacy for various psychiatric disorders is currently not clear. DATA SOURCES: A literature search was performed from 1966 through October 2008 using PubMed, Ovid Medline, Embase Psychiatry, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, and PsycINFO. The following search terms were used: transcranial magnetic stimulation, TMS, repetitive TMS, psychiatry, mental disorder, psychiatric disorder, anxiety disorder, attention-deficit hyperactivity disorder, bipolar disorder, catatonia, mania, depression, obsessive-compulsive disorder, psychosis, posttraumatic stress disorder, schizophrenia, Tourette's syndrome, bulimia nervosa, and addiction. STUDY SELECTION: Data were obtained from randomized, sham-controlled studies of rTMS treatment for depression (34 studies), auditory verbal hallucinations (AVH, 7 studies), negative symptoms in schizophrenia (7 studies), and obsessive-compulsive disorder (OCD, 3 studies). Studies of rTMS versus electroconvulsive treatment (ECT, 6 studies) for depression were meta-analyzed. DATA EXTRACTION: Standardized mean effect sizes of rTMS versus sham were computed based on pretreatment-posttreatment comparisons. DATA SYNTHESIS: The mean weighted effect size of rTMS versus sham for depression was 0.55 ($P < .001$). Monotherapy with rTMS was more effective than rTMS as adjunctive to antidepressant medication. ECT was superior to rTMS in the treatment of depression (mean weighted effect size -0.47, $P = .004$). In the treatment of AVH, rTMS was superior to sham treatment, with a mean weighted effect size of 0.54 ($P < .001$). The mean weighted effect size for rTMS versus sham in the treatment of negative symptoms in schizophrenia was 0.39 ($P = .11$) and for OCD, 0.15 ($P = .52$). Side effects were mild, yet more prevalent with high-frequency rTMS at frontal locations. CONCLUSIONS: It is time to provide rTMS as a clinical treatment method for depression, for auditory verbal hallucinations, and possibly for negative symptoms. We do not recommend rTMS for the treatment of OCD.

Jaafari N, Rachid F, et al. Safety and efficacy of repetitive transcranial magnetic stimulation in the treatment of obsessive-compulsive disorder: a review. World J Biol Psychiatry. 2012;13(3):164-77.

OBJECTIVES: Obsessive-compulsive disorder (OCD) is a chronic, often severe, neuropsychiatric disorder leading to a dramatic impairment in interpersonal and occupational functions. rTMS has been tried out in several studies in patients with OCD with different characteristics. In this paper, we review the safety and efficacy of rTMS in the treatment of mostly severe resistant OCD. METHODS: A review of the English literature from 1966 to 2010 pertaining to rTMS in the treatment of OCD was conducted using MEDLINE by selectively entering the search terms "transcranial magnetic stimulation", "repetitive transcranial magnetic stimulation", "obsessive-compulsive disorder" and "OCD". Twelve studies including open and randomized, sham-controlled trials were included in this review. RESULTS: Although available data about the use of rTMS in OCD treatment are quite heterogeneous in terms of sample size, study design, stimulus parameters used and stimulation areas targeted, promising findings regarding rTMS efficacy appeared for two structures based on recent controlled studies: the supplementary motor area and the orbitofrontal cortex. On the other hand, rTMS of the dorsolateral prefrontal cortex is not significantly effective when compared to sham rTMS. CONCLUSIONS: Three target areas have already been selected of which the supplementary motor area in particular and the orbitofrontal cortex seem to be the most promising in terms of potential efficacy and could more accurately be targeted with the help of neuronavigational techniques. Larger randomized controlled trials should be conducted in order to better clarify the therapeutic role of rTMS in OCD.

Berlim MT, Neufeld NH, et al. Repetitive transcranial magnetic stimulation (rTMS) for obsessive-compulsive disorder (OCD): an exploratory meta-analysis of randomized and sham-controlled trials. J Psychiatr Res. 2013;47(8):999-1006.

OBJECTIVE: Randomized and sham-controlled trials (RCTs) on repetitive transcranial magnetic stimulation (rTMS) for treating obsessive-compulsive disorder (OCD) have yielded conflicting results that may be due to limited statistical power among individual studies. We pursued the present systematic review and meta-analysis to assess the efficacy of rTMS for OCD and to generate hypotheses for more robustly powered RCTs. METHOD: We searched the literature for RCTs on rTMS for OCD from 1995 through December 2012 using MEDLINE, EMBASE, PsycINFO, Cochrane Central Register of Controlled Trials, and SCOPUS. We then performed an exploratory random-effects meta-analysis with the main outcome measures as pre-post changes in Yale-Brown Obsessive Compulsive Scale (Y-BOCS) scores, response to treatment and overall dropout rates at study end. RESULTS: Data were obtained from 10 RCTs, totaling 282 subjects with OCD. The pooled Hedges' g for pre-post Y-BOCS scores was 0.59 ($z = 2.73$, $p = 0.006$), indicating a significant and medium-sized difference in outcome favoring active rTMS. Furthermore, response rates were 35% and 13% for patients receiving active and sham rTMS, respectively (OR = 3.4, $p = 0.002$). Sub-group analyses indicated that LF-rTMS and rTMS protocols targeting non-DLPFC regions (i.e., orbitofrontal cortex or supplementary motor area) seem to be the most promising for reducing OCD-related symptoms. No differences on baseline depression scores or dropout rates at study end were observed between active and sham rTMS groups, although OCD severity at baseline was higher in the active group. CONCLUSIONS: Our exploratory analyses show that active rTMS seems to be efficacious for treating OCD. Moreover, LF-rTMS and protocols targeting the orbitofrontal cortex or the supplementary motor area seem to be the most promising. Nevertheless, future RCTs on rTMS for OCD should include larger sample sizes and be more homogeneous in terms of demographic/clinical variables as well as stimulation parameters and brain targets.

Radhu N, de Jesus DR, et al. A meta-analysis of cortical inhibition and excitability using transcranial magnetic stimulation in psychiatric disorders. Clin Neurophysiol. 2013;124(7):1309-20.

OBJECTIVE: To evaluate transcranial magnetic stimulation (TMS) measures of inhibition and excitation in obsessive-compulsive disorder (OCD), major depressive disorder (MDD) and schizophrenia (SCZ). METHODS: Paradigms included: short-interval cortical inhibition (SICI), cortical silent period (CSP), resting motor threshold, intracortical facilitation, and motor evoked potential amplitude. A literature search was performed using PubMed, Ovid Medline, Embase Psychiatry and PsycINFO 1990 through April 2012. RESULTS: A significant Hedge's g was found for decreased SICI (g=0.572, 95% confidence interval [0.179, 0.966], p=0.004), enhanced intracortical facilitation (g=0.446, 95% confidence interval [0.042, 0.849], p=0.030) and decreased CSP (g=-0.466, 95% confidence interval [-0.881, -0.052], p=0.027) within the OCD population. For MDD, significant effect sizes were demonstrated for decreased SICI (g=0.641, 95% confidence interval [0.384, 0.898], p=0.000) and shortened CSP (g=-1.232, 95% confidence interval [-1.530, -0.933], p=0.000). In SCZ, a significant Hedge's g was shown for decreased SICI (g=0.476, 95% confidence interval [0.331, 0.620], p=0.000). CONCLUSION:

Inhibitory deficits are a ubiquitous finding across OCD, MDD, SCZ and enhancement of intracortical facilitation is specific to OCD. SIGNIFICANCE: Provides a clear platform from which diagnostic procedures can be developed.

Hamani C, Pilitsis J, et al. Deep brain stimulation for obsessive-compulsive disorder: systematic review and evidence-based guideline sponsored by the American Society for Stereotactic and Functional Neurosurgery and the Congress of Neurological Surgeons (CNS) and endorsed by the CNS and American Association of Neurological Surgeons. Neurosurgery. 2014;75(4):327-33; quiz 333.

BACKGROUND: It is estimated that 40% to 60% of patients with obsessive-compulsive disorder (OCD) continue to experience symptoms despite adequate medical management. For this population of treatment-refractory patients, promising results have been reported with the use of deep brain stimulation (DBS). OBJECTIVE: To conduct a systematic review of the literature and develop evidence-based guidelines on DBS for OCD. METHODS: A systematic literature search was undertaken using the PubMed database for articles published between 1966 and October 2012 combining the following words: "deep brain stimulation and obsessive-compulsive disorder" or "electrical stimulation and obsessive-compulsive disorder." Of 353 articles, 7 were retrieved for full-text review and analysis. The quality of the articles was assigned to each study and the strength of recommendation graded according to the guidelines development methodology of the American Association of Neurological Surgeons/Congress of Neurological Surgeons Joint Guidelines Committee. RESULTS: Of the 7 studies, 1 class I and 2 class II double-blind, randomized, controlled trials reported that bilateral DBS is more effective in improving OCD symptoms than sham treatment. CONCLUSION: Based on the data published in the literature, the following recommendations can be made: (1) There is Level I evidence, based on a single class I study, for the use of bilateral subthalamic nucleus DBS for the treatment of medically refractory OCD. (2) There is Level II evidence, based on a single class II study, for the use of bilateral nucleus accumbens DBS for the treatment of medically refractory OCD. (3) There is insufficient evidence to make a recommendation for the use of unilateral DBS for the treatment of medically refractory OCD.

Kisely S, Hall K, et al. Deep brain stimulation for obsessive-compulsive disorder: a systematic review and meta-analysis. Psychol Med. 2014;44(16):3533-42.

BACKGROUND: Deep brain stimulation (DBS) is increasingly being applied to psychiatric conditions such as obsessive-compulsive disorder (OCD), major depression and anorexia nervosa. Double-blind, randomized controlled trials (RCTs) of active versus sham treatment have been limited to small numbers. We therefore undertook a systematic review and meta-analysis of the effectiveness of DBS in psychiatric conditions to maximize study power. METHOD: We conducted a systematic literature search for double-blind, RCTs of active versus sham treatment using Pubmed/Medline and EMBASE up to April 2013. Where possible, we combined results from studies in a meta-analysis. We assessed differences in final values between the active and sham treatments for parallel-group studies and compared changes from baseline score for cross-over designs. RESULTS: Inclusion criteria were met by five studies, all of which were of OCD. Forty-four subjects provided data for the meta-analysis. The main outcome was a reduction in obsessive symptoms as measured by the Yale-Brown Obsessive Compulsive Scale (YBOCS). Patients on active, as opposed to sham, treatment had a significantly lower mean score [mean difference (MD) -8.93, 95% confidence interval (CI) -13.35 to -5.76, $p < 0.001$], representing partial remission. However, one-third of patients experienced significant adverse effects ($n = 16$). There were no differences between the two groups in terms of other outcomes. CONCLUSIONS: DBS may show promise for treatment-resistant OCD but there are insufficient randomized controlled data for other psychiatric conditions. DBS remains an experimental treatment in adults for severe, medically refractory conditions until further data are available.

Kohl S, Schonherr DM, et al. Deep brain stimulation for treatment-refractory obsessive compulsive disorder: a systematic review. BMC Psychiatry. 2014;14:214.

BACKGROUND: Obsessive-compulsive disorder is one of the most disabling of all psychiatric illnesses. Despite available pharmacological and psychotherapeutic treatments about 10% of patients remain severely affected and are considered treatment-refractory. For some of these patients deep brain stimulation offers an appropriate treatment method. The scope of this article is to review the published data and to compare different target structures and their effectiveness. METHODS: PubMed search, last update June 2013, was conducted using the terms "deep brain stimulation" and "obsessive compulsive disorder". RESULTS: In total 25 studies were found that reported five deep brain stimulation target structures to treat obsessive-compulsive disorder: the anterior limb of the internal capsule (five studies including 14 patients), nucleus accumbens (eight studies includ-

ing 37 patients), ventral capsule/ventral striatum (four studies including 29 patients), subthalamic nucleus (five studies including 23 patients) and inferior thalamic peduncle (two studies including 6 patients). Despite the anatomical diversity, deep brain stimulation treatment results in similar response rates for the first four target structures. Inferior thalamic peduncle deep brain stimulation results in higher response rates but these results have to be interpreted with caution due to a very small number of cases. Procedure and device related adverse events are relatively low, as well as stimulation or therapy related side effects. Most stimulation related side effects are transient and decline after stimulation parameters have been changed. CONCLUSION: Deep brain stimulation in treatment-refractory obsessive-compulsive disorder seems to be a relatively safe and promising treatment option. However, based on these studies no superior target structure could be identified. More research is needed to better understand mechanisms of action and response predictors that may help to develop a more personalized approach for these severely affected obsessive compulsive patients.

Fontenelle LF, Coutinho ES, et al. Electroconvulsive therapy for obsessive-compulsive disorder: a systematic review. J Clin Psychiatry. 2015;76(7):949-57.

OBJECTIVE: Surgical therapies for treatment-refractory obsessive-compulsive disorder (OCD), such as deep brain stimulation or psychosurgery, remain unattainable for many patients. Despite the long-held view that electroconvulsive therapy (ECT) is an ineffective treatment for OCD, there is no systematic review to support or refute this claim, which is the basis of the current review. DATA SOURCES: A systematic search of MEDLINE, Web of Science, Scopus, and LILACS databases was conducted on December 22, 2013, using the terms obsessive-compulsive disorder and electroconvulsive therapy. Reference lists, specific journals, and clinical trial registries were also scrutinized. No date or language limitation was imposed on the search. STUDY SELECTION: After irrelevant and redundant records from the 500 identified titles were excluded, the 50 articles reporting the acute treatment effects of ECT in OCD and related constructs (involving a total of 279 patients) were analyzed for this study. DATA EXTRACTION: The relevant sociodemographic, clinical, and outcome data of individual cases were extracted. Data from individual cases were used to compare the characteristics of responders versus nonresponders to ECT. RESULTS: Most selected records were case reports/series; there were no randomized controlled trials. A positive response was reported in 60.4% of the 265 cases in which individual responses to ECT were available. ECT responders exhibited a significantly later onset of OCD symptoms (P = .003), were more frequently nondepressed (P = .009), more commonly reported being treated with ECT for severe OCD (P = .01), and received a fewer number of ECT sessions (P = .03). ECT responders were also less frequently previously treated with adequate trials of serotonin reuptake inhibitors (P = .05) and cognitive-behavioral therapy (P = .005). CONCLUSIONS: Although 60% of the reported cases reviewed exhibited some form of a positive response to ECT, it cannot be stated that this provides evidence that ECT is indeed effective for OCD.

5.3.7. Comparación de estrategias de potenciación

No hemos encontrado revisiones sistemáticas.

5.3.8. Efecto a plazo de la potenciación

No hemos encontrado revisiones sistemáticas.

5.4. Cambio (incluye cambio a i.v.)

No hemos encontrado revisiones sistemáticas.

APÉNDICE 3

Búsqueda bibliográfica trastorno obsesivo-compulsivo/embarazo y lactancia

ESTRATEGIA DE BÚSQUEDA

PUBMED (82 refs)
Search, Query, Items found
TOC (Mesh)
#1, "Search ("Compulsive Behavior"[Mesh] OR "Obsessive Behavior"[Mesh] OR "Obsessive-Compulsive Disorder"[Mesh]), 21378
TOC (Mesh) + (words or phrases)
#2,"Search ("Compulsive Behavior"[Mesh] OR "Obsessive Behavior"[Mesh] OR "Obsessive-Compulsive Disorder"[Mesh]) AND ("checking behavior"[tab] OR "checking behaviors"[tab] OR compulsion[tab] OR compulsions[tab] OR compulsive[tab] OR hoarding[tab] OR obsession[tab] OR obsessional[tab] OR obsessions[tab] OR obsessive[tab] OR rituals[tab]),11643
EMBARAZO O LACTANCIA
#3, "Search (pregnancy OR pregnant OR gestation* OR childbirth OR perinatal OR post-natal OR postnatal OR post-partum OR post-partum OR breastfeeding OR lactating)", 1052965
#4, "Search (pregnancy [Mesh] OR "pregnant women"[Mesh] OR "post-partum period"[Mesh] OR breastfeeding [Mesh])", 823170
#5, "Search #3 OR #4", 1052965
#6, "Search #2 AND #5", 152
#7 "Search #6 AND (therapy OR therapeutic OR management OR guidelines OR recommendations OR treatment), 82 (excluded rats and rabbit)
PSYCINFO (65 refs)
TOC (Mesh)
MJSUB.EXACT("Obsessive Compulsive Disorder") 10122
(words or phrases)
TI,AB("checking behavior") OR TI,AB("checking behaviors") OR TI,AB(compulsion) OR TI,AB(compulsions) OR TI,AB(compulsive) OR TI,AB(hoarding) OR TI,AB(obsession) OR TI,AB(obsessional) OR TI,AB(obsessions) OR TI,AB(obsessive) OR TI,AB(rituals) 37061

TOC (Mesh) + (words or phrases)
MJSUB.EXACT("Obsessive Compulsive Disorder") AND (TI,AB("checking behavior") OR TI,AB("checking behaviors") OR TI,AB(compulsion) OR TI,AB(compulsions) OR TI,AB(compulsive) OR TI,AB(hoarding) OR TI,AB(obsession) OR TI,AB(obsessional) OR TI,AB(obsessions) OR TI,AB(obsessive) OR TI,AB(rituals)) 9896
EMBARAZO O LACTANCIA
TI,AB(pregnancy) OR TI,AB(pregnant) OR TI,AB(gestation*) OR TI,AB(childbirth) OR TI,AB(perinatal) OR TI,AB(post-natal) OR TI,AB(postnatal) OR TI,AB(post-partum) OR TI,AB(post-partum) OR TI,AB(breastfeeding) OR TI,AB(lactating), 67304
if (PREGNANCY) OR IF (PREGNANT WOMEN) OR if (POST-PARTUM) OR if (BREASTFEEDING), 29664
((TI,AB(pregnancy) OR TI,AB(pregnant) OR TI,AB(gestation*) OR TI,AB(childbirth) OR TI,AB(perinatal) OR TI,AB(post-natal) OR TI,AB(postnatal) OR TI,AB(post-partum) OR TI,AB(post-partum) OR TI,AB(breastfeeding) OR TI,AB(lactating))) OR ((if(PREGNANCY) OR IF(PREGNANT WOMEN) OR if(POST-PARTUM) OR if(BREASTFEEDING))), 69104
TOC (9896) AND (EMBARAZO/LACTANCIA), 127
TOC AND (EMBARAZO/LACTANCIA) AND (therapy OR therapeutic OR management OR guidelines OR recommendations OR treatment), 65
COCHRANE (26 refs)
TOC (Mesh)
#1 MeSH descriptor: [Compulsive Behavior] explode all trees 440
#2 MeSH descriptor: [Obsessive Behavior] explode all trees 36
#3 MeSH descriptor: [Obsessive-Compulsive Disorder] explode all trees 725
#4 (#1 or #2 or #3) 1175
(words or phrases)
#5 (checking behavior: tab OR "checking behaviors": tab OR compulsion: tab OR compulsions: tab OR compulsive: tab OR hoarding: tab OR obsession: tab OR obsessional: tab OR obsessions: tab OR obsessive: tab OR rituals: tab) 1933
TOC (Mesh) + (words or phrases)
#6 (#4 OR #5) 2394
EMBARAZO O LACTANCIA
(pregnancy OR pregnant OR gestation* OR childbirth OR perinatal OR post-natal OR postnatal OR post-partum OR post-partum OR breastfeeding OR lactating), 42997
(pregnancy [Mesh] OR "pregnant women"[Mesh] OR "post-partum period"[Mesh] OR breastfeeding [Mesh]), 8665
TOC + EMBARAZO/LACTANCIA
30 refs
and (therapy or therapeutic or management or guidelines or recommendations or treatment), 26 refs.

RESULTADOS DE LA BÚSQUEDA

The mind-body connection--anxiety, panic, mood and compulsion. Int J Fertil Menopausal Stud. 1996;41(6):498-505.

Use of psychoactive medication during pregnancy and possible effects on the fetus and newborn. Committee on Drugs. American Academy of Pediatrics. Pediatrics. 2000;105(4 Pt 1):880-7.

Psychoactive drugs are those psychotherapeutic drugs used to modify emotions and behavior in the treatment of psychiatric illnesses. This statement will limit its scope to drug selection guidelines for those psychoactive agents used during pregnancy for prevention or treatment of the following common psychiatric disorders: schizophrenia, major depression, bipolar disorder, panic disorder, and obsessive-compulsive disorder. The statement assumes that pharmacologic therapy is needed to manage the psychiatric disorder. This decision requires thoughtful psychiatric and obstetric advice.

Current treatments of obsessive-compulsive disorder (2nd ed.), American Psychiatric Association, Arlington, VA; 2001.

During the 10 years since publication of the 1st edition of this book, progress in neuroscience has had direct and immediate clinical implications in both the pharmacological and psychological treatment of obsessive-compulsive disorder (OCD). This 2nd edition reflects this progress. Chapters include the latest data on the use of all current OCD treatments in special populations, such as the strictly religious, the elderly, children, adolescents, and those who are pregnant, and all are illustrated with detailed case histories that highlight specific treatments and diagnostic issues. This edition also includes 3 new pharmacotherapy chapters that discuss the use of sertraline, paroxetine, and citalopram and updates of the original edition's chapters on clomipramine, fluoxetine and fluvoxamine; an expanded chapter on children and adolescents that incorporates the latest findings in immunological research, with particular regard to pediatric autoimmune neurologic disorders associated with streptococcal infection; and an expanded behavioral therapy chapter with detailed treatment plans for individuals and groups as well as up-to-date empirical data to support their use. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (jacket)

CNS digest: In the journal of 2003. CNS Spectrums. 2003;8(6):415.

Presents a collection of abstracts on migraine treatment. One of the abstracts "Venlafaxine Treatment of Obsessive-Compulsive Disorder: Case Reports" presents a clinical case of a 50-year-old housewife who had her first symptoms of Obsessive-Compulsive Disorder after her second pregnancy at 27 years of age. The second abstract "Topiramate in the Preventive Treatment of Episodic Migraine: A Combined Analysis from Pilot, Double-Blind, Placebo-Controlled Trials" evaluates the drug efficacy of antiepileptic topiramate in migraine treatment. The article "The Comorbidity of Migraine" studies association between migraine and other disorders. "Migraine and Glutamate: How Are They Related?" studies excessive glutamate-medicated excitation in migraine. "Restless Legs Syndrome and Drug-Induced Akathisia in Headache Patients" studies treatment of drug-induced side effects in patients with headache. (PsycINFO Database Record (c) 2012 APA, all rights reserved)

Clinical Updates in Neuropsychiatry. CNS Spectrums. 2004;9(5):329-32.

The article presents a collection of articles presented at the 24th Annual Conference of the Anxiety Disorders Association of America. The first article focuses on the efficacy of risperidone for patients suffering from depression and anxiety disorders. The second article studies the effectiveness of antidepressants in the treatment of social anxiety disorder in UK patients. The third article focuses on the effect of parent-child group cognitive behavior therapy in alleviating obsessive compulsive disorder symptoms. The fourth article discusses side-effects profile of atypical antipsychotics in the treatment of women schizophrenic patients. The fifth article focuses on the prenatal depression as a forecast for post-partum depression in adolescent mothers. (PsycINFO Database Record (c) 2012 APA, all rights reserved)

Meetings, new data, thorough reviews, and farewell to a friend. Annals of Clinical Psychiatry. 2011;23(1):1.

The upcoming meeting of the American Academy of Clinical Psychiatrists in collaboration with Current Psychiatry will take place in Chicago, II, on April 15-17, 2011. The meeting's topic is "Psychotic and cognitive disorders: Solving clinical challenges, improving patient care." Presentations will address psychotic and cognitive disorders across the lifespan, best practices for treatment resistant schizophrenia, managing dementia pharmacologically and behaviorally, evaluating risk for vio-

lence and suicide, and treating psychotic disorders during pregnancy and post-partum. This issue of Annals features several important articles. The articles discuss about psychological disorders. Other contributions include a review showing that patients with bipolar disorder have a 2-fold greater risk of cardiovascular mortality compared with the general population. The authors discuss the concept of pathological guilt as a mediating factor in obsessive-compulsive disorder. Annals editorial board member Dr. Jerry Lewis died unexpectedly on September 13, 2010, while on a bicycle ride in Minnesota. Jerry was a valued friend and colleague who served as a Clinical Professor of Psychiatry and Director of Electrotherapy at the University of Iowa Carver College of Medicine. He also was a loyal and contributing member of the American Academy of Clinical Psychiatrists. (PsycINFO Database Record (c) 2012 APA, all rights reserved)

Eye movement desensitization and reprocessing (EMDR) therapy scripted protocols and summary sheets: Treating anxiety, obsessive-compulsive, and mood-related conditions, Springer Publishing Co, New York, NY; 2016.

Eye Movement Desensitization and Reprocessing (EMDR) Therapy is a psychotherapy approach based on standard procedures and protocols. This book is an important resource that focuses on applying EMDR Therapy to anxiety, obsessive-compulsive, and mood-related conditions using EMDR Therapy's standard procedures and protocols as its template. The scripts distill the essence of the Standard EMDR Protocols and reinforce the specific parts, sequence, and language used to create an effective outcome. Also, it illustrates how clinicians are using this framework to work with a variety of conditions while maintaining the integrity of the Adaptive Information Processing (AIP) model. The book delivers step-by-step protocols that enable beginning practitioners as well as seasoned EMDR clinicians, trainers, and consultants to enhance their expertise more quickly when treating clients or groups of clients with these conditions. These chapters reflect the expertise of EMDR clinicians treating anxiety disorders including specific phobia, panic disorder, and generalized anxiety disorder; obsessive-compulsive disorders including body dysmorphic disorder, olfactory reference syndrome, and hoarding behaviors; and mood disorders including bipolar disorder, major depression, and post-partum depression. For each topic, the authors include relevant questions for history taking, helpful resources and explanations, frequently used negative and positive cognitions, and information on case conceptualization and treatment planning. Consisting of past, present, and future templates, the scripts are conveniently presented in an easy-to-use, manual-style format that facilitates a reliable, consistent procedure. Summary sheets for each protocol support quick retrieval of essential issues and components for the clinician when putting together a treatment plan for the client. These scripted protocols and completed summary sheets can be inserted right into a client's chart for easy documentation. (PsycINFO Database Record (c) 2016 APA, all rights reserved) (cover)

Abramowitz J, Moore K, et al. Acute onset of obsessive-compulsive disorder in males following childbirth. Psychosomatics: Journal of Consultation and Liaison Psychiatry. 2001;42(5):429-31.

Presents 4 cases of males (aged 28–40 years) with obsessive-compulsive disorder (OCD) onset that coincide with a spouse's pregnancy or delivery. The rapid onset and content of obsessions and compulsions are remarkably like those reported in previous studies of post-partum OCD in females. Each patient also responded to cognitive-behavioral therapy using exposure procedures. The implications of these cases for etiological models of post-partum OCD and future research directions are discussed. (PsycINFO Database Record (c) 2013 APA, all rights reserved)

Abramowitz J, Moore K, et al. Acute onset of obsessive-compulsive disorder in males following childbirth. Psychosomatics. 2001;42(5):429-31.

Research on post-partum onset obsessive-compulsive disorder (OCD) has focused exclusively on females. However, the authors present four cases of males with OCD onset that coincide with a spouse's pregnancy or delivery. The rapid onset and content of obsessions and compulsions are remarkably like those reported in previous studies of post-partum OCD in females. Each patient also responded to cognitive-behavioral therapy using exposure procedures. The implications of these cases for etiological models of post-partum OCD and future research directions are discussed.

Abramowitz JS, Fairbrother N. Post-partum obsessive-compulsive disorder. Clinical handbook of obsessive-compulsive disorder and related problems., Johns Hopkins University Press, Baltimore, MD; 2008; p. 139-55.

Much attention has focused on post-partum depression and psychosis, with much less attention on perinatal anxiety disorders, post-partum obsessive-compulsive disorder (ppOCD). The opening section of this chapter provides an overview and description of ppOCD, including a case example

to illustrate the cardinal features of this presentation or "subtype" of OCD. We then consider the relationship between ppOCD and OCD in general. Theoretical perspectives on ppOCD are presented in the second section of the chapter. The third section, which is concerned with treatment issues, includes a discussion of two interventions for ppOCD that have been shown to be effective: cognitive-behavioral therapy (CBT) and pharmacotherapy. A case vignette illustrating the treatment of a patient with ppOCD is presented, along with a discussion of relevant clinical considerations and suggestions for troubleshooting. (PsycINFO Database Record (c) 2015 APA, all rights reserved) (chapter)

Abramowitz JS, Meltzer-Brody S, et al. Obsessional thoughts and compulsive behaviors in a sample of women with post-partum mood symptoms. Arch Women's Mental Health. 2010;13(6):523-30.

Post-partum psychiatric disorders are widely recognized by clinicians and researchers, yet while much attention has been paid to perinatal mood disorders, considerably less has been given to anxiety and obsessive-compulsive symptoms in this population. The present study examined anxiety and obsessive-compulsive symptoms among post-partum women with mood complaints, with the aim of delineating the relationship between these symptoms. Sixty post-partum women seeking treatment in a perinatal mood disorders clinic completed measures of depression, anxiety, and obsessive-compulsive symptoms. Obsession-like thoughts and compulsive-like ("neutralizing") strategies were present among much of the sample, yet the severity of these symptoms ranged widely. Depressive and anxiety symptoms were associated with obsessive and neutralizing compulsive symptoms. It may be helpful to consider anxiety and depressive symptoms as part of a broad spectrum of perinatal psychiatric illness. Clinicians should assess for anxiety and obsessive-compulsive symptoms as routinely as they assess for depressive symptoms in the perinatal period.

Abramowitz JS, Nelson CA, et al. The cognitive mediation of obsessive-compulsive symptoms: a longitudinal study. J Anxiety Disord. 2007;21(1):91-104.

Contemporary cognitive models of obsessive-compulsive disorder (OCD) posit that OC symptoms arise from negative interpretations of intrusive thoughts, which are derived from trait-like dysfunctional assumptions ("obsessive beliefs;" e.g., concerning overestimates of responsibility). Although correlational studies suggest that obsessive beliefs, negative interpretations of intrusions, and OC symptoms are interrelated, prospective studies evaluating the directional hypotheses implied in the cognitive model are lacking. In the present longitudinal study, 76 first time expecting parents were followed through the post-partum. Results indicated that the tendency to negatively interpret the presence and meaning of unwanted intrusive infant-related thoughts early in the post-partum period (3-4 weeks) mediated the relationship between pre-childbirth obsessive-beliefs and late post-partum (12 weeks) OC symptoms. Results are discussed in terms of their theoretical and treatment implications.

Abramowitz JS, Schwartz SA, et al. Obsessive-compulsive symptoms in pregnancy and the puerperium: A review of the literature. Journal of Anxiety Disorders. 2003;17(4):461-78.

In this article, we review the available research on post-partum obsessive-compulsive disorder (OCD). Most studies are retrospective in nature, thus not answering questions as to overall prevalence of such symptoms. However, there are consistent findings regarding symptom profile: obsessional thoughts in post-partum OCD tend to concern fears of harm to the infant. We discuss distinctions between post-partum OCD symptoms and post-partum depression and psychosis. Although preliminary, research on treatments for post-partum OCD indicates the effectiveness of medications and cognitive-behavioral therapy. We explore the relationship between OCD symptoms and post-partum depression and offer possible directions for future study. We also consider the proposed etiological models and offer a fresh conceptualization of this condition. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract).

Abramowitz JS, Schwartz SA, et al. Obsessive-compulsive symptoms in pregnancy and the puerperium: a review of the literature. J Anxiety Disord. 2003;17(4):461-78.

In this article, we review the available research on post-partum obsessive-compulsive disorder (OCD). Most studies are retrospective in nature, thus not answering questions as to overall prevalence of such symptoms. However, there are consistent findings regarding symptom profile: obsessional thoughts in post-partum OCD tend to concern fears of harm to the infant. We discuss distinctions between post-partum OCD symptoms and post-partum depression and psychosis. Although preliminary, research on treatments for post-partum OCD indicates the effectiveness of medications and cognitive-behavioral therapy. We explore the relationship between OCD symptoms and post-

partum depression and offer possible directions for future study. We also consider the proposed etiological models and offer a fresh conceptualization of this condition.

Ahuja I. Home based treatment of obsessive-compulsive disorder by behavioral technique. Indian Journal of Clinical Psychology. 1979;6(1):39-42.

A case of obsessive-compulsive disorder (preoccupation with cleanliness and washing) in a 26-yr-old married woman was treated successfully at home using sensory flooding under supervision of a therapist, combined with self-directed techniques between therapy sessions. The disorder was precipitated by fears for the health of her baby during pregnancy and after birth, as she had a history of difficulty in becoming pregnant. (5 ref) (PsycINFO Database Record (c) 2012 APA, all rights reserved)

Akl Elie A, Oxman Andrew D, et al. Framing of health information messages. Cochrane Database of Systematic Reviews. 2011. DOI: 10.1002/14651858.CD006777.pub2.

Background: The same information about the evidence on health effects can be framed either in positive words or in negative words. Some research suggests that positive versus negative framing can lead to different decisions, a phenomenon described as the framing effect. Attribute framing is the positive versus negative description of a specific attribute of a single item or a state, for example, "the chance of survival with cancer is 2/3" versus "the chance of mortality with cancer is 1/3". Goal framing is the description of the consequences of performing or not performing an act as a gain versus a loss, for example, "if you undergo a screening test for cancer, your survival will be prolonged" versus "if you don't undergo screening test for cancer, your survival will be shortened". Objectives: To evaluate the effects of attribute (positive versus negative) framing and of goal (gain versus loss) framing of the same health information, on understanding, perception of effectiveness, persuasiveness, and behavior of health professionals, policy makers, and consumers. Search methods: We searched the Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, issue 3 2007), MEDLINE (Ovid) (1966 to October 2007), EMBASE (Ovid) (1980 to October 2007), PsycINFO (Ovid) (1887 to October 2007). There were no language restrictions. We reviewed the reference lists of related systematic reviews, included studies and of excluded but closely related studies. We also contacted experts in the field. Selection criteria: We included randomized controlled trials, quasi-randomized controlled trials, and cross-over studies with health professionals, policy makers, and consumers evaluating one of the two types of framing. Data collection and analysis: Two review authors extracted data in duplicate and independently. We graded the quality of evidence for each outcome using the GRADE approach. We standardized the outcome effects using standardized mean difference (SMD). We stratified the analysis by the type of framing (attribute, goal) and conducted pre-planned subgroup analyses based on the type of message (screening, prevention, and treatment). The primary outcome was behavior. We did not assess any adverse outcomes. Main results: We included 35 studies involving 16,342 participants (all health consumers) and reporting 51 comparisons. In the context of attribute framing, participants in one included study understood the message better when it was framed negatively than when it was framed positively (1 study; SMD -0.58 (95% confidence interval (CI) -0.94 to -0.22); moderate effect size; low quality evidence). Although positively-framed messages may have led to more positive perception of effectiveness than negatively-framed messages (2 studies; SMD 0.36 (95% CI -0.13 to 0.85); small effect size; low quality evidence), there was little or no difference in persuasiveness (11 studies; SMD 0.07 (95% CI -0.23 to 0.37); low quality evidence) and behavior (1 study; SMD 0.09 (95% CI -0.14 to 0.31); moderate quality evidence).In the context of goal framing, loss messages led to a more positive perception of effectiveness compared to gain messages for screening messages (5 studies; SMD -0.30 (95% CI -0.49 to -0.10); small effect size; moderate quality evidence) and may have been more persuasive for treatment messages (3 studies; SMD -0.50 (95% CI -1.04 to 0.04); moderate effect size; very low quality evidence). There was little or no difference in behavior (16 studies; SMD -0.06 (95% CI -0.15 to 0.03); low quality evidence). No study assessed the effect on understanding. Authors' conclusions: Contrary to commonly held beliefs, the available low to moderate quality evidence suggests that both attribute and goal framing may have little if any consistent effect on health consumers' behavior. The unexplained heterogeneity between studies suggests the possibility of a framing effect under specific conditions. Future research needs to investigate these conditions.

Albert U, Maina G, et al. Obsessive-compulsive disorder (OCD) and triggering life events. The European Journal of Psychiatry. 2000;14(3):180-8.

Reviewed literature data on obsessive-compulsive disorder (OCD) onset in order to investigate whether OCD onset is significantly associated with the frequency and/or the severity of life events occurring in the year before, and whether these are specific events related to the onset of OCD. Re-

sults from studies performed on OCD samples did not point toward a higher number or a higher severity of life events prior to OCD onset as compared to non-psychiatric samples drawn from the general population. The difference between OCD patients and comparison Ss emerged when considering specific life events related to OCD onset. Delivery and streptococcal infections have been proven to exert an influence on triggering some forms of OCD. OCD whose onset is related to delivery (post-partum OCD) or to a streptococcal infection appears to be characterized by peculiar clinical features that allow clinicians to postulate that these forms are distinct clinical entities within the OCD spectrum. The better clinical characterization of these forms and the confirmation of the role of these life events in triggering OCD onset would provide researchers with models of pathogenesis that could be useful in identifying more effective therapeutic approaches at least to the treatment of these forms of OCD. (PsycINFO Database Record (c) 2012 APA, all rights reserved)

Allen G. Perinatal obsessive-compulsive disorder. Br J Gen Pract. 2013;63(612):347.

Altemus M. Obsessive-compulsive disorder during pregnancy and post-partum. Management of psychiatric disorders in pregnancy., Oxford University Press, New York, NY: 2001; p. 149-63.

Reviews research from primarily retrospective surveys and case reports on obsessive-compulsive disorder (OCD) during pregnancy and post-partum. Pregnancy and the post-partum period appear to be associated with the onset of OCD and possibly the exacerbation of pre-existing OCD. There is no evidence that lactation affects OCD symptom severity, but it may reduce subclinical symptoms which develop during pregnancy. Pregnancy-associated OCD is often characterized by comorbid major depression, and intrusive violent thoughts, contamination obsessions. Early detection and treatment of OCD during pregnancy and the post-partum period is important for the care of the mother and to minimize disruption and conflict within the family and mother–infant bonding. Two effective treatment strategies for OCD that have been identified are behavior therapy and pharmacologic treatments, particularly serotonin reuptake inhibitors. Identification of the physiological processes underlying the effects of hormonal fluxes on OCD in pregnancy and the post-partum period should clarify the pathophysiology of OCD in provided new treatment approaches. (PsycINFO Database Record (c) 2015 APA, all rights reserved) (chapter)

Andrews KH, Bracero LA. Cannabinoid Hyperemesis Syndrome During Pregnancy: A Case Report. J Reprod Med. 2015;60(9-10):430-2.

BACKGROUND: Cannabinoid hyperemesis syndrome (CHS) is a syndrome characterized by chronic marijuana use, cyclic vomiting, and compulsive bathing. Given the similarities this syndrome shares with hyperemesis gravidarum, it is likely that this is a highly underdiagnosed syndrome. We present a case of severe nausea and vomiting during pregnancy that met the criteria for CHS. CASE: This case outlines the course of recurrent nausea and vomiting due to cannabinoid hyperemesis in a pregnant patient and illustrates the similarities between hyperemesis gravidarum and CHS and the value of obtaining a complete history that includes the use of marijuana. CONCLUSION: Recognition of this syndrome will aid in patient care, lessen the economic burden of an extensive workup, and hopefully lessen provider frustration with diagnosis and treatment of a common and underdiagnosed entity.

Apter A, Ratzoni G, et al. Fluvoxamine open-label treatment of adolescent inpatients with obsessive-compulsive disorder or depression. J Am Acad Child Adolesc Psychiatry. 1994;33(3):342-8.

OBJECTIVE: Fluvoxamine, a monocyclic, specific serotonin uptake inhibitor with demonstrated efficacy in obsessive-compulsive disorder (OCD) and depression in adults, is marketed in more than 30 countries worldwide, including Israel. In the United States, where fluvoxamine is available only on an investigational basis, marketing appears imminent. This study evaluates the safety and efficacy of fluvoxamine in adolescents. METHOD: In an 8-week, open-label trial of fluvoxamine, 20 adolescent inpatients, ages 13 to 18 years, were treated for OCD (n = 14) or major depressive disorder (MDD)(n = 6) with daily doses ranging from 100 to 300 mg. Target symptoms were rated at regular intervals with the Yale-Brown Obsessive Compulsive Scale (Y-BOCS); Suicide Potential Scales (SPS); Beck Depression Inventory (BDI); the Overt Aggression Scale (OAS); and the Children's Global Adjustment Scale (CGAS). RESULTS: Fluvoxamine proved relatively safe and was especially effective in the patients with OCD; mean Y-BOCS scores decreased significantly ($p < .0001$) from 28.0 to 19.8 on medication. Although fluvoxamine also appeared effective in decreasing depression and bulimic symptoms, its impact on impulsive, suicidal, and anorectic symptoms was less clear. The commonest side effects (n > or = 3) were dermatitis, insomnia, hyperactivity, excitement, anxiety, tremor, and nausea. Fluvoxamine was discontinued in four patients because of side effects; the most serious side

effect occurred in two debilitated anorexic patients, of whom one became delirious and the other developed hallucinations. CONCLUSION: Preliminary evidence suggests that short-term treatment of adolescents with fluvoxamine is relatively safe and may be effective for OCD and some affective spectrum symptoms.

Arai M, Koike S, et al. Idiopathic carbonyl stress in a drug- naive case of at- risk mental state. Psychiatry and Clinical Neurosciences. 2011;65(6) 606-7.

Presents a case report of a 21-year-old male college student, who was born at full term after an uneventful pregnancy and delivery. He first developed obsessive thoughts at age 18 and sought medical help because of communication difficulties and depression. He was diagnosed with obsessive and compulsive disorder (OCD). Biweekly counseling and psychotherapy temporarily reduced his symptoms but a persistence of confused thoughts, hearing hypersensitivity and delusional ideation of persecution and reference led to a diagnosis of at-risk mental state, 10 months after his initial consultation. He was put on drug therapy. The present case report does not demonstrate a direct link between carbonyl stress and the disease development. It is not known whether carbonyl stress is a cause or consequence of the disease. In addition, it cannot be ruled out that other physical conditions or drugs affected the pentosidine levels. Additional data are needed to clarify a possible relationship between carbonyl stress and mental disorders. (PsycINFO Database Record (c) 2012 APA, all rights reserved)

Barpal H. [Theoretical transference and inference aspects of a case of defloration and pregnancy phobia (a contribution to the study of Melanie Klein with regard to female anxiety about the internal body)]. Rev Psicoanal. 1982;19:49-54.

Bhatia MS, Gupta R. Pica responding to SSRI: an OCD spectrum disorder? World J Biol Psychiatry. 2009;10(4 Pt 3):936-8.

Pica is a common disorder in childhood, however, in adults it is associated with mental retardation, psychosis and pregnancy. A few case reports have described it being associated with obsessive compulsive disorder in adults. We describe the case of an adult female patient who developed an impulse to ingest chalk only in stressful situations. These thoughts were ego-dystonic and kept on hammering her mind until she ate it. She was diagnosed as having Major Depressive Disorder with relational problems and pica. We prescribed her escitalopram with clonazepam and asked her to ventilate her feelings during stressful situations. Her depression improved within three weeks, with remarkable improvement in pica symptoms. We concluded that stress may induce the pica in some adults and that such feelings have impulsive/compulsive characters. In addition, appropriate management of stress may help to alleviate the symptoms of pica.

Bjarnason NH, Rode L, et al. Fetal exposure to pimozide: a case report. J Reprod Med. 2006;51(5):443-4.

BACKGROUND: Pimozide is an antidopaminergic, antipsychotic drug. Exposure during human pregnancy has not been reported previously, and recommendations on its use are based on extrapolation from other antipsychotics with antidopaminergic activity. CASE: A 26-year-old woman had Gilles de la Tourette syndrome and obsessive-compulsive disorder. It was not possible to discontinue pimozide during pregnancy, although the dosage was reduced to 1 mg daily. In addition, she was treated with 20 mg fluoxetine until gestational week 27. By request of the patient, elective cesarean section was scheduled for week 38. As a precaution, pimozide was withdrawn 2 weeks prior to the section. During this period the patient's symptoms severely intensified, and an emergency cesarean section had to be performed at 36 weeks. A healthy male infant weighing 2,448 g was delivered. Pediatric examination of the infant and electroencephalogram demonstrated no neurologic abnormalities. On day 4 both mother and infant were discharged. CONCLUSION: This is the first published report on fetal exposure to pimozide.

Brandes M, Soares CN, et al. Post-partum onset obsessive-compulsive disorder: diagnosis and management. Arch Women's Mental Health. 2004;7(2):99-110.

The post-partum period is associated with an increased risk of developing obsessive-compulsive disorder (OCD) in women. Post-partum onset OCD is often undiagnosed and untreated resulting in serious consequences for the patient, her family and the newborn. The symptoms of post-partum onset OCD may consist of obsessional intrusive thoughts about harming the newborn without compulsions or with both obsessions and compulsions. In this review, the phenomenology of post-partum onset OCD is described as well as strategies for screening and diagnosis. The review also characterizes the differences between post-partum onset OCD and post-partum depression and

post-partum psychosis and explores strategies for managing post-partum onset OCD patients. Issues regarding pharmacologic treatment of OCD in breastfeeding mothers are also reviewed.

Brandt KR, Mackenzie TB. Obsessive-compulsive disorder exacerbated during pregnancy: a case report. Int J Psychiatry Med. 1987;17(4):361-6.

An established obsessive-compulsive disorder (OCD) in a twenty-six-year-old woman, characterized by obsessional fear of rat germs and ritualistic cleansing, was observed to worsen during pregnancy. The patient's OCD had followed a fluctuating course for three years, but she had not previously experienced a decompensation of such duration and severity. During her pregnancy she became depressed and suicidal, was unable to care for her family and spent much of her confinement in the hospital. Several mechanisms are discussed which might explain the exacerbation.

Brieger P, Bolling S. [Compulsive disorder with homicidal impulses and paranoid symptoms in vascular encephalopathy]. Psychiatr Prax. 1997;24(5):245-7.

We report on the case of a 45-year old man with OCD who had the obsessive impulse to kill his 3-year old son. The patient showed signs of vascular encephalopathy after perinatal brain damage; besides that, he had developed a mild "explanatory" delusional system. Under treatment with SSRI and clozapine he improved remarkably. Presenting this case, we discuss the connection between organic disorders and OCD, and especially its relationship to perinatal brain damage.

Brockington I. Post-partum psychiatric disorders. Lancet. 2004;363(9405):303-10.

This review summarizes the psychiatry of the puerperium, in the light of publications during the past 5 years. A wide variety of disorders are seen. Recognition of disorders of the mother-infant relationship is important, because these have pernicious long-term effects but generally respond to treatment. Psychoses complicate about one in 1000 deliveries. The most common is related to manic depression, in which neuroleptic drugs should be used with caution. Post-traumatic stress disorder, obsessions of child harm, and a range of anxiety disorders all require specific psychological treatments. Post-partum depression necessitates thorough exploration. Cessation of breastfeeding is not necessary, because most antidepressant drugs seem not to affect the infant. Controlled trials have shown the benefit of involving the child's father in therapy and of interventions promoting interaction between mother and infant. Owing to its complexity, multidisciplinary specialist teams have an important place in post-partum psychiatry.

Brockington IF, Macdonald E, et al. Anxiety, obsessions and morbid preoccupations in pregnancy and the puerperium. Arch Women's Mental Health. 2006;9(5):253-63.

129 mothers referred to specialist psychiatric services in Birmingham and Christchurch were interviewed with the Birmingham Interview. Anxiety disorders were more frequent than depression during pregnancy, and equally frequent after delivery. The focus of pre- and post-partum anxiety may be important for psychological treatment. At a severe level, the most common prepartum theme was fear of fetal death; this was associated with a history of reproductive losses or infertility. After delivery the commonest themes were the pathological fear of cot death and fear of the criticism of mothering skills (which was a clue to a disordered mother-infant relationship). Clinicians should be vigilant for obsessional disorders, querulant (complaining) disorders, post-traumatic stress disorder, conjugal jealousy and dysmorphophobia states, which are all quite common. Patients with "post-partum depression" usually had at least one other (co-morbid) disorder, and 27% had two or more. These findings emphasize the diversity of post-partum psychiatric illness.

Buckley S. Editorial. Down Syndrome: Research & Practice. 2"6;10(1):v-vi.

In this issue, we have six papers, with some common themes. The first paper reports on the successful identification and treatment of a case series of four adults with Down syndrome with symptoms consistent with obsessive compulsive disorder (OCD). The next paper highlights the value of specific specialist clinics for children with Down syndrome. The third paper addresses the important issue of speech intelligibility and verbal apraxia (in some countries verbal dyspraxia) in children with Down syndrome. The fourth paper explores the development of behavioral difficulties and links with temperament, longitudinally from 12 - 45 months of age, in children with Down syndrome. The next paper, from Brian Trenholm and Pat Mirenda, Vancouver, Canada, explores the literacy skills and literacy related experiences and opportunities of children and adults with Down syndrome through a survey of 224 families across Canada. The final paper reports important changes in patterns of maternal age for conceptions and births of babies with Down syndrome. (PsycINFO Database Record (c) 2012 APA, all rights reserved)

Bulik CM, Carter FA, et al. Self-induced abortion in a bulimic woman. Int J Eat Disord. 1994;15(3):297-9.

We report the case of a woman with bulimia nervosa, several personality disorders, and a history of anorexia nervosa who deliberately induced an abortion via self-imposed starvation and vigorous exercise. Her history reveals severe obsessive-compulsive and narcissistic personality disorders as well as a lifelong pattern of denial of affect and illness.

Burt VK, Rudolph M. Treating an Orthodox Jewish woman with obsessive-compulsive disorder: maintaining reproductive and psychologic stability in the context of normative religious rituals. Am J Psychiatry. 2000;157(4):620-4.

Carter D, Misri S, et al. Psychologic aspects of early pregnancy loss. Clin Obstet Gynecol. 2007;50(1):154-65.

Early pregnancy loss is a complicated psychologic event that occurs in 12% to 24% of recognized pregnancies. Women who have experienced miscarriage often have common bereavement reactions and while the intensity and experience of these reactions diminishes over time for most women, a substantial minority will develop long-term psychiatric consequences. Depression, symptoms of anxiety, obsessive-compulsive disorder, and posttraumatic stress disorder are the most commonly reported psychologic reactions to miscarriage. The course and impact of these disorders on a grieving mother and her partner are discussed and treatment recommendations are made. The psychologic effects of therapeutic abortion are also be briefly discussed.

Case WA, Dubey BL. The mutilated breast syndrome--SIS augmentation of psychotherapy in post-partum onset OCD. Journal of Projective Psychology & Mental Health. 2008;15(2):103-12.

The Somatic Inkblot Series-II was administered to OCD patient as an aide in cognitive behavioral psychotherapy. Content analysis of SIS projected symbolic imagery was able to bring to the surface long-forgotten, unresolved stressors. The SIS could stimulate in memory long forgotten posttraumatic dreams and providing clinically relevant information for treatment plan. The SIS therapeutic intervention can be implemented to undermine affect linked irrational obsessions and thereby reduce compulsive behaviors. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract).

Challacombe F, Salkovskis P, et al. Interactions and attachment in infants of mothers with OCD. Archives of women's mental health. 2015;18:287. DOI: 10.1007/s00737-014-0488-6.

Objective / Background OCD is a relatively common and often disabling disorder that can have serious effects for the sufferer and those around them. Mothers may be more vulnerable to developing OCD after having a child, yet almost nothing is known about the adverse consequences on parenting and infants, and further whether treatment ameliorates such effects. Methods A group of 37 mothers with postnatally occurring OCD were recruited and assessed at home on symptom and parenting variables when their infants were 6 months old using a variety of methods including clinical interview, self-report questionnaires and observed mother-infant interactions. They were compared with a community group of 37 mothers without OCD who were assessed using the same methodology in order to clearly delineate the effect on parenting of obsessive-compulsive symptomatology. Interactions were rated blindly using Ainsworth's sensitivity scales and other scales devised for the study. Following assessment at 6 months, mothers entered pilot randomized controlled trial. mothers received wither intensive cognitive behavior therapy (CBT) over a 2-week period with 1-3 monthly follow ups or treatment as usual. They were reassessed at 12 months using the same procedures from the 6-month assessment. In addition, mothers and infants were assessed using the lab-based strange situation procedure. Control mothers were also reassessed at 12 months. Results Mothers with OCD were less sensitive in interactions with infants across a range of everyday parenting situations (Effect size=0.8) and reported significant interference with parenting. CBT was successful in ameliorating symptoms and the effect was maintained 5 months later (ES=0.92-1.09). However, mother-infant interactions were relatively unchanged after treatment. The distribution of attachment categories was similar in both treated and untreated clinical groups and healthy controls, with 71% of infants categorized as securely attached in all groups. Rates of attachment disorganization were low (4 % in the OCD group v 6 % in the control group). Conclusion Mothers with postnatal OCD are troubled by their symptoms for many hours per day and report that these symptoms interfere directly with the tasks of caregiving as well as their enjoyment of being a parent. Objectively, maternal sensitivity appears to be affected by OCD. However, the mother-infant attachment relationship appears to be resilient to these difficulties. Mothers with OCD may be able

to compensate for the difficulties caused by the disorder in ways that facilitate secure attachment relationships. CBT is effective for postnatal OCD and intensive treatments can achieve significant and lasting symptomatic change in a short space of time. This format may be preferred by women with young babies who can access treatment more easily.

Challacombe FL, Salkovskis PM. Intensive cognitive-behavioral treatment for women with postnatal obsessive-compulsive disorder: a consecutive case series. Behav Res Ther. 2011;49(6-7):422-6.

The postnatal period has been identified as a time of increased risk for the development of OCD. Obsessions and compulsions at this time frequently focus on accidental or deliberate harm coming to the infant and may impact on the sufferer's capacities as a parent. Given the similarities in presentation between OCD at this and other times, cognitive-behavior therapy is likely to be effective, but there is little information on whether or how adaptations of CBT can be made to maximize effectiveness and acceptability for mothers. There are no data on the impact of successful treatment on parenting. Six consecutively referred cases of postnatal OCD were treated using cognitive-behavioral therapy (CBT) intensively delivered over a two-week period. All mothers improved on self-report and clinician-rated measures which were sustained at 3-5-month follow-up. Mothers reported significant benefits in terms of their own symptoms and in parenting in general. The intensive mode of delivery appears to be effective and acceptable for this group. Future work should explore whether difficulties in terms of parenting are experienced by this group and whether these persist beyond the remission of the maternal disorder.

Challacombe FL, Wroe AL. A hidden problem: consequences of the misdiagnosis of perinatal obsessive-compulsive disorder. Br J Gen Pract. 2013;63(610):275-6.

Charlton BG. Self-management and pregnancy-safe interventions for panic, phobia and other anxiety-disorders might include over-the counter (OTC) 'SSRF antihistamines such as diphenhydramine and chlorpheniramine. Acta Psychiatrica Scandinavica. 2005;112(4):323.

Comments on an article by Julie H. Barlow et al (see record 2005-06257-003). The authors recently described a range of self-management psychological therapies which were an effective treatment for anxiety disorders such as panic, phobias and obsessive-compulsive disorder. This principle of self-management might be extended to include some of the early 'first generation' antihistamines which probably have properties similar to the selective serotonin-reuptake inhibitors (SSRIs), and which have been available 'over the counter' (OTC) for many decades - used mainly in the treatment of allergies such as hay fever, and as cough suppressants. (PsycINFO Database Record (c) 2012 APA, all rights reserved)

Chelmow D, Halfin VP. Pregnancy complicated by obsessive-compulsive disorder. J Matern Fetal Med. 1997;6(1):31-4.

Obsessive-compulsive disorder (OCD) is a well-recognized psychiatric disorder often beginning in reproductive age. A case of OCD in pregnancy is presented and its management discussed. A 28-year-old G3P2 woman presented at 8 weeks' gestation for prenatal care. She had been diagnosed with OCD following her prior pregnancy. Her symptoms primarily involved obsessions about infectious disease and compulsive cleaning and organization of household items, both of which greatly distressed her and interfered with caring for her children. She had been managed with clomipramine between pregnancies and was beginning a clinical trial of fluvoxamine when pregnancy was diagnosed. She discontinued medication when she realized she was pregnant. Her symptoms were managed during the pregnancy with frequent appointments with her obstetrician and her psychiatrist. She used a behavioral technique, "thought-stopping", as well. Her symptoms worsened in the last month of pregnancy and immediately after delivery; she delivered a normal infant. The clomipramine was restarted post-partum. She has done well since then, with minimal psychiatric symptoms. OCD is a disabling psychiatric disorder that occurs in women of reproductive age. With careful management, pregnancy without disabling psychiatric symptoms can occur.

Chowdhury AN, Mukherjee H, et al. Puppy pregnancy in humans: a culture-bound disorder in rural West Bengal, India. Int J Soc Psychiatry. 2003;49(1):35-42.

BACKGROUND: Delusion of pregnancy in males, though uncommon, has been reported in the literature. Delusion of animal pregnancy in humans is unreported until now, and we are reporting here cases of puppy pregnancy in human beings from a part of rural West Bengal, India. MATERIAL: Studies of six male cases and one female case of delusion of puppy pregnancy after an alleged touch or bite of a dog are presented. DISCUSSION: Detailed phenomenological analysis revealed

that there exists a strong cultural belief that dog bite may evolve into a puppy pregnancy even in the human male. Psychiatric status showed that there was a clear association of obsessive-compulsive disorder in two cases, anxiety-phobic locus in one and three showed no other mental symptom except this solitary false belief and preoccupation about the puppy pregnancy. All the cases were from rural areas and their communities endorse this pathogenic event of puppy pregnancy in humans. One case (11-year-old child) exemplified how the social imposition of this cultural belief made him a case that allegedly vomited out an embryo of a dog fetus. CONCLUSION: Although the belief in puppy pregnancy is culturally shared, the cases presented a mix of somatic and psychological complaints and their help-seeking behavior was marked. These features prompted us to identify these phenomena as a culture-bound disorder which needs proper cultural understanding for its effective management.

Christian LM, Storch EA. Cognitive behavioral treatment of post-partum onset: Obsessive compulsive disorder with aggressive obsessions. Clinical Case Studies. 2009;8(1):72-83.

This case study describes the application of cognitive behavioral therapy (CBT) for obsessive compulsive disorder (OCD) with post-partum onset. Sara, a 29-year-old woman, presented with aggressive obsessions of strangling and drowning her 5-month-old son. When she presented at the clinic, Sara had recently begun pharmacological treatment and was highly motivated to supplement this treatment with CBT. She showed marked improvement over the course of 8 CBT sessions using exposure and ritual prevention. This case study highlights cognitive and behavioral risk factors for OCD with post-partum onset, key considerations in differential diagnosis, and the utility of CBT for OCD with this population. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract).

Cornee J, Measson A, et al. Obsessional symptoms in expectant women and outcome of their pregnancy. J Psychosom Obstet Gynaecol. 1994;15(4):197-24.

The aim of this investigation was to explore whether, within the scope of personality traits and their modifications during pregnancy, the obsessional dimension may have a protective role against premature birth. In fact, obsessional characterology with its tendency to control may suggest that the women with these traits do not passively experience their pregnancy and may try to control its evolution, at least in their fantasies. Personality dimensions have been recorded using Derogatis' psychological self-administered questionnaire, in which women were asked to assess their level on the Derogatis symptom scale before and during pregnancy. The survey involved 351 women (117 premature and 234 term deliveries) who had both completed the self-administered questionnaire on the 6-month pregnancy visit and answered a specific interview at birth. Our results have shown that the existence of obsessional traits before pregnancy apparently does not have a protective role against premature delivery (odds ratio = 1.40; NS). Conversely, intensified obsessional symptoms during pregnancy are associated with a decreased premature birth rate (odds ratio = 0.44; $p < 0.05$). These results remain when the presence of obsessional traits before pregnancy is considered (adjusted odds ratio = 0.38; $p < 0.02$). The possibility of a defense reaction to this situation of pregnancy is discussed.

Curtis A, Clarke Carl E, et al. Cannabinoids for Tourette's Syndrome. Cochrane Database of Systematic Reviews. 2009. DOI: 10.1002/14651858.CD006565.pub2.

Background: Gilles de la Tourette Syndrome (GTS) is a developmental neuropsychiatric disorder characterized by the presence of chronic motor and phonic tics. Drugs currently used in the treatment of GTS either lack efficacy or are associated with intolerable side effects. There is some anecdotal and experimental evidence that cannabinoids may be effective in treating tics and compulsive behavior in patients with GTS. There are currently no systematic Cochrane reviews of treatments used in GTS. There is one other Cochrane review being undertaken at present, on the use of fluoxetine for tics in GTS. Aims: To evaluate the efficacy and safety of cannabinoids as compared to placebo or other drugs in treating tics, premonitory urges and obsessive-compulsive symptoms (OCS), in patients with GTS. Search methods: We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (in The Cochrane Library Issue 4 2008) , MEDLINE (January 1996 to date), EMBASE (January 1974 to date), PsycINFO (January 1887 to date), CINAHL (January 1982 to date), AMED (January 1985 to date), British Nursing Index (January 1994 to date) and DH DATA (January 1994 to date). We also searched the reference lists of located trials and review articles for further information. Selection criteria: We included randomized controlled trials (RCTs) comparing any cannabinoid preparation with placebo or other drugs used in the treatment of tics and OCS in patients with GTS. Information collection and analysis: Two authors abstracted data independently and settled any differences by

argument. Main results: Only two trials were found that met the inclusion criteria. Both compared a cannabinoid, delta-9-Tetrahydrocannabinol (?9THC), either as monotherapy or as adjuvant therapy, with placebo. One was a double blind, single dose crossover trial and the other was a double blind, parallel group study. A total of 28 different patients were studied. Although both trials reported a positive effect from ?9THC, the improvements in tic frequency and severity were small and were only detected by some of the outcome trials. Authors' conclusions: Not enough evidence to support the use of cannabinoids in treating tics and obsessive-compulsive behavior in people with Tourette's syndrome.

Darling E. Worried sick: Post-partum obsessive-compulsive disorder. Motherhood, mental illness and recovery: Stories of hope., Springer International Publishing, Cham; 2014; p. 241-8.

This chapter presents the experiences of the author, who is a doctoral student in Clinical Psychology, tells the story of a mother's experience with post-partum depression and obsessive-compulsive disorder. Written following an interview with this mother, who is also a psychiatrist, the story emphasizes the importance of access to support and treatment for mental health recovery. (PsycINFO Database Record (c) 2015 APA, all rights reserved) (chapter)

Davidson J, Robertson E. A follow-up study of post-partum illness, 1946-1978. Acta Psychiatr Scand. 1985;71(5):451-7.

Eighty-two patients, who were treated for post-partum illness between 1946 and 1971, were identified and followed up. Diagnostically, the sample comprised unipolar depression (52%), bipolar disorder (18%), schizophrenia (16%), abnormal personality with depression (8%), organic disorder (2%), and obsessional state with depression and paranoid disorder (1% each). The overall prognosis was good, except for schizophrenia, in which more than 50% of patients had chronic disability. Further childbirth intensified, and caused deterioration of, the underlying schizophrenia process. Following an initial illness in the puerperium, the probability of a recurrent affective illness was 43% for unipolar and 66% for bipolar disorder. The risk of developing another post-partum illness varied from 1 in 3 to 1 in 5 pregnancies. Five percent of the sample ultimately committed suicide, and the probable incidence of infanticide was 4%.

Di Mario S, Basevi V, et al. Prenatal education for congenital toxoplasmosis. Cochrane Database of Systematic Reviews. 2015. DOI: 10.1002/14651858.CD006171.pub4.

Background: Congenital toxoplasmosis is considered a rare but potentially severe infection. Prenatal education about congenital toxoplasmosis could be the most efficient and least harmful intervention, yet its effectiveness is uncertain. Objectives: To assess the effects of prenatal education for preventing congenital toxoplasmosis. Search methods: We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (31 May 2015), and reference lists of relevant papers, reviews and websites. Selection criteria: Randomized and quasi-randomized controlled trials of all types of prenatal education on toxoplasmosis infection during pregnancy. Cluster-randomized trials were eligible for inclusion. Data collection and analysis: Two review authors independently assessed trials for inclusion and risk of bias, extracted data and checked them for accuracy. Main results: Two cluster-randomized controlled trials (RCTs) (involving a total of 5455 women) met the inclusion criteria. The two included trials measured the effectiveness of the intervention in different ways, which meant that meta-analysis of the results was not possible. The overall quality of the two studies, as assessed using the GRADE approach, was low, with high risk of detection and attrition bias in both included trials. One trial (432 women enrolled) conducted in Canada was judged of low methodological quality. This trial did not report on any of the review's pre-specified primary outcomes and the secondary outcomes reported results only as P values. Moreover, losses to follow-up were high (34%, 147 out of 432 women initially enrolled). The authors concluded that prenatal education can effectively change pregnant women's behavior as its increased pet, personal and food hygiene. The second trial conducted in France was also judged of low methodological quality. Losses to follow-up were also high (44.5%, 2233 out of 5023 women initially enrolled) and differential (40% in the intervention group and 52% in the control group). The authors concluded that prenatal education for congenital toxoplasmosis has a significant effect on improving women's knowledge, whereas it has no effect on changing women's behavior. In this trial 17/3949 pregnant women seroconverted for toxoplasmosis: 13/2591 (0.5%) in the intervention group and 4/1358 (0.3%) in the control group. The rate of seroconversion detected during the study did not differ between groups (risk ratio (RR) 1.70, 95% confidence interval (CI) 0.56 to 5.21; participants = 3949; studies = one, low quality evidence). The number of events was too small to reach conclusions about the effect of prenatal education on seroconversion rate during gestation. No other randomized trials on the effect of prenatal

education on congenital toxoplasmosis rate, or toxoplasmosis seroconversion rate during pregnancy were detected. Authors' conclusions: Even though primary prevention of congenital toxoplasmosis is considered a desirable intervention, given the lack of related risks compared to secondary and tertiary prevention, its effectiveness has not been adequately evaluated. There is very little evidence from RCTs that prenatal education is effective in reducing congenital toxoplasmosis even though evidence from observational studies suggests it is. Given the lack of good evidence supporting prenatal education for congenital toxoplasmosis prevention, further RCTs are needed to confirm any potential benefits and to further quantify the impact of different sets of educational intervention.

Diaz SF, Grush LR, et al. Obsessive-compulsive disorder in pregnancy and the puerperium. American Psychiatric Press review of psychiatry, Vol. 16., American Psychiatric Association, Arlington, VA; 1997; III-97-III-112.

The authors review the literature on obsessive-compulsive disorder (OCD) in pregnancy and the puerperium. Preliminary data from a naturalistic study that followed 19 women with OCD through their pregnancies is presented. Epidemiology, etiology, and treatment recommendations (psychotherapy and pharmacotherapy) are discussed. Case examples are used to familiarize the clinician with ways in which the illness may present during pregnancy and the puerperium. The cases also illustrate the variability in illness course and severity during pregnancy and the post-partum period. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (chapter)

Draper R. Clinical experience with Ro 5-3350 (bromazepam). J Int Med Res. 1975;3(3):214-22.

A pilot study using Ro 5-3350 was followed by a double-blind trial comparing Ro 5-3350 and chlordiazepoxide in a total of 25 patients who were either hospital in-patients or previous in-patients attending an out-patients follow-up clinic. The patients all had a long history of obsessive-compulsive or phobic symptoms. The visual analogue scale, the Taylor Manifest Anxiety Scale and clinical ratings were used to measure the response to treatment. In all three rating methods used, those patients who had received Ro 5-3350, chlordiazepoxide and then Ro 5-3350 in that order, consistently favored Ro 5-3350. When the clinical ratings were examined by diagnostic groups, it was found that the phobic patients all gave positive responses to Ro 5-3350. Two of the six patients with severe anxiety or agoraphobic states who had been treated with Ro 5-3350 over periods ranging from three to five years received the medication during the whole term of pregnancy and they were delivered of full-term normal babies. The results suggest that Ro 5-3350 (bromazepam) is a potent anxiolytic most likely to be effective in the relief of visceral manifestations of anxiety. The incidence of side-effects was low and there were no toxic effects reported.

Draper R. Clinical experience with Ro 5-3350 (bromazepam). The Journal of international medical research. 1975;3:214-22.

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Elkins R, Rapoport JL, et al. Obsessive-compulsive disorder of childhood and adolescence. A neurobiological viewpoint. J Am Acad Child Psychiatry. 1980;19(3):511-24.

Faggiano F, Minozzi S, et al. Universal school-based prevention for illicit drug use. Cochrane Database of Systematic Reviews. 2014. DOI: 10.1002/14651858.CD003020.pub3.

Background: Drug addiction is a chronic, relapsing disease. Primary interventions should aim to reduce first use or to prevent the transition from experimental use to addiction. School is the appropriate setting for preventive interventions. Objectives: To evaluate the effectiveness of universal school-based interventions in reducing drug use compared to usual curricular activities or no in-

tervention. Search methods: We searched the Cochrane Drugs and Alcohol Group's Trials Register (September 2013), the Cochrane Central Register of Controlled Trials (2013, Issue 9), PubMed (1966 to September 2013), EMBASE (1988 to September 2013) and other databases. We also contacted researchers in the field and checked reference lists of articles. Selection criteria: Randomized controlled trials (RCT) evaluating school-based interventions designed to prevent illicit drugs use. Data collection and analysis: We used the standard methodological procedures expected by The Cochrane Collaboration. Main results: We included 51 studies, with 127,146 participants. Programmed were mainly delivered in sixth and seventh grade pupils. Most of the trials were conducted in the USA. Social competence approach versus usual curricula or no intervention Marijuana use at < 12 months follow-up: the results favored the social competence intervention (risk ratio (RR) 0.90; 95% confidence interval (CI) 0.81 to 1.01, four studies, 9456 participants, moderate quality evidence). Seven studies assessed this outcome (no data for meta-analysis): two showed a positive significant effect of intervention, three showed a non-significant effect, one found a significant effect in favour of the control group and one found a trend in favour of the control group. Marijuana use at 12+ months: the results favored the social competence intervention (RR 0.86; 95% CI 0.74 to 1.00, one study, 2678 participants, high quality evidence). Seven studies assessed this outcome (no data for meta-analysis): two showed a significant positive effect of intervention, three showed a non-significant effect, one found a significant effect in favour of the control group and one a trend in favour of the control group. Hard drug use at < 12 months: we found no difference (RR 0.69; 95% CI 0.40 to 1.18, one study, 2090 participants, moderate quality evidence). Two studies assessed this outcome (no data for meta-analysis): one showed comparable results for the intervention and control group; one found a statistically non-significant trend in favour of the social competence approach. Hard drug use at 12+ months: we found no difference (mean difference (MD) -0.01; 95% CI -0.06 to 0.04), one study, 1075 participants, high quality evidence). One study with no data for meta-analysis showed comparable results for the intervention and control group. Any drug use at < 12 months: the results favoured social competence interventions (RR 0.27; 95% CI 0.14 to 0.51, two studies, 2512 participants, moderate quality evidence). One study with 1566 participants provided continuous data showing no difference (MD 0.02; 95% CI -0.05 to 0.09, moderate quality evidence). Social influence approach versus usual curricula or no intervention. Marijuana use at < 12 months: we found a nearly statistically significant effect in favour of the social influence approach (RR 0.88; 95% CI 0.72 to 1.07, three studies, 10,716 participants, moderate quality evidence). One study with 764 participants provided continuous data showing results that favoured the social influence intervention (MD -0.26; 95% CI -0.48 to -0.04).Marijuana use at 12+ months: we found no difference (RR 0.95; 95% CI 0.81 to 1.13, one study, 5862 participants, moderate quality evidence). One study with 764 participants provided continuous data and showed nearly statistically significant results in favour of the social influence intervention (MD -0.22; 95% CI -0.46 to 0.02). Of the four studies not providing data for meta-analysis a statistically significant protective effect was only found by one study. Hard drug use at 12+ months: one study not providing data for meta-a lysis found a significant protective effect of the social influence approach. Any drug use: no studies assessed this outcome. Combined approach versus usual curricula or no intervention Marijuana use at < 12 months: there was a trend in favour of intervention (RR 0.79; 95% CI 0.59 to 1.05, three studies, 8701 participants, moderate quality evidence). One study with 693 participants provided continuous data and showed no difference (MD -1.90; 95% CI -5.83 to 2.03).Marijuana use at 12+ months: the results favoured combined intervention (RR 0.83; 95% CI 0.69 to 0.99, six studies, 26,910 participants, moderate quality evidence). One study with 690 participants provided continuous data and showed no difference (MD -0.80; 95% CI -4.39 to 2.79). Two studies not providing data for meta-analysis did not find a significant effect. Hard drug use at < 12 months: one study with 693 participants provided both dichotomous and continuous data and showed conflicting results: no difference for dichotomous outcomes (RR 0.85; 95% CI 0.63 to 1.14), but results in favour of the combined intervention for the continuous outcome (MD -3.10; 95% CI -5.90 to -0.30). The quality of evidence was high. Hard drug use at 12+ months: we found no difference (RR 0.86; 95% CI 0.39 to 1.90, two studies, 1066 participants, high quality evidence). One study with 690 participants provided continuous data and showed no difference (MD 0.30; 95% CI -1.36 to 1.96). Two studies not providing data for meta-analysis showed a significant effect of treatment. Any drug use at < 12 months: the results favoured combined intervention (RR 0.76; 95% CI 0.64 to 0.89, one study, 6362 participants).Only one study assessed the effect of a knowledge-focused intervention on drug use and found no effect. The types of comparisons and the programs assessed in the other two groups of studies were very heterogeneous and difficult to synthesize. Authors' conclusions: School programs based on a combination of social competence and social influence approaches showed, on average, small but consistent protective effects in preventing drug use, even if some outcomes did not show statistical significance. Some programs based on the social competence approach also showed protective effects for some outcomes. Since the effects of school-based pro-

grams are small, they should form part of more comprehensive strategies for drug use prevention in order to achieve a population-level impact.

Fairbrother N, Abramowitz JS. New parenthood as a risk factor for the development of obsessional problems. Behav Res Ther. 2007;45(9):2155-63.

Research on emotional disturbance during pregnancy and the post-partum period has focused primarily on mood disorders and psychosis, yet preliminary evidence suggests that early parenthood is also associated with an increased risk for the development and exacerbation of obsessional problems. In this article we describe the nature of "post-partum obsessive-compulsive disorder" (ppOCD) and present a cognitive-behavioral model to account for these signs and symptoms. The model outlines feature of early parenthood that might increase vulnerability to ppOCD and proposes a conceptual framework similar to that described in cognitive-behavioral models of OCD in general. The empirical status of the model described herein is discussed, along with suggestions for future research and implications for treatment.

Fields L. An integrative brief treatment approach for obsessive-compulsive disorder. Journal of Psychotherapy Integration. 1998;8(3):161-72.

This article reports on the integrated application of cognitive therapy, transactional analysis techniques, and the behavioral technique of response prevention using self-instructional training and behavioral substitution in a brief therapy approach. These methods were applied in the case of a young man who presented with compulsions to perform repetitive and ordering rituals with the belief that it would prevent his girlfriend from becoming pregnant. A 21-year-old White male who had performed 3 to 5 hours of rituals daily for several years was able to eliminate many of his compulsive behaviors and reduce his level of anxiety after eight clinical therapy sessions. Results were maintained at 6-month follow-up. The clear precipitating factors and the unusual maintaining variables for the disorder in the client are described. The author discusses the case considering current theoretical, therapeutic, and biomedical understandings of the disorder. (PsycINFO Database Record (c) 2015 APA, all rights reserved)

Frías Á, Palma C, et al. Obsessive-compulsive disorder in the perinatal period: Epidemiology, phenomenology, pathogenesis, and treatment. Anales de Psicología. 2015;31(1):1-7.

The aim of this review is to describe the main theoretical findings and research conclusions about obsessive-compulsive disorder (CCD) in the perinatal period. On one hand, epidemiological studies show that the risk of OCD onset and/or exacerbation could increase in this period, particularly in the puerperium. Phenomenologically, in these stage aggressive and contamination obsessions are very common and are related to the fetus or newborn. On the other hand, regarding OCD pathogenesis in this period, there is indirect evidence to suggest the participation of neuroendocrine (e.g. female gonadal steroids and oxytocin) and cognitive behavioral variables (e.g. hyper-responsibility, threat overestimation, and mental control). In terms of research, more empirical studies are needed to contrast these specific vulnerability factors. Moreover, no empirically validated psychotherapeutic treatments (controlled trials) adapted to this OCD subgroup were found, although some studies highlight the role of cognitive behavioral therapy (CBT) as an effective intervention in the context of selective primary prevention. (PsycINFO Database Record (c) 2015 APA, all rights reserved) (journal abstract).

Fukuchi T, Okada Y, et al. [A case of pregnant woman with severe obsessive-compulsive disorder successfully treated by modified-electroconvulsive therapy]. Seishin Shinkeigaku Zasshi. 2003;105(7):927-32.

Obsessive-compulsive disorder (OCD) is rare psychiatric disorder during pregnancy and is often therapy resistant. We report a 36-year-old pregnant woman with severe obsessive-compulsive disorder successfully treated by modified-electroconvulsive therapy. During the pregnancy, severe mysophobia and compulsive washing appeared, so severely that she was unable to lie down, endangering the life of the fetus. Since the pharmacotherapy was ineffective, modified electroconvulsive therapy (m-ECT) was performed in cooperation with the obstetrician and the anesthesiologist, along with monitored cardiotocography throughout the procedure. During the second therapy late deceleration on the fetal cardiogram occurred, but rapid intravenous administration of ritodrine led to the cessation of abnormal uterine contraction. Two courses of m-ECT markedly diminished her symptoms, and she delivered a healthy infant without complications. M-ECT can be an alternative treatment for pregnant patients with OCD.

Geller D, Biederman J, et al. Is juvenile obsessive-compulsive disorder a developmental subtype of the disorder? A review of the pediatric literature. J Am Acad Child Adolesc Psychiatry. 1998;37(4):420-7.

OBJECTIVE: To examine the clinical correlates of obsessive-compulsive disorder (OCD) in children and adolescents. METHOD: A systematic review of the extant literature on juvenile OCD was conducted examining age at onset, gender distribution, symptom phenomenology, psychiatric comorbidity, neurological and perinatal history, family psychiatric history, cognitive and neuropsychological profiles, and treatment and outcome in juvenile OCD subjects. RESULTS: Juvenile OCD was associated with a unique peak of age at onset indicating a bimodal incidence of the disorder, male preponderance, a distinct pattern of comorbidity with attention-deficit/hyperactivity disorder and other developmental disorders as well as frequent associated neuropsychological deficits, an increased familial loading for OCD, and frequent absence of insight. CONCLUSION: These findings show that juvenile OCD is associated with a unique set of correlates that appear to differ from findings reported in studies of adult OCD subjects. Although in need of confirmation, these findings suggest that juvenile OCD may be a developmental subtype of the disorder. Since juvenile OCD is likely to continue into adulthood, these findings stress the importance of considering age at onset in clinical and research studies of adults with OCD.

Geller DA, Wieland N, et al. Perinatal factors affecting expression of obsessive-compulsive disorder in children and adolescents. J Child Adolesc Psychopharmacol. 2008;18(4):373-9.

OBJECTIVE: To examine whether adverse perinatal experiences of children are associated with obsessive compulsive disorder (OCD) in youth. METHODS: Subjects were 130 children and adolescents with OCD recruited from a family genetic study of pediatric OCD and 49 matched controls from a contemporaneous family case-control study of attention-deficit/hyperactivity disorder (ADHD). Subjects were comprehensively assessed in multiple domains of function. A systematic history of pregnancy, delivery, and infancy complications was obtained. RESULTS: Compared to normal controls, children with OCD had mothers with significantly higher rates of illness during pregnancy requiring medical care (chi(2) +/- 8.61, p +/- 0.003) and more birth difficulties (induced labor, forceps delivery, nuchal cord, or prolonged labor) (chi(2) +/- 7.51, p +/- 0.006). Among the OCD-affected children, we found several significant associations between adverse perinatal experiences and earlier age at onset, increased OCD severity, and increased risk for comorbid ADHD, chronic tic disorder, anxiety disorder, and major depressive disorder. CONCLUSION: Although exploratory, our analyses found that children with OCD had higher rates of several adverse perinatal experiences compared with controls. Among OCD-affected children, comorbid psychopathology was predicted by specific perinatal risk factors. Prospective studies of perinatal adverse events that minimize potential recall bias and type I errors are needed.

Gold KJ, Boggs ME, et al. Anxiety disorders and obsessive-compulsive disorder 9 months after perinatal loss. Gen Hosp Psychiatry. 2014;36(6):650-4.

OBJECTIVE: Perinatal loss (stillbirth after 20 weeks of gestational age or infant death in the first month) impacts one to two infants per hundred live births in the United States and can be a devastating experience for parents. We assessed prevalence of anxiety disorders and obsessive-compulsive disorder (OCD) among bereaved and live-birth mothers. METHODS: We collaborated with the Michigan Department of Community Health to survey Michigan mothers with perinatal death or live birth. We measured symptoms of generalized anxiety disorder, social phobia, panic disorder and OCD using validated written self-report screens and collected data on maternal demographics, psychiatric history, social support and intimate partner violence. RESULTS: A total 609/1400 mothers (44%) participated, returning surveys 9 months postdelivery. Two hundred thirty-two mothers had live birth, and 377 had perinatal loss. In unadjusted analyses, bereaved mothers had higher odds of all four disorders. In logistic regression adjusted for covariates, bereaved mothers still had higher odds of moderate-severe generalized anxiety disorder [odds ratio (OR): 2.39, confidence interval (CI): 1.10-5.18, P = .028] and social phobia (OR: 2.32, CI: 1.52-3.54, P < .0005) but not panic disorder or OCD. CONCLUSION: Bereaved mothers struggle with clinically significant anxiety disorders in the first year after perinatal loss; improved identification and treatment are essential to improve mental health for this vulnerable population.

Goldstein DJ. Effects of third trimester fluoxetine exposure on the newborn. J Clin Psychopharmacol. 1995;15(6):417-20.

Prospectively identified fluoxetine-exposed pregnancies were evaluated to determine whether fluoxetine, a serotonin reuptake inhibitor commonly used for the treatment of depression and obses-

sive-compulsive disorder, might be associated with neonatal complications after maternal fluoxetine exposure during the third trimester through delivery. The outcomes of all prospectively identified, spontaneously reported pregnancies with confirmed fluoxetine exposure during the third trimester through delivery were evaluated. Postnatal complications unrelated to malformations were reported in 15 of the 112 identified pregnancies (115 infants), but there was neither a consistent or recurring pattern nor a dose relationship. Based on this survey and comparison with reported rates from the National Hospital Discharge Survey, it is unlikely that maternal fluoxetine use during the third trimester results in significant postnatal complications.

Gross ER. Common causes of hair loss in male and female and some recommendations as to treatment. Del Med J. 1964;36:1-5.

Guglielmi V, Vulink NC, et al. Obsessive-compulsive disorder and female reproductive cycle events: results from the OCD and reproduction collaborative study. Depress Anxiety. 2014;31(12):979-87.

BACKGROUND: Women with obsessive-compulsive disorder (OCD) often report that symptoms first appear or exacerbate during reproductive cycle events; however, little is known about these relationships. The goals of this study were to examine, in a US and a European female OCD sample, onset and exacerbation of OCD in reproductive cycle events, and to investigate the likelihood of repeat exacerbation in subsequent pregnancies and post-partum periods. METHODS: Five hundred forty-two women (United States, n = 352; Dutch, n = 190) who met DSM-IV criteria for OCD, completed self-report questionnaires designed to assess OCD onset and symptom exacerbation associated with reproductive events. RESULTS: OCD onset occurred within 12 months after menarche in 13.0%, during pregnancy in 5.1%, at post-partum in 4.7%, and at menopause in 3.7%. Worsening of pre-existing OCD was reported by 37.6% of women at premenstrual, 33.0% during pregnancy, 46.6% post-partum, and 32.7% at menopause. Exacerbation in first pregnancy was significantly associated with exacerbation in second pregnancy (OR = 10.82, 95% CI 4.48-26.16), as was exacerbation in first post-partum with exacerbation in second post-partum (OR = 6.86, 95% CI 3.27-14.36). Results were replicated in both samples. CONCLUSIONS: Reproductive cycle events are periods of increased risk for onset and exacerbation of OCD in women. The present study is the first to provide significant evidence that exacerbation in or after first pregnancy is a substantial risk factor for exacerbation in or after a subsequent pregnancy. Further research is needed to identify factors related to exacerbation, so that physicians may provide appropriate recommendations to women regarding clinical issues involving OCD and reproductive cycle events.

Guglielmi V, Vulink NCC, et al. Obsessive–compulsive disorder and female reproductive cycle events: Results from the ocd and reproduction collaborative study. Depression and Anxiety. 2014;31(12):979-87.

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Hallion LS, Sockol LE, et al. Obsessive-compulsive disorder. Anxiety disorders and gender, Springer International Publishing, Cham; 2015; p. 69-87.

This chapter discusses obsessive-compulsive disorder (OCD). A small but growing body of research suggests several differences in the prevalence, clinical features, and genetic underpinnings of OCD. In pediatric samples, OCD is twice as common in males than females, corresponding to an earlier age of onset in males than females. In adult community samples, the gender distribution is roughly equal, whereas treatment-seeking samples are characterized by a slightly higher percentage of women. Phenomenologically, women are more likely than men to report cleaning and contamination obsessions, particularly in the context of perinatal OCD, whereas men are more likely to report sexual and symmetry-related obsessions. Patterns of comorbidity correspond to commonly observed gender differences in other disorders; for example, men with OCD are more likely to experience comorbid substance-related disorders, whereas women more commonly experience comorbid mood and anxiety disorders. Corresponding to these epidemiological and phenomenological differences, genetic research hints at sex differences in the genetic underpinnings of OCD. Few gender-related differences in OCD treatment responsivity have been identified. As such, cognitive- behavioral therapy and pharmacotherapy with SSRIs are considered frontline treatments for OCD irrespective of gender (PsycINFO Database Record (c) 2016 APA, all rights reserved) (chapter)

Hodgman CH. Current issues in adolescent psychiatry. Hosp Community Psychiatry. 1983;34(6):514-21.

Adolescent psychiatry as a body of knowledge has shown encouraging growth in recent years, as research findings from general psychiatry have been added to new data on adolescent psychological and physical development. The author reviews recent findings on selected topics in adolescent psychopathology, including adaptive disorders, obsessive-compulsive disorders, phobias, attention deficit disorders, depression, manic-depressive illness, suicidal impulses, schizophrenia, anorexia nervosa, and borderline states. He also outlines findings on normal adolescent development and discusses the problems of diagnosing children and adolescents with psychological problems. Studies in anxiety, attention deficit, and conduct disorders, he says, are yielding important new findings by combining biological and psychological insights.

Hollander E. Muscarinic targets for cognition in schizophrenia; ADHD comorbidity; perinatal risks, treatment resistance and SRIs; and brain lesions presenting as psychiatric illness. CNS Spectrums. 2008;13(11):938-9.

This month's CNS Spectrums examines cholinergic mechanisms of cognitive dysfunction in schizophrenia, how attention-deficit/hyperactivity disorder may complicate the course of other psychiatric illness, whether serotonin reuptake inhibitors may induce spontaneous abortions, the combination of citalopram + clomipramine in treatment-resistant obsessive compulsive disorder, and how silent brain lesions can present as psychiatric illness. (PsycINFO Database Record (c) 2012 APA, all rights reserved)

Hudak R, Wisner KL. Diagnosis and treatment of post-partum obsessions and compulsions that involve infant harm. Am J Psychiatry. 2012;169(4):360-3.

Obsessive-compulsive symptoms in the post-partum period often include intrusive thoughts of harming the infant and rituals that result in avoidance of the baby. The differential diagnosis of women who develop these symptoms includes post-partum major mood disorders, obsessive-compulsive disorder, and psychosis with infanticidal thoughts. The treatment of the most common diagnoses, mood disorders and obsessive-compulsive disorder, includes serotonergic drugs, psychoeducation to help the patient understand that she is highly unlikely to harm her infant, and exposure with response prevention therapy. This intervention involves exposure of the patient to the feared situations, which are usually related to infant care, while simultaneously preventing the compulsive rituals.

Iida J, Iwasaka H, et al. Clinical features of childhood-onset schizophrenia with obsessive-compulsive symptoms during the prodromal phase. Psychiatry Clin Neurosci. 1995;49(4):201-7.

Thirty-nine patients with schizophrenia, diagnosed according to DSM-III-R, who were under 15 years of age, were studied in two groups; 16 subjects with obsessive-compulsive symptoms during the prodromal phase, and 23 with no obsessive-compulsive disorders. The group with obsessive-compulsive symptoms during the prodromal phase was characterized by a higher ratio of males, higher incidences of perinatal and brain computed tomography (CT) abnormalities, fewer hereditary factors, longer duration of the prodromal phase, and a higher incidence of insidious onset and negative symptoms compared with the group without such prodromal symptoms. Schizophrenic

patients with obsessive-compulsive symptoms during the prodromal phase were clinically distinct from those without, which suggests the possibility of subtype categorization.

James Anthony C, James G, et al. Cognitive behavioral therapy for anxiety disorders in children and adolescents. Cochrane Database of Systematic Reviews. 2015. DOI: 10.1002/14651858.CD004690.pub4.

Background: A previous Cochrane review (James 2005) showed that cognitive behavioral therapy (CBT) was effective in treating childhood anxiety disorders; however, questions remain regarding (1) the relative efficacy of CBT versus non-CBT active treatments; (2) the relative efficacy of CBT versus medication and the combination of CBT and medication versus placebo; and (3) the long-term effects of CBT. Objectives: To examine (1) whether CBT is an effective treatment for childhood and adolescent anxiety disorders in comparison with (a) wait-list controls; (b) active non-CBT treatments (i.e. psychological placebo, bibliotherapy and treatment as usual (TAU)); and (c) medication and the combination of medication and CBT versus placebo; and (2) the long-term effects of CBT. Search methods: Searches for this review included the Cochrane Central Register of Controlled Trials (CENTRAL) and the Cochrane Depression, Anxiety and Neurosis Group Register, which consists of relevant randomized controlled trials from the bibliographic databases. The Cochrane Library (1970 to July 2012), EMBASE, (1970 to July 2012) MEDLINE (1970 to July 2012) and PsycINFO (1970 to July 2012). Selection criteria: All randomized controlled trials (RCTs) of CBT versus waiting list, active control conditions, TAU or medication were reviewed. All participants must have met the criteria of the Diagnostic and Statistical Manual (DSM) or the International Classification of Diseases (ICD) for an anxiety diagnosis, excluding simple phobia, obsessive-compulsive disorder, posttraumatic stress disorder and elective mutism. Data collection and analysis: The methodological quality of included trials was assessed by three reviewers independently. For the dichotomous outcome of remission of anxiety diagnosis, the odds ratio (OR) with 95% confidence interval (CI) based on the random-effects model, with pooling of data via the inverse variance method of weighting, was used. Significance was set at $P < 0.05$. Continuous data on each child anxiety symptoms were pooled using the standardized mean difference (SMD). Main results: Forty-one studies consisting of 1806 participants were included in the analyses. The studies involved children and adolescents with anxiety of mild to moderate severity in university and community clinics and school settings. For the primary outcome of remission of any anxiety diagnosis for CBT versus waiting list controls, intention-to-treat (ITT) analyses with 26 studies and 1350 participants showed an OR of 7.85 (95% CI 5.31 to 11.60, $Z = 10.26$, $P < 0.0001$), but with evidence of moderate heterogeneity ($P = 0.04$, $I^2 = 33\%$). The number needed to treat (NNT) was 6.0 (95% CI 7.5 to 4.6). No difference in outcome was noted between individual, group and family/parental formats. ITT analyses revealed that CBT was no more effective than non-CBT active control treatments (six studies, 426 participants) or TAU in reducing anxiety diagnoses (two studies, 88 participants). The few controlled follow-up studies (n = 4) indicate that treatment gains in the remission of anxiety diagnosis are not statistically significant. Authors' conclusions: Cognitive behavioral therapy is an effective treatment for childhood and adolescent anxiety disorders; however, the evidence suggesting that CBT is more effective than active controls or TAU or medication at follow-up, is limited and inconclusive.

Katzman MA, Bleau P, et al. Canadian clinical practice guidelines for the management of anxiety, posttraumatic stress and obsessive-compulsive disorders. BMC Psychiatry. 2014;14(Suppl 1).

Background: Anxiety and related disorders are among the most common mental disorders, with lifetime prevalence reportedly as high as 31%. Unfortunately, anxiety disorders are under-diagnosed and under-treated. Methods: These guidelines were developed by Canadian experts in anxiety and related disorders through a consensus process. Data on the epidemiology, diagnosis, and treatment (psychological and pharmacological) were obtained through MEDLINE, PsycINFO, and manual searches (1980–2012). Treatment strategies were rated on strength of evidence, and a clinical recommendation for each intervention was made, based on global impression of efficacy, effectiveness, and side effects, using a modified version of the periodic health examination guidelines. Results: These guidelines are presented in 10 sections, including an introduction, principles of diagnosis and management, six sections (Sections 3 through 8) on the specific anxiety-related disorders (panic disorder, agoraphobia, specific phobia, social anxiety disorder, generalized anxiety disorder, obsessive-compulsive disorder, and posttraumatic stress disorder), and two additional sections on special populations (children/adolescents, pregnant/lactating women, and the elderly) and clinical issues in patients with comorbid conditions. Conclusions: Anxiety and related disorders are very common in clinical practice, and frequently comorbid with other psychiatric and medical conditions. Optimal management requires a good understanding of the efficacy and side effect profiles of pharmacological and psychological treatments. (PsycINFO Database Record (c) 2016 APA, all rights reserved) (journal abstract).

Katzman MA, Bleau P, et al. Canadian clinical practice guidelines for the management of anxiety, posttraumatic stress and obsessive-compulsive disorders. BMC Psychiatry. 2014;14 Suppl 1: S1.

BACKGROUND: Anxiety and related disorders are among the most common mental disorders, with lifetime prevalence reportedly as high as 31%. Unfortunately, anxiety disorders are underdiagnosed and under-treated. METHODS: These guidelines were developed by Canadian experts in anxiety and related disorders through a consensus process. Data on the epidemiology, diagnosis, and treatment (psychological and pharmacological) were obtained through MEDLINE, PsycINFO, and manual searches (1980-2012). Treatment strategies were rated on strength of evidence, and a clinical recommendation for each intervention was made, based on global impression of efficacy, effectiveness, and side effects, using a modified version of the periodic health examination guidelines. RESULTS: These guidelines are presented in 10 sections, including an introduction, principles of diagnosis and management, six sections (Sections 3 through 8) on the specific anxiety-related disorders (panic disorder, agoraphobia, specific phobia, social anxiety disorder, generalized anxiety disorder, obsessive-compulsive disorder, and posttraumatic stress disorder), and two additional sections on special populations (children/adolescents, pregnant/lactating women, and the elderly) and clinical issues in patients with comorbid conditions. CONCLUSIONS: Anxiety and related disorders are very common in clinical practice, and frequently comorbid with other psychiatric and medical conditions. Optimal management requires a good understanding of the efficacy and side effect profiles of pharmacological and psychological treatments.

Kesebir S, Isitmez S, et al. Compulsive buying in bipolar disorder: is it a comorbidity or a complication? J Affect Disord. 2012;136(3):797-802.

BACKGROUND: The objective of this study was to investigate the frequency of compulsive buying in bipolar disorder (BD), to compare it with healthy controls, and to search if there is a difference between bipolar cases with and without compulsive buying in terms of sociodemographic qualities, temperament, clinical characteristics and comorbid diagnoses. METHODS: One-hundred outpatient cases diagnosed as BD according to DSM-IV were evaluated consecutively. Following the diagnosis interview (SCID-I and II) the subjects completed the mood disorders registry form, Compulsive Buying Scale and TEMPS-A. RESULTS: Compulsive buying scores were higher in bipolar patients than healthy controls ($p<0.001$). Cases with compulsive buying revealed higher cyclothymic and irritable temperament scores than other bipolar patients ($p=0.029$ vs 0.045). Premenstrual syndrome and post-partum onset were more frequent, while psychotic symptoms were less in compulsive buyer bipolar patients ($p=0.002$, 0.009 vs 0.034). Severity of episode was lower ($p=0.01$), number of episodes was higher ($p=0.009$). Acute onset and remission before and after maintenance treatment were more frequent in patients with compulsive buying ($p=0.011$ and $p=0.011$). Full remission between episodes was 100%. Cases with axis-1 and axis-2 comorbidities demonstrated higher compulsive buying scores ($p=0.025$ and 0.005). LIMITATIONS: Treatment regimen differences between patients are a limitation of the study. CONCLUSIONS: This is the first study to relate compulsive buying with the clinical characteristics of BD. Our results reveal that compulsive buying in BD occurs together with mood episodes which are not very severe, but frequent and with abrupt onset.

Keuthen NJ, O'Sullivan RL, et al. The relationship of menstrual cycle and pregnancy to compulsive hairpulling. Psychother Psychosom. 1997;66(1):33-7.

BACKGROUND: Trichotillomania (TTM) or compulsive hairpulling is a cyclical disorder that presents predominantly in females. Anecdotal reports of symptom worsening in the premenstrual and during pregnancy led us to retrospectively study the role of these events in hairpulling behavior. METHODS: Questionnaires assessing demographics, current hairpulling behavior, and the reported effects of menstruation and pregnancy on urges, actual hairpulling and behavioral control were administered to clinic patients and volunteers at a hairpulling conference. The MGH Hairpulling Scale, Beck Depression Inventory and Beck Anxiety Inventory were also completed. Data from 59 hairpullers were analyzed. RESULTS: Premenstrual symptom exacerbation was reported for actual hairpulling urge intensity and frequency, and ability to control pulling and was alleviated during menstruation and shortly thereafter. The impact of pregnancy was less unidirectional, with both symptom exacerbation and lessening reported. CONCLUSIONS: The menstrual cycle appears to affect compulsive hairpulling and deserves recognition in both the assessment and treatment of this disorder. The impact of pregnancy on TTM is less clear.

Konuk N, Öztürk Ü, et al. Post-partum obsesif kompulsif bozukluk: Bir gözden geçirme. Klinik Psikofarmakoloji Bülteni / Bulletin of Clinical Psychopharmacology. 2007;17(3):142-6.

Post-partum period is a vulnerable period for development of psychiatric disorders. Despite large number of studies focusing on post-partum depression and psychosis, there are few other studies reporting that aggravation or even alleviation of anxiety disorders such as obsessive-compulsive disorder in this period. Therefore, the presence of obsessions and/or compulsions should be carefully evaluated among all patients in post-partum period. In this article, the epidemiology, etiology and clinical features of post-partum obsessive compulsive disorder are reviewed and management through cognitive behavioral therapy and pharmacotherapy in comparison with other obsessive-compulsive patients are evaluated based on previous literature. (PsycINFO Database Record (c) 2013 APA, all rights reserved) (journal abstract).

Kopyta I, Szwed-Bialozyt B, et al. [The analysis of the clinical symptoms and social conditionings of the tic disorder in children]. Wiad Lek. 2011;64(4):320-3.

A tic is a rapid, involuntary and stereotypical motor movement or vocalization. The exact cause of tic disorder is unknown, but it is well established that both genetic and environmental factors are involved. Tic occurrence in population was estimated on 5-100/10 000. AIM: The purpose of the research was to analyze the clinical symptoms and social conditionings of tic disorder in children. MATERIAL AND METHOD: The analysis was conducted on a group of 42 patients (8 girls, 34 boys) at the age of 3 to 15 years, admitted to Department of Neuropediatric of Medical University of Silesia to diagnose and treatment of tic disorder. The children's family history was analyzed. The patients were physically, neurological, radiologically and psychologically examined. RESULTS: The majority group were boys and the time of the symptoms appearance was an early school age. The tics were associated with emotional and anxiety disorders, compulsive behavior, psychological obsession. 9% of patients had family history of tic disorder. Pregnancy-birth history was complicated in 24% of cases. There were not abnormalities in physical, neurological and radiological examination in most cases. The majority group (83%) lives in the cities. The most parents have vocational training. CONCLUSION: In case of appearance of twitching during suspicious behavior of child, we need to carry out an inquiring research targeted to widely understated social issues.

Koran LM, Hanna GL, et al. Practice guideline for the treatment of patients with obsessive-compulsive disorder. Am J Psychiatry. 2007;164(7 Suppl):5-53.

Labad J, Menchon JM, et al. Female reproductive cycle and obsessive-compulsive disorder. J Clin Psychiatry. 2005;66(4):428-35; quiz 546.

BACKGROUND: The aim of our study was to assess whether there is a relationship between reproductive cycle events and the initiation or changes in symptoms of obsessive-compulsive disorder (OCD). METHOD: Forty-six female outpatients meeting DSM-IV criteria for OCD completed a semi structured interview at our OCD unit to assess the relationship between reproductive cycle events and OCD. Dates of data collection were from January 2001 to December 2003. RESULTS: In our sample, OCD onset occurred in the same year as menarche in 22% (N = 10), at pregnancy in 2% (N = 1), at post-partum in 7% (N = 3), and at menopause in 2% (N = 1). Worsening of preexisting OCD was reported by 20% of patients (9/45) at premenstrual, 8% (1/12) at pregnancy, 50% (6/12) at post-partum, and 8% (1/12) at menopause. The number of premenstrual mood symptoms, which included anxiety, irritability, mood lability and depressed mood, was associated with both premenstrual worsening of OCD (OR = 5.1, $p < .01$) and onset or worsening of OCD at post-partum (OR = 2.7, $p < .05$). Patients with an onset or worsening of OCD at post-partum also more frequently reported pre-menstrual worsening of OCD and previous history of major depressive disorder, including post-partum depression ($p <$ or =.05 for all). CONCLUSION: In a substantial number of patients, the onset or worsening of OCD was related to reproductive cycle events, especially at menarche and post-partum. Certain women with OCD seem to be vulnerable to worsening of OCD at different reproductive periods that imply hormonal fluctuations, and premenstrual and post-partum were the 2 reproductive events with a greater vulnerability. Those patients whose OCD symptoms appeared to be related to reproductive events also exhibited a greater history of mood symptoms (premenstrual depression and major depressive episodes).

Larden CN, Palmer ML, et al. Efficacy of therapeutic touch in treating pregnant inpatients who have a chemical dependency. Journal of holistic nursing: official journal of the American Holistic Nurses' Association. 2004;22:320-32. DOI: 10.1177/0898010104269242.

Chemical dependency is known to complicate about 3.8% of pregnancies in Vancouver, British Columbia, Canada. In this study, 54 English-speaking, hospitalized women were randomly assigned

to receive either (a) daily Therapeutic Touch over a 7-day period for 20 minutes each day, (b) shared activity with a registered nurse for 20 minutes over a 7-day period, or (c) standard ward care. Anxiety was measured using Spielberger's State-Trait Anxiety Inventory. Withdrawal symptoms were measured using a standardized Symptom Checklist. Anxiety scores were significantly less on Days 1, 2, and 3 ($p<.05$) for the group receiving Therapeutic Touch. Therapeutic Touch may be of value as an adjunctive measure in the treatment of chemical dependency among pregnant women.

Lieberman J. Evidence for a biological hypothesis of obsessive-compulsive disorder. Neuropsychobiology. 1984;11(1):14-21.

There is scant but provocative evidence to support the concept of a biological etiology in obsessive-compulsive disorder (OCD). This evidence includes the phenomenological similarities and associations with other major psychiatric disorders for which there is evidence of biologic etiologies; the genetic studies that show an increased familial occurrence of psychiatric illness including OCD and concordance for this disorder in monozygotic twins; biologic evidence and the historical association of OCD and CNS damage; the treatment response of OCD to antidepressant medication and possibly those medications that selectively modify serotonin neuronal activity and to selective anterior limbic leukotomy. This evidence and the evidence linking OCD to depressive illness are specifically reviewed and discussed.

Lipper S, Feigenbaum WM. Obsessive-compulsive neurosis after viewing the fetus during therapeutic abortion. Am J Psychother. 1976;30(4):666-74.

A case of obsessive-compulsive neurosis which developed in a young woman after she had viewed the fetus expelled during a therapeutic abortion with hypertonic saline is reported. The treatment, involving both psychodynamic psychotherapy and behavior therapy, illustrates the use and possible interaction of these therapies in the same patient.

Lochner C, Hemmings SM, et al. Corrigendum to gender in obsessive-compulsive disorder: clinical and genetic findings [Eur Neuropsychopharmacol. 2004;14:105-13]. Eur Neuropsychopharmacol. 2004;14(5):437-45.

BACKGROUND: There is increasing recognition that obsessive-compulsive disorder (OCD) is not a homogeneous entity. It has been suggested that gender may contribute to the clinical and biological heterogeneity of OCD. METHODS: Two hundred and twenty patients (n=220; 107 males, 113 female) with DSM-IV OCD (age: 36.40 +/- 13.46) underwent structured interviews. A subset of Caucasian subjects (n=178), including subjects from the genetically homogeneous Afrikaner population (n=81), and of matched control subjects (n=161), was genotyped for polymorphisms in genes involved in monoamine function. Clinical and genetic data were statistically analyzed across gender. RESULTS: Compared with females, males with OCD (1) had an earlier age of onset, and a trend toward having more tics and worse outcome, (2) had somewhat differing patterns of OCD symptomatology and axis I comorbidity, and (3) in the Caucasian group, were more likely to have the high activity T allele of the EcoRV variant of the monoamine oxidase A (MAO-A) gene compared to controls, and (4) in the Afrikaner subgroup, were more frequently homozygous for the G allele at the G861C variant of the 5HT1Dbeta gene than controls. Females with OCD (1) reported more sexual abuse during childhood than males, (2) often noted changes in obsessive-compulsive symptoms in the premenstrual/menstrual period as well as during/shortly after pregnancy, and with menopause, and (3) in the Caucasian subgroup, were more frequently homozygous for the low activity C allele of the EcoRV variant of the MAO-A gene compared to controls, with this allele also more frequent in female patients than controls. CONCLUSION: This study supports the hypothesis that gender contributes to the clinical and biological heterogeneity of OCD. A sexually dimorphic pattern of genetic susceptibility to OCD may be present. Further work is, however, needed to delineate the mechanisms that are responsible for mediating the effects of gender.

Lochner C, Seedat S, et al. Obsessive-compulsive disorder and trichotillomania: a phenomenological comparison. BMC Psychiatry. 2005;5:2.

BACKGROUND: Similarities between obsessive-compulsive disorder (OCD) and trichotillomania (TTM) have been widely recognized. Nevertheless, there is evidence of important differences between these two disorders. Some authors have conceptualized the disorders as lying on an OCD spectrum of conditions. METHODS: Two hundred and seventy-eight OCD patients (n = 278: 148 males; 130 female) and 54 TTM patients (n = 54; 5 males; 49 female) of all ages were interviewed. Female patients were compared on select demographic and clinical variables, including comorbid axis I and II disorders, and temperament/character profiles. RESULTS: OCD patients reported sig-

nificantly more lifetime disability, but fewer TTM patients reported response to treatment. OCD patients reported higher comorbidity, more harm avoidance and less novelty seeking, more maladaptive beliefs, and more sexual abuse. OCD and TTM symptoms were equally likely to worsen during menstruation, but OCD onset or worsening was more likely associated with pregnancy/puerperium. CONCLUSIONS: These findings support previous work demonstrating significant differences between OCD and TTM. The classification of TTM as an impulse control disorder is also problematic, and TTM may have more in common with conditions characterized by stereotypical self-injurious symptoms, such as skin-picking. Differences between OCD and TTM may reflect differences in underlying psychobiology and may necessitate contrasting treatment approaches.

Lochner C, Seedat S, et al. Obsessive-compulsive disorder and trichotillomania: A phenomenological comparison. BMC Psychiatry. 2005;5.

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Lochner C, Stein DJ. Gender in obsessive-compulsive disorder and obsessive-compulsive spectrum disorders. Archives of Women's Mental Health. 2001;4(1):19-26.

There is increasing recognition that obsessive-compulsive disorder (OCD) and putative OCD spectrum disorders (OCSDs) are not homogenous entities. A MEDLINE review of gender issues in OCD and putative OCD spectrum disorders was undertaken (1965-2000). These included demographic variables, clinical phenomenology, etiological factors, and treatment implications. OCD differs from other anxiety disorders in having an approximately equal male: female gender ratio. OCSDs may have an equal gender ratio, may be more common in women or may be more common in men. Etiological factors may differ across gender, an association between perinatal or early brain injury and OCD or Tourette's appears particularly important in males, while OCD and trichotillomania may also begin during pregnancy or shortly after childbirth with exacerbation of symptoms during menstruation. It is not clear that anti-androgens are effective in OCD, nor that gender predicts response to serotonin reuptake inhibitors in this disorder. There is a relative scarcity of literature addressing gender issues in OCD and putative OCSDs. That literature which does exist is not entirely conclusive but raises a few interesting questions for future research. (PsycINFO Database Record (c) 2012 APA, all rights reserved)

Lopez Laureen M, Tolley Elizabeth E, et al. Theory-based interventions for contraception. Cochrane Database of Systematic Reviews. 2013. DOI: 10.1002/14651858.CD007249.pub4.

Background: The explicit use of theory in research helps expand the knowledge base. Theories and models have been used extensively in HIV-prevention research and in interventions for preventing sexually transmitted infections (STIs). The health behavior field uses many theories or models of change. However, educational interventions addressing contraception often have no stated theoretical base. Objectives: Review randomized controlled trials (RCTs) that tested a theoretical approach to inform contraceptive choice; encourage contraceptive use; or promote adherence to, or continuation of, a contraceptive regimen. Search methods: Through June 2013, we searched computerized databases for trials that tested a theory-based intervention for improving contraceptive use (MEDLINE, POPLINE, CENTRAL, PsycINFO, ClinicalTrials.gov, and ICTRP). Previous searches also included EMBASE. For the initial review, we wrote to investigators to find other trials. Selection criteria: Trials tested a theory-based intervention for improving contraceptive use. We excluded trials

focused on high-risk groups and preventing sexually transmitted infections or HIV. Interventions addressed the use of one or more contraceptive methods for contraception. The reports provided evidence that the intervention was based on a specific theory or model. The primary outcomes were pregnancy, contraceptive choice or use, and contraceptive adherence or continuation. Data collection and analysis: The primary author evaluated abstracts for eligibility. Two authors extracted data from included studies. For the dichotomous outcomes, the Mantel-Haenszel odds ratio (OR) with 95% CI was calculated using a fixed-effect model. Cluster randomized trials used various methods of accounting for the clustering, such as multilevel modeling. Most reports did not provide information to calculate the effective sample size. Therefore, we presented the results as reported by the investigators. No meta-analysis was conducted due to differences in interventions and outcome measures. Main results: We included three new trials for a total of 17. Ten randomly assigned individuals and seven were cluster randomized. Eight trials showed some intervention effect. Two of 12 trials with pregnancy or birth data showed some effect. A theory-based group was less likely than the comparison group to have a second birth (OR 0.41; 95% CI 0.17 to 1.00) or to report a pregnancy (OR 0.24 (95% CI 0.10 to 0.56); OR 0.27 (95% CI 0.11 to 0.66)). The theoretical bases were social cognitive theory (SCT) and another social cognition model. Of 12 trials with data on contraceptive use (non-condom), six showed some effect. A theory-based group was more likely to consistently use oral contraceptives (OR 1.41; 95% CI 1.06 to 1.87), hormonal contraceptives (reported relative risk (RR) 1.30; 95% CI 1.06 to 1.58) or dual methods (reported RR 1.36; 95% CI 1.01 to 1.85); to use an effective contraceptive method (reported effect size 1.76; OR 2.04 (95% CI 1.47 to 2.83)) or use more habitual contraception (reported $P < 0.05$); and were less likely to use ineffective contraception (OR 0.56; 95% CI 0.31 to 0.98). Theories and models included the Health Belief Model (HBM), SCT, SCT plus another theory, other social cognition, and motivational interviewing (MI). For condom use, a theory-based group had favorable results in 5 of 11 trials. The main differences were reporting more consistent condom use (reported RR 1.57; 95% CI 1.28 to 1.94) and more condom use during last sex (reported results: risk ratio 1.47 (95% CI 1.12 to 1.93); effect size 1.68; OR 2.12 (95% CI 1.24 to 3.56); OR 1.45 (95% CI 1.03 to 2.03)). The theories were SCT, SCT plus another theory, and HBM. Nearly all trials provided multiple sessions or contacts. SCT provided the basis for seven trials focused on adolescents, of which five reported some effectiveness. Two others based on other social cognition models had favorable results with adolescents. Of six trials including adult women, five provided individual sessions. Some effect was seen in two using MI and one using the HBM. Two based on the Transtheoretical Model did not show any effect. Authors' conclusions: Eight trials provided evidence of high or moderate quality. Family planning researchers and practitioners could adapt the effective interventions, although most provided group sessions for adolescents. Three were conducted outside the USA. Clinics and low-resource settings need high-quality evidence on changing behavior. Thorough use of single theories would help in identifying what works, as would better reporting on research design and intervention implementation.

Malouf R, Grimley Evans J. Folic acid with or without vitamin B12 for the prevention and treatment of healthy elderly and demented people. Cochrane Database of Systematic Reviews. 2008. DOI: 10.1002/14651858.CD004514.pub2.

Background: Folate deficiency can result in congenital neural tube defects and megaloblastic anemia. Low folate levels may be due to insufficient dietary intake or inefficient absorption, but impaired metabolic utilization also occurs. Because B12 deficiency can produce a similar anemia to folate deficiency, there is a risk that folate supplementation can delay the diagnosis of B12 deficiency, which can cause irreversible neurological damage. Folic acid supplements may sometimes therefore include vitamin B12 supplements with simultaneous administration of vitamin B12.Lesser degrees of folate inadequacy are associated with high blood levels of the amino acid homocysteine which has been linked with the risk of arterial disease, dementia and Alzheimer's disease. There is therefore interest in whether dietary supplementation can improve cognitive function in the elderly. However, any apparent benefit from folic acid which was given in combination with B12 needs to be "corrected" for any effect of vitamin B12 alone. A separate Cochrane review of vitamin B12 and cognitive function has therefore been published. Objectives: To examine the effects of folic acid supplementation, with or without vitamin B12, on elderly healthy or demented people, in preventing cognitive impairment or retarding its progress. Search methods: Trials were identified from a search of the Cochrane Dementia and Cognitive Improvement Group's Specialized Register on 10 October 2007 using the terms: folic acid, folate, vitamin B9, leucovorin, methyltetrahydrofolate, vitamin B12, cobalamin and cyanocobalamin. This Register contains references from all major health care databases and many ongoing trials databases. In addition, MEDLINE, EMBASE, CINAHL, PsychINFO and LILACS were searched (years 2003-2007) for additional trials of folate with or without vitamin B12 on healthy elderly people. Selection criteria: All double-blind, placebo-controlled, randomized

trials, in which supplements of folic acid with or without vitamin B12 were compared with placebo for elderly healthy people or people with any type of dementia or cognitive impairment. Data collection and analysis: The reviewers independently applied the selection criteria and assessed study quality. One reviewer extracted and analyzed the data. In comparing intervention with placebo, weighted mean differences and standardized mean difference or odds ratios were estimated. Main results: Eight randomized controlled trials fulfilled the inclusion criteria for this review. Four trials enrolled healthy older people, and four recruited participants with mild to moderate cognitive impairment or dementia with or without diagnosed folate deficiency. Pooling the data was not possible owing to heterogeneity in sample selections, outcomes, trial duration, and dosage. Two studies involved a combination of folic acid and vitamin B12.There is no adequate evidence of benefit from folic acid supplementation with or without vitamin B12 on cognitive function and mood of unselected healthy elderly people. However, in one trial enrolling a selected group of healthy elderly people with high homocysteine levels, 800 mcg/day folic acid supplementation over three years was associated with significant benefit in terms of global functioning (WMD 0.05, 95% CI 0.004 to 0.096, P = 0.033); memory storage (WMD 0.14, 95% CI 0.04 to 0.24, P = 0.006) and information-processing speed (WMD 0.09, 95% CI 0.02 to 0.16, P = 0.016).Four trials involved people with cognitive impairment. In one pilot trial enrolling people with Alzheimer's disease, the overall response to cholinesterase inhibitors significantly improved with folic acid at a dose of 1mg/day (odds ratio: 4.06, 95% CI 1.22 to 13.53; P = 0.02) and there was a significant improvement in scores on the Instrumental Activities of Daily Living and the Social Behavior subscale of the Nurse's Observation Scale for Geriatric Patients (WMD 4.01, 95% CI 0.50 to 7.52, P = 0.02). Other trials involving people with cognitive impairment did not show any benefit in measures of cognitive function f om folic acid, with or without vitamin B12.Folic acid plus vitamin B12 was effective in reducing serum homocysteine concentrations (WMD -5.90, 95% CI -8.43 to -3.37, P < 0.00001). Folic acid was well tolerated, and no adverse effects were reported. Authors' conclusions: The small number of studies which have been done provide no consistent evidence either way that folic acid, with or without vitamin B12, has a beneficial effect on cognitive function of unselected healthy or cognitively impaired older people. In a preliminary study, folic acid was associated with improvement in the response of people with Alzheimer's disease to cholinesterase inhibitors. In another, long-term use appeared to improve the cognitive function of healthy older people with high homocysteine levels. More studies are needed on this important issue.

Man SC, Hung BH, et al. A pilot-controlled trial of a combination of dense cranial electroacupuncture stimulation and body acupuncture for post-stroke depression. BMC complementary and alternative medicine. 2014;14:255. DOI: 10.1186/1472-6882-14-255.

BACKGROUND: Our previous studies have demonstrated the treatment benefits of dense cranial electroacupuncture stimulation (DCEAS), a novel brain stimulation therapy in patients with major depression, post-partum depression and obsessive-compulsive disorder. The purpose of the present study was to further evaluate the effectiveness of DCEAS combined with body acupuncture and selective serotonin reuptake inhibitors (SSRIs) in patients with post-stroke depression (PSD). METHODS: In a single-blind, randomized controlled trial, 43 patients with PSD were randomly assigned to 12 sessions of DCEAS plus SSRI plus body electroacupuncture (n = 23), or sham (non-invasive cranial electroacupuncture, n-CEA) plus SSRI plus body electroacupuncture (n = 20) for 3 sessions per week over 4 weeks. Treatment outcomes were measured using the 17-item Hamilton Depression Rating Scale (HAMD-17), the Clinical Global Impression - Severity scale (CGI-S) and Barthel Index (BI), a measure used to evaluate movement ability associated with daily self-caring activity. RESULTS: DCEAS produced a significantly greater reduction of both HAMD-17 and CGI-S as early as week 1 and CGI-S at endpoint compared to n-CEA, but subjects of n-CEA group exhibited a significantly greater improvement on BI at week 4 than DCEAS. Incidence of adverse events was not different in the two groups. CONCLUSIONS: These results indicate that DCEAS could be effective in reducing stroke patients' depressive symptoms. Superficial electrical stimulation in n-CEA group may be beneficial in improving movement disability of stroke patients. A combination of DCEAS and body acupuncture can be considered a treatment option for neuropsychiatric sequelae of stroke. TRIAL REGISTRATION: http://www.clinicaltrials.gov, NCT01174394.

Man SC, Hung BHB, et al. A pilot-controlled trial of a combination of dense cranial electroacupuncture stimulation and body acupuncture for post-stroke depression. BMC complementary and alternative medicine. 2014;14. DOI: 10.1186/1472-6882-14-255.

Background: Our previous studies have demonstrated the treatment benefits of dense cranial electroacupuncture stimulation (DCEAS), a novel brain stimulation therapy in patients with major de-

pression, post-partum depression and obsessive-compulsive disorder. The purpose of the present study was to further evaluate the effectiveness of DCEAS combined with body acupuncture and selective serotonin reuptake inhibitors (SSRIs) in patients with post-stroke depression (PSD).Methods: In a single-blind, randomized controlled trial, 43 patients with PSD were randomly assigned to 12 sessions of DCEAS plus SSRI plus body electroacupuncture (n = 23), or sham (non-invasive cranial electroacupuncture, n-CEA) plus SSRI plus body electroacupuncture (n = 20) for 3 sessions per week over 4 weeks. Treatment outcomes were measured using the 17-item Hamilton Depression Rating Scale (HAMD-17), the Clinical Global Impression - Severity scale (CGI-S) and Barthel Index (BI), a measure used to evaluate movement ability associated with daily self-caring activity. Results: DCEAS produced a significantly greater reduction of both HAMD-17 and CGI-S as early as week 1 and CGI-S at endpoint compared to n-CEA, but subjects of n-CEA group exhibited a significantly greater improvement on BI at week 4 than DCEAS. Incidence of adverse events was not different in the two groups. Conclusions: These results indicate that DCEAS could be effective in reducing stroke patients' depressive symptoms. Superficial electrical stimulation in n-CEA group may be beneficial in improving movement disability of stroke patients. A combination of DCEAS and body acupuncture can be considered a treatment option for neuropsychiatric sequelae of stroke. Trial registration: http://www.clinicaltrials.gov, NCT01174394. 2014 Man et al.; licensee BioMed Central Ltd.

Marchesi C, Ossola P, et al. Clinical management of perinatal anxiety disorders: A systematic review. Journal of Affective Disorders. 2016;190:543-50.

Background: In the last few decades, there has been a growing interest in anxiety disorders (AnxD) in the perinatal period. Although AnxD are diagnosed in 4–39% of pregnant women and in up to 16% of women after delivery, evidence on their clinical management is limited. Methods: A systematic review was conducted on pharmacological and non-pharmacological treatment of AnxD in the perinatal period. Relevant papers published from January 1st, 2015 were identified searching the electronic databases MEDLINE, Embase, PsycINFO and the Cochrane Library. Results: 18 articles met inclusion criteria. Selected studies supported the use of cognitive-behavioral therapy (CBT) for obsessive–compulsive disorder (OCD), panic disorder (PD) and specific phobia both in pregnancy and post-partum. Selective serotonin reuptake inhibitors (SSRIs) led to significant OCD and PD improvement both in pregnancy and post-partum with no side effects for the babies. In the largest clinical sample to date, 65% of post-partum patients who entered the open-label trial of fluvoxamine (up to 300 mg/day) experienced a 30% or greater decrease in the total score of the Yale–Brown Obsessive– Compulsive Scale (Y-BOCS). During pregnancy, SSRIs and tricyclic antidepressants (TCAs) led to remission of panic symptoms and healthy outcomes for the babies. Limitations: Study design, mostly case reports, and enrolment of subjects mainly from outpatient specialty units might have limited community-wide generalizability. Conclusions: Keeping in mind the scantiness and heterogeneity of the available literature, the best interpretation of the available evidence appears to be that CBT should be the first treatment offered to pregnant and breastfeeding women with AnxD. However, SSRIs can represent a first line treatment strategy, and not exclusively in cases where AnxD is refractory to CBT. (PsycINFO Database Record (c) 2016 APA, all rights reserved) (journal abstract).

Masand PS, Gupta S. Selective serotonin-reuptake inhibitors: an update. Harv Rev Psychiatry. 1999;7(2):69-84.

Selective serotonin-reuptake inhibitors (SSRIs), including fluoxetine, sertraline, paroxetine, fluvoxamine, and citalopram, represent an important advance in the pharmacotherapy of mood and other disorders. They are chemically unrelated to tricyclic, heterocyclic, and other first-generation antidepressants. SSRIs are the treatment of choice for many indications, including major depression, dysthymia, panic disorder, obsessive-compulsive disorder, eating disorders, and premenstrual dysphoric disorder, because of their efficacy, good side-effect profile, tolerability, and safety in overdose, as well as patient compliance. A review of the literature was conducted using Medline and the terms "SSRIs," "fluoxetine," "sertraline," "paroxetine," "fluvoxamine," and "citalopram." Articles were limited to those published in English within the last 15 years. The search revealed that indications for antidepressants include unipolar depression, dysthymia, bipolar depression, treatment-resistant depression, depression in the medically ill, panic disorder, obsessive-compulsive disorder, eating disorders, social phobia, and premenstrual dysphoric disorder. One SSRI, fluoxetine, has demonstrated safety in pregnancy. Side effects of SSRIs include gastrointestinal disturbances, headache, sedation, insomnia, activation, weight gain, impaired memory, excessive perspiration, paresthesia, and sexual dysfunction.

Mavrogiorgou P, Illes F, et al. [Perinatal obsessive-compulsive disorder]. Fortschr Neurol Psychiatr. 2011;79(9):507-16.

A perinatal obsessive-compulsive disorder (OCD) is defined as an illness exhibiting first symptoms in the context of pregnancy and the postpartum period. There are no valid data up to date concerning the incidence of OCD, which might be of multifactorial origin, in this period in which females are highly vulnerable for psychiatric diseases. From a clinical point of view, obsessions and compulsions are mainly related to the well-being of the fetus or newborn baby. Differential diagnosis of perinatal OCD including pregnancy psychosis and post-partum depression is often difficult. Concerning treatment, non-pharmacological approaches should be preferred. Administration of SSRIs should be strongly restricted. However, there are no controlled therapy studies in patients with perinatal OCD. Furthermore, current knowledge about these patients is still limited. The aim of this review article is the presentation of phenomenology, pathogenesis, differential diagnosis and treatment of perinatal OCD. The mental situation of the female patients can be improved and stabilized if early diagnosis of a perinatal OCD leads to early initiation of an adequate therapy. This will then enable a good and stable mother-child relationship to develop.

Mavrogiorgou P, Illes F, et al. Perinatal Zwangsstörungen. Fortschritte der Neurologie, Psychiatrie. 2011;79(9):507-16.

A perinatal obsessive-compulsive disorder (OCD) is defined as an illness exhibiting first symptoms in the context of pregnancy and the postpartum period. There are no valid data up to date concerning the incidence of OCD, which might be of multifactorial origin, in this period in which females are highly vulnerable for psychiatric diseases. From a clinical point of view, obsessions and compulsions are mainly related to the well-being of the fetus or newborn baby. Differential diagnosis of perinatal OCD including pregnancy psychosis and post-partum depression is often difficult. Concerning treatment, non-pharmacological approaches should be preferred. Administration of SSRIs should be strongly restricted. However, there are no controlled therapy studies in patients with perinatal OCD. Furthermore, current knowledge about these patients is still limited. The aim of this review article is the presentation of phenomenology, pathogenesis, differential diagnosis and treatment of perinatal OCD. The mental situation of the female patients can be improved and stabilized if early diagnosis of a perinatal OCD leads to early initiation of an adequate therapy. This will then enable a good and stable mother-child relationship to develop. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract).

McCraw RK. Obsessive-compulsive disorder apparently related to abortion. Am J Psychother. 1989;43(2):269-76.

This case study presents a young woman who developed a severe obsessive-compulsive disorder after a routine medical procedure. It is suggested that this procedure brought back repressed guilt from three abortions and thus led to the onset of symptoms. The case is discussed in relationship to available research and theory.

PIP: Although most women experience no long-term significant psychopathology following an elective abortion, up to 5% exhibit severe psychiatric sequelae. Reported here is the case of a woman with an obsessive-compulsive disorder apparently related to abortions at ages 14 and 15 years of age. In her mid-20s, during her fourth marriage, the woman became convinced that she had been impregnated by a physician in the course of a pelvic exam and a proctosigmoidoscopy. At the time, she was obsessed that she would sabotage her marriage by becoming pregnant with a man other than her husband. The obsession later expanded to include a fear of contracting a sexually transmitted disease. In psychotherapy, the etiology of this disorder was linked to the patient's guilt and fear of punishment connected to her early abortions. The invasiveness of the sigmoidoscopy procedure triggered memories of these abortions and was subconsciously viewed as another pregnancy termination. A review of this woman's history revealed most of the factors considered to promote psychiatric problems after abortion, including young age, unmarried status, passivity, lack of social support, reservations about the abortions, parental pressure to abort, immaturity, and unstable relationships with the fathers. Counseling before and after abortion for women identified as having risk factors for emotional problems is recommended.

McDonough M, Kennedy N. Pharmacological management of obsessive-compulsive disorder: a review for clinicians. Harv Rev Psychiatry. 2002;10(3):127-37.

Obsessive-compulsive disorder (OCD) has been treated pharmacologically with drugs that enhance availability of the neurotransmitter serotonin. This review summarizes the available literature on

the pharmacological treatments of OCD. Numerous randomized controlled trials have attested to the efficacy of serotonin-reuptake inhibitors (SRIs) in treating this disorder, although a coherent model of serotonin dysfunction in OCD has not been established. Meta-analyses of randomized controlled trials have found better results with clomipramine than with other SRIs, but comparative studies have so far not replicated this finding. Aspects of the methodology in these studies that might explain this discrepancy are considered. Tolerability, side effects, dosing, and safety during pregnancy of the SRIs are discussed. Treatment of OCD with poor insight and of OCD comorbid with a tic disorder, augmentation strategies, and management of partial response to SRIs are reviewed. Finally, the available interventions for refractory OCD are considered.

McGuinness M, Blissett J, et al. OCD in the perinatal period: is post-partum OCD (ppOCD) a distinct subtype? A review of the literature. Behav Cogn Psychother. 2011;39(3):285-310.

BACKGROUND: It has been suggested that the perinatal period is a period of increased risk for the development and/or exacerbation of OCD and that post-partum OCD (ppOCD) presents a distinct clinical picture. This raises the possibility that ppOCD might be a distinct subtype of OCD. This review examines this contention. METHOD: A search using Ovid (Medline, PsycINFO and Embase), EBSCO, Cochrane Library, Web of Science (ISI), Pubmed databases and Google Scholar was carried out using the key words: "obsessive compulsive disorder" (and derivatives), "perinatal", "pregnancy", "postnatal", "post-partum", "mothers" (and derivatives), "anxiety disorders" and "subtypes." These articles and their references were reviewed. RESULTS: Most studies reviewed were retrospective, which makes it impossible to infer causality. Two prospective studies found a higher incidence of OCD in the post-partum period. These were carried out in Turkey and Brazil and, as such, may be limited in their applicability to other cultural groups. CONCLUSION: The concept of ppOCD as a specific subtype has not been robustly demonstrated. The evidence that OCD is more prevalent in the post-partum period is mixed. The evidence that OCD in the post-partum period presents a distinctive clinical picture with specific symptomatology and course is more compelling. In view of the impact of culture and religion on the expression of OCD, collaborative, international, prospective studies that consider the methodological and definitional issues raised in this review are necessary to provide clarification.

Meltzer-Brody S, Stuebe A. The long-term psychiatric and medical prognosis of perinatal mental illness. Best Pract Res Clin Obstet Gynaecol. 2014;28(1):49-60.

The perinatal period provides an important window into a woman's long-term health. Perinatal mental illness is a common condition conferring potential serious long-term psychiatric and medical consequences for the mother and family. It is known that childbirth acts as a powerful trigger for depressive episodes in some women, and that women with histories of a mood disorder are particularly vulnerable. Some evidence links perinatal mental illness with obstetrical complications and reduced lactation initiation and duration. Therefore, perinatal mental illness may be a marker for long-term risk and may contribute directly to subsequent cardiometabolic disease through both neuroendocrine mechanisms and the effects of mental illness on health behaviors. In clinical practice, these associations underscore the importance of screening and treating women with perinatal mental illness to ensure best possible long-term outcomes. Early screening and treatment may both mitigate the primary disease process and reduce the risk of comorbid medical conditions.

Merlino G, Lorenzut S, et al. Pharmacotherapy of restless legs syndrome with pramipexole. Clinical Medicine Insights: Therapeutics. 2010;2:407-15.

Restless Legs Syndrome (RLS) is one of the most common neurological diseases characterized by an urge to move the legs, often associated with unpleasant sensations relieved by movement. It is engendered by rest and is worse in the evening or at night. Patients affected by severe RLS should be treated pharmacologically. Dopamine-agonists represent the first-line treatment for RLS symptoms. Pramipexole is a non-ergot derived dopamine agonist with a high selectivity for D₂ and D₃ receptors. At doses comprised between 0.125 and 0.75 mg, pramipexole improves subjective symptoms and objective signs of primary RLS even after the first administration. In addition, pramipexole seems to be safe and well tolerated. However, physicians should be aware that augmentation and compulsive behaviors might occur in their RLS patients treated with pramipexole. Further studies are needed to confirm the efficacy of pramipexole in uremic RLS and in children affected by the sleep disorder. the author(s), publisher and licensee Libertas Academica Ltd.

Miller ES, Hoxha D, et al. The impact of perinatal depression on the evolution of anxiety and obsessive-compulsive symptoms. Arch Women's Mental Health. 2015;18(3):457-61.

We sought to examine the evolution of post-partum anxiety, obsessions and compulsions over time, and the influence of depression on their clinical course. This was a prospective cohort of obstetric patients enrolled at a tertiary care women's hospital. Women were recruited immediately post-partum and followed for 6 months. Women were screened for depression, state-trait anxiety, and obsessive-compulsive symptoms and dichotomized by the presence of depression. Four hundred sixty-one women agreed to participate in the study and completed the 2 weeks post-partum assessment; 331 (72 %) women completed the assessment at 6 months post-partum. At 2 weeks post-partum, 28 (19.9 %) women with depression had anxiety symptoms, compared to 4 (1.3 %) women who screened negative for depression ($p < 0.001$). Similarly, 36 (25.7 %) women with depression endorsed obsessions and compulsions compared to 19 (8.4 %) women without depression ($p < 0.001$). A significant interaction effect was present with anxiety over time such that by 6 months post-partum, there were no differences in symptoms in women with and without depression ($p = 0.860$). Conversely, the differences in obsessions and compulsions between depressed and non-depressed women persisted ($p = 0.017$). Women with post-partum depression are more likely to experience comorbid state-trait anxiety and obsessive-compulsive symptoms in the immediate post-partum period. While state-trait anxiety symptoms tend to resolve with time, obsessive-compulsive symptoms persist. Understanding these temporal trends is critical to tailor appropriate monitoring and treatment.

Millet B, Kochman F, et al. Phenomenological and comorbid features associated in obsessive-compulsive disorder: influence of age of onset. J Affect Disord. 2004;79(1-3):241-6.

BACKGROUND: To explore clinical features of symptoms and comorbidity according to the age of onset of patients suffering from obsessive-compulsive disorder (OCD). METHODS: The survey involved collecting data from both patient members of an OCD association, and a sample of 175 OCD patients seen in OCD specialty practice. All the patients (n=617) responded to a questionnaire on family and personal psychiatric OCD history, phenomenological features of OCD and comorbidity. They were classified according to OCD age at onset [group early age of onset (EO): under 15, group late age of onset (LO): older than 15]. RESULTS: A higher percentage of patients from Group LO complained of OCD triggering by factors such as professional difficulties and childbirth ($P<0.05$); also, they more often had ($P=0.05$) a sudden onset of symptoms. On the other hand, clinical features, such as superstition and magic thoughts, parasite obsessions and repeating, counting, hoarding, tapping/rubbing and collecting compulsions were significantly more frequent ($P<0.05$) in EO; likewise, history of tics was more frequent in this group. The existence of comorbid depression (at least one episode) did not show any significant difference between groups. However, depression preceding OCD was more frequent in LO. There was no significant difference in treatment response according to age of onset OCD. CONCLUSIONS: The results showed a clear association of EO with obsessions of superstition and parasites, repetitive compulsions and motor and vocal tics, whereas a sudden onset, triggering factors and a more frequent depression preceding OCD characterized LO.

Misri S, Milis L. Obsessive-compulsive disorder in the post-partum: open-label trial of quetiapine augmentation. J Clin Psychopharmacol. 2004;24(6):624-7.

OBJECTIVE: Post-partum nonpsychotic conditions are routinely treated with antidepressant therapy. However, a subset of this population with comorbid obsessive-compulsive disorder (OCD) is treatment resistant. Optimal response is obtained by augmentation therapy with novel antipsychotics. The objective of this open-label study was to evaluate clinical response to quetiapine augmentation of SSRIs or SNRIs in treatment-resistant OCD in the post-partum. METHODS: Twenty-two post-partum women diagnosed with OCD as per DSM-IV criteria, who did not respond to at least 8 weeks of SSRI or SNRI monotherapy, were offered a trial of quetiapine augmentation for 12 weeks. Response (defined as >50% reduction in scores) was assessed using the Yale Brown Obsessive-Compulsive Scale (YBOCS) and Clinical Global Impressions scale (CGI). RESULTS: Seventeen patients agreed to a trial of quetiapine augmentation. Three withdrew early due to side effects, and 14 completed the 12-week trial. Of these, 11 responded to treatment within 12 weeks, with a mean (SD) response time of 5.9 (2.6) weeks. The mean (SD) baseline YBOCS score of 24.7 (6.8) dropped to a mean of 10.3 (9.0), with a mean reduction of 59.6%. Mean CGI scores at outcome were 1.9 (1.2). The average dose of response was 112.5 mg (76.4 mg). Sedation was the most commonly reported side effect. CONCLUSIONS: Although limited by lack of controls, this is the first study in a post-partum population where the addition of quetiapine to antidepressant therapy has been shown to be effective for treatment-refractory OCD. Quetiapine deserves further controlled study in this context.

Misri S, Reebye P, et al. The use of paroxetine and cognitive-behavioral therapy in post-partum depression and anxiety: a randomized controlled trial. The Journal of clinical psychiatry. 2204;65:1236-41.

BACKGROUND: Approximately 10% to 16% of women experience a major depressive episode after childbirth. A significant proportion of these women also suffer from comorbid anxiety disorders. The purpose of this study was to evaluate whether the addition of cognitive-behavioral therapy (CBT) to standard antidepressant therapy offers additional benefits in the treatment of post-partum depression with comorbid anxiety disorders. METHOD: Thirty-five women referred to a tertiary care hospital outpatient program with a DSM-IV diagnosis of post-partum depression with comorbid anxiety disorder were randomly assigned to 1 of 2 treatment groups-paroxetine-only monotherapy group (N = 16) or paroxetine plus 12 sessions of CBT combination therapy group (N = 19)-for a 12-week trial. Progress was monitored by a psychiatrist blinded to treatment group, using the Hamilton Rating Scale for Depression, Hamilton Rating Scale for Anxiety, Yale-Brown Obsessive-Compulsive Scale, Clinical Global Impressions scale, and Edinburgh Postnatal Depression Scale. Data were analyzed using 2-tailed statistical tests at an alpha level of.05. The study was conducted from April 1, 2002, to June 30, 2003. RESULTS: Both treatment groups showed a highly significant improvement ($p < .01$) in mood and anxiety symptoms. Groups did not differ significantly in week of recovery, dose of paroxetine at remission, or measures of depression, anxiety, and obsessive-compulsive symptoms at outcome. CONCLUSION: Antidepressant monotherapy and combination therapy with antidepressants and CBT were both efficacious in reducing depression and anxiety symptoms. However, in this sample of acutely depressed/anxious post-partum women, there were no additional benefits from combining the 2 treatment modalities. Further research into the efficacy of combination therapy in the treatment of moderate-to-severe depression with comorbid disorders in post-partum women is recommended.

Moore Elizabeth R, Anderson Gene C, et al. Early skin-to-skin contact for mothers and their healthy newborn infants. Cochrane Database of Systematic Reviews. 2012. DOI: 10.1002/14651858.CD003519.pub3.

Background: Mother-infant separation post birth is common in Western culture. Early skin-to-skin contact (SSC) begins ideally at birth and involves placing the naked baby, head covered with a dry cap and a warm blanket across the back, prone on the mother's bare chest. According to mammalian neuroscience, the intimate contact inherent in this place (habitat) evokes neurobehaviors ensuring fulfillment of basic biological needs. This time may represent a psychophysiological 'sensitive period' for programming future physiology and behavior. Objectives: To assess the effects of early SSC on breastfeeding, physiological adaptation, and behavior in healthy mother-newborn dyads. Search methods: We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (30 November 2011), made personal contact with trialists, and consulted the bibliography on kangaroo mother care (KMC) maintained by Dr. Susan Ludington. Selection criteria: Randomized controlled trials comparing early SSC with usual hospital care. Data collection and analysis: We independently assessed trial quality and extracted data. Study authors were contacted for additional information. Main results: Thirty-four randomized controlled trials were included involving 2177 participants (mother-infant dyads). Data from more than two trials were available for only eight outcome measures. For primary outcomes, we found a statistically significant positive effect of early SSC on breastfeeding at one to four months post birth (13 trials; 702 participants) (risk ratio (RR) 1.27, 95% confidence interval (CI) 1.06 to 1.53, and SSC increased breastfeeding duration (seven trials; 324 participants) (mean difference (MD) 42.55 days, 95% CI -1.69 to 86.79) but the results did not quite reach statistical significance ($P = 0.06$). Late preterm infants had better cardio-respiratory stability with early SSC (one trial; 31 participants) (MD 2.88, 95% CI 0.53 to 5.23). Blood glucose 75 to 90 minutes following the birth was significantly higher in SSC infants (two trials, 94 infants) (MD 10.56 mg/dL, 95% CI 8.40 to 12.72). The overall methodological quality of trials was mixed, and there was high heterogeneity for some outcomes. Authors' conclusions: Limitations included methodological quality, variations in intervention implementation, and outcomes. The intervention appears to benefit breastfeeding outcomes, and cardio-respiratory stability and decrease infant crying, and has no apparent short- or long-term negative effects. Further investigation is recommended. To facilitate meta-analysis, future research should be done using outcome measures consistent with those in the studies included here. Published reports should clearly indicate if the intervention was SSC with time of initiation and duration and include means, standard deviations and exact probability values.

Munhoz C. Um par analítico e uma gravidez prenhe de sentidos. Percurso Revista de Psicanálise. 2004;17(33):67-74.

A particularly intense series of sessions during an analytic treatment leads to questions about how psychoanalysis and psychiatry relate differently to obsessional compulsive organizations. A male patient's relation to his mother proves decisive to establish an analytic perspective upon a classic syndrome also described by psychiatrists. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract).

Namouz-Haddad S, Nulman I. Safety of treatment of obsessive-compulsive disorder in pregnancy and puerperium. Can Fam Physician. 2014;60(2):133-6.

QUESTION: My patient is 3 weeks post-partum and has experienced repetitive checking and washing of her newborn as a result of obsessive concerns with the newborn's safety. Should I refer her for a psychiatric assessment to rule out obsessive compulsive disorder (OCD) or should I reassure her that her behavior is normal? ANSWER: Current data suggest that pregnancy and the post-partum period are times of high risk of OCD onset and exacerbation. The presenting symptoms of OCD overlap with normal concerns and behavior during the perinatal period; however, an undiagnosed or untreated disorder could have adverse consequences for both the mother and her newborn. Therefore, it is strongly recommended that this patient undergo screening and psychiatric assessment in order to be appropriately managed.

O'Kearney Richard T, Anstey K, et al. Behavioral and cognitive behavioral therapy for obsessive compulsive disorder in children and adolescents. Cochrane Database of Systematic Reviews. 2006. DOI: 10.1002/14651858.CD004856.pub2.

Background: This is an update of a Cochrane Review first published in The Cochrane Library in Issue 4, 2006.Obsessive-compulsive disorder (OCD) in children and adolescents is characterized by persistent intrusive thoughts, inappropriate impulses or images which cause marked anxiety, and/or by persistent repetitive behaviors such as hand washing, checking and ordering. Along with antidepressant medication, behavioral or cognitive-behavioral therapy (BT/CBT) is recommended as the treatment of choice for pediatric obsessive-compulsive disorder (OCD).Objectives: This review examines the overall efficacy of BT/CBT for pediatric OCD, its relative efficacy against medication and whether there are benefits in using BT/CBT combined with medication. Search methods: We searched CCDANCTR-Studies, CCDANCTR-References (16/3/2009), MEDLINE, EMBASE, PsycINFO, national trials registers, reference lists of all selected studies and hand searched journals related to cognitive behavioral treatment of OCD. Selection criteria: Included studies were randomized or quasi-randomized controlled trials with participants 18 years of age or younger with a diagnosis of OCD, established by clinical assessment or standardized diagnostic interview. Reviewed studies included standard behavioral or cognitive-behavioral techniques, either alone or in combination, compared with waitlist, attention placebo, pill placebo or medication. Data collection and analysis: The quality of selected studies was assessed independently by two review authors. Using Review Manager software, weighted mean differences were calculated for the total severity of OCD symptoms at post treatment and relative risks for having OCD at post treatment. Main results: Eight studies with 343 participants were included. The review found evidence for lower post-treatment OCD severity and reduced risk of continuing with OCD for the BT/CBT group compared to pill placebo or wait-list comparisons. There was no evidence found that the efficacy of BT/CBT alone and medication alone differ in terms of post treatment symptom severity or in the risk of having OCD. There was some evidence of a benefit for combined BT/CBT and medication compared to medication alone but not relative to BT/CBT alone. The low rates of drop out suggested BT/CBT is an acceptable treatment to child and adolescent patients and their families. Authors' conclusions: Although only based on a small number of studies which vary in quality, behavioral or cognitive-behavior therapy alone appears to be an effective treatment for OCD in children and adolescents. It is as effective as medication alone and may lead to better outcomes when combined with medication compared to medication alone. Additional higher quality trials are needed to confirm these findings.

Olthuis Janine V, Watt Margo C, et al. Therapist-supported Internet cognitive behavioral therapy for anxiety disorders in adults. Cochrane Database of Systematic Reviews. 2016. DOI: 10.1002/14651858.CD011565.pub2.

Background: Cognitive behavioral therapy (CBT) is an evidence-based treatment for anxiety disorders. Many people have difficulty accessing treatment, due to a variety of obstacles. Researchers have therefore explored the possibility of using the Internet to deliver CBT; it is important to ensure

the decision to promote such treatment is grounded in high quality evidence. Objectives: To assess the effects of therapist-supported Internet CBT (ICBT) on remission of anxiety disorder diagnosis and reduction of anxiety symptoms in adults as compared to waiting list control, unguided CBT, or face-to-face CBT. Effects of treatment on quality of life and patient satisfaction with the intervention were also assessed. Search methods: We searched the Cochrane Depression, Anxiety and Neurosis Review Group Specialized Register (CCDANCTR) to 16 March 2015. The CCDANCTR includes relevant randomized controlled trials from MEDLINE, EMBASE, PsycINFO and CENTRAL. We also searched online clinical trial registries and reference lists of included studies. We contacted authors to locate additional trials. Selection criteria: Each identified study was independently assessed for inclusion by two authors. To be included, studies had to be randomized controlled trials of therapist supported ICBT compared to a waiting list, attention, information, or online discussion group; unguided CBT (that is, self-help); or face-to-face CBT. We included studies that treated adults with an anxiety disorder (panic disorder, agoraphobia, social phobia, post-traumatic stress disorder, acute stress disorder, generalized anxiety disorder, obsessive compulsive disorder, and specific phobia) defined according to the Diagnostic and Statistical Manual of Mental Disorders III, III-R, IV, IV-TR or the International Classification of Diseases 9 or 10.Data collection and analysis: Two authors independently assessed the risk of bias of included studies and judged overall study quality. We used data from intention-to-treat analyses wherever possible. We assessed treatment effect for the dichotomous outcome of clinically important improvement in anxiety using a risk ratio (RR) with 95% confidence interval (CI). For disorder-specific and general anxiety symptom measures and quality of life we assessed continuous scores using standardized mean differences (SMD). We examined statistical heterogeneity using the I2 statistic. Main results: We screened 1736 citations and selected 38 studies (3214 participants) for inclusion. The studies examined social phobia (11 trials), panic disorder with or without agoraphobia (8 trials), generalized anxiety disorder (5 trials), post-traumatic stress disorder (2 trials), obsessive compulsive disorder (2 trials), and specific phobia (2 trials). Eight remaining studies included a range of anxiety disorder diagnoses. Studies were conducted in Sweden (18 trials), Australia (14 trials), Switzerland (3 trials), the Netherlands (2 trials), and the USA (1 trial) and investigated a variety of ICBT protocols. Three primary comparisons were identified, therapist-supported ICBT versus waiting list control, therapist-supported versus unguided ICBT, and therapist-supported ICBT versus face-to-face CBT. Low quality evidence from 11 studies (866 participants) contributed to a pooled risk ratio (RR) of 3.75 (95% CI 2.51 to 5.60; I2 = 50%) for clinically important improvement in anxiety at post-treatment, favoring therapist-supported ICBT over a waiting list, attention, information, or online discussion group only. The SMD for disorder-specific symptoms at post-treatment (28 studies, 2147 participants; SMD -1.06, 95% CI -1.29 to -0.82; I2 = 83%) and general anxiety symptoms at post-treatment (19 studies, 1496 participants; SMD -0.75, 95% CI -0.98 to -0.52; I2 = 78%) favored therapist-supported ICBT; the quality of the evidence for both outcomes was low. One study compared unguided CBT to therapist supported ICBT for clinically important improvement in anxiety at post-treatment, showing no difference in outcome between treatments (54 participants; very low-quality evidence). At post-treatment there were no clear differences between unguided CBT and therapist-supported ICBT for disorder-specific anxiety symptoms (5 studies, 312 participants; SMD -0.22, 95% CI -0.56 to 0.13; I2 = 58%; very low quality evidence) or general anxiety symptoms (2 studies, 138 participants; SMD 0.28, 95% CI -2.21 to 2.78; I2 = 0%; very low quality evidence).Compared to face-to-face CBT, therapist-supported ICBT showed no significant differences in clinically important improvement in anxiety at post-treatment (4 studies, 365 participants; RR 1.09, 95% CI 0.89 to 1.34; I2 = 0%; low quality evidence). There were also no clear differences between face-to-face and therapist supported ICBT for disorder-specific anxiety symptoms at post-treatment (7 studies, 450 participants; SMD 0.06, 95% CI -0.25 to 0.37; I2 = 60%; low quality evidence) or general anxiety symptoms at post-treatment (5 studies, 317 participants; SMD 0.17, 95% CI -0.35 to 0.69; I2 = 78%; low quality evidence).Overall, risk of bias in included studies was low or unclear for most domains. However, due to the nature of psychosocial intervention trials, blinding of participants and personnel, and outcome assessment tended to have a high risk of bias. Heterogeneity across several the meta-analyses was substantial, some was explained by type of anxiety disorder or may be meta-analytic measurement artefact due to combining many assessment measures. Adverse events were rarely reported. Authors' conclusions: Therapist-supported ICBT appears to be an efficacious treatment for anxiety in adults. The evidence comparing therapist-supported ICBT to waiting list, attention, information, or online discussion group only control was low to moderate quality, the evidence comparing therapist-supported ICBT to unguided ICBT was very low quality, and comparisons of therapist-supported ICBT to face-to-face CBT were low quality. Further research is needed to better define and measure any potential harms resulting from treatment. These findings suggest that therapist-supported ICBT is more efficacious than a waiting list, attention, information, or

online discussion group only control, and that there may not be a significant difference in outcome between unguided CBT and therapist-supported ICBT; however, this latter finding must be interpreted with caution due to imprecision. The evidence suggests that therapist supported ICBT may not be significantly different from face-to-face CBT in reducing anxiety. Future research should explore heterogeneity among studies which is reducing the quality of the evidence body, involve equivalence trials comparing ICBT and face-to-face CBT, examine the importance of the role of the therapist in ICBT, and include effectiveness trials of ICBT in real-world settings. A timely update to this review is needed given the fast pace of this area of research.

O'Neill MT, Davis JM, et al. Pharmacotherapy. Handbook of comparative interventions for adult disorders (2nd ed.). John Wiley & Sons Inc, Hoboken, NJ; 1999; p. 378-413.

In this chapter, the authors provide a comprehensive review of the available pharmacotherapy options for obsessive-compulsive disorder (OCD). Topics addressed in the chapter include diagnosis and clinical features; epidemiology, course, and genetics; overview of treatment (clomipramine, selective serotonin reuptake inhibitors, other agents); augmentation (serotonergic agents, dopaminergic agents); maintenance treatment and discontinuation studies; refractory OCD; neurosurgery; experimental agents and somatic treatments; obsessive compulsive spectrum disorders (trichotillomania, body dysmorphic disorder); special populations (children and adolescents, pregnancy and puerperium, developmentally disabled, elderly and neurologically impaired); and OCD and managed care. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (chapter)

Ori R, Amos T, et al. Augmentation of cognitive and behavioral therapies (CBT) with d-cycloserine for anxiety and related disorders. Cochrane Database of Systematic Reviews. 2015. DOI: 10.1002/14651858.CD007803.pub2.

Background: A significant number of patients who suffer with anxiety and related disorders (that is post-traumatic stress disorder (PTSD), social anxiety disorder (SAnD), panic disorder with or without agoraphobia (PD), specific phobia (SPh) and obsessive compulsive disorder (OCD)) fail to respond optimally to first-line treatment with medication or cognitive and behavioral therapies. The addition of d-cycloserine (DCS) to cognitive and behavioral therapies may improve treatment response by impacting the glutamatergic system. This systematic review aimed to investigate the effects of adding DCS to cognitive and behavioral therapies by synthesizing data from relevant randomized controlled trials and following the guidelines recommended by Cochrane. Objectives: To assess the effect of DCS augmentation of cognitive and behavioral therapies compared to placebo augmentation of cognitive and behavioral therapies in the treatment of anxiety and related disorders. Additionally, to assess the efficacy and tolerability of DCS across different anxiety and related disorders. Search methods: This review fully incorporates studies identified from a search of the Cochrane Depression, Anxiety and Neurosis Controlled Trials Register (CCDANCTR) to 12 March 2015. This register includes relevant randomized controlled trials (RCTs) from: the Cochrane Library (all years), EMBASE (1974 to date), MEDLINE (1950 to date), PsycINFO (1967 to date), the World Health Organization? s trials portal (ICTRP) and ClinicalTrials.gov. Reference lists from previous meta-analyses and reports of RCTs were also checked. No restrictions were placed on language, setting, date or publication status. Selection criteria: All RCTs of DCS augmentation of cognitive and behavioral therapies versus placebo augmentation of cognitive and behavioral therapies for anxiety and related disorders were included. Data collection and analysis: Two authors (RO and TA) independently assessed RCTs for eligibility and inclusion, extracted outcomes and risk of bias data and entered these into a customized extraction form. Investigators were contacted to obtain missing data. In addition, data entry and analysis were performed by two review authors (KSW and HB). Main results: Twenty-one published RCTs, with 788 participants in outpatient settings, were included in the review. Sixteen studies had an age range of 18 to 75 years, while four investigated pediatric populations aged 8 to 17 years and one included children, adolescents and adults. The 21 RCTs investigated OCD (number of RCTs (N) = 6), PTSD (N = 5), SAnD (N = 5), SPh (N = 3) and PD (N = 2). Most information from the studies was rated as having either low risk or unclear risk of bias. There was no evidence of a difference between DCS augmentation of cognitive and behavioral therapies and placebo augmentation of cognitive and behavioral therapies for the treatment of anxiety and related disorders in adults at the endpoint (treatment responders, N = 9, risk ratio (RR) 1.10; 95% confidence interval (CI) 0.89 to 1.34; number of participants (n) = 449; low quality evidence) and between 1 and 12 months follow-up (N = 7, RR 1.08; 95% CI 0.90 to 1.31; n = 383). DCS augmentation of cognitive and behavioral therapies was not superior to placebo augmentation of cognitive and behavioral therapies for children and adolescents, both at the endpoint (N = 4, RR 1.01; 95% CI 0.78 to 1.31; n = 121; low quality evidence) and between 3 and 12 months follow-up (N = 3, RR 0.86; 95% CI 0.67 to 1.09; n = 91).There was no evidence of a difference in treatment

acceptability for DCS augmentation of cognitive and behavioral therapies compared with placebo augmentation of cognitive and behavioral therapies in adults (N = 16, RR 0.88; 95% CI 0.61 to 1.25; n = 740), nor in children and adolescents (N = 4, RR 0.90; 95% CI 0.17 to 4.69; n = 131). These conclusions were based on moderate quality evidence for adults, and very low-quality evidence for children and adolescents. Although the observed difference was small, it is noteworthy that there was a high efficacy of exposure-based therapies alone in the included trials. Due to the limited number of studies, subgroup analysis of moderating factors for clinical and methodological effect could not take place. Authors' conclusions: This review found no evidence of a difference between DCS augmentation of cognitive and behavioral therapies and placebo augmentation of cognitive and behavioral therapies for treating anxiety and related disorders in children, adolescents and adults. These findings are based on low quality evidence from heterogenous studies with small sample sizes and incomplete data for clinical response, which precludes us from drawing conclusions on the use of DCS augmentation of cognitive and behavioral therapies at this stage. Given there is some promising preliminary data from individual studies, further research is necessary to assess DCS compared with placebo augmentation of cognitive and behavioral therapies and determine mechanisms of action as well as magnitude of effect in anxiety and related disorders.

Pani Pier P, Trogu R, et al. Antidepressants for cocaine dependence and problematic cocaine use. Cochrane Database of Systematic Reviews. 2011. DOI: 10.1002/14651858.CD002950.pub3.

Background: Cocaine dependence is a disorder for which no pharmacological treatment of proven efficacy exists, advances in the neurobiology could guide future medication development. Objectives: To investigate the efficacy and acceptability of antidepressants alone or in combination with any psychosocial intervention for the treatment of cocaine dependence and problematic cocaine use. Search methods: We searched the Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, EMBASE and CINAHL in July 2011 and researchers for unpublished trials. Selection criteria: Randomized clinical trials comparing antidepressants alone or associated with psychosocial intervention with placebo, no treatment, other pharmacological or psychosocial interventions. Data collection and analysis: Two authors independently assessed trial quality and extracted information. Main results: 37 studies were included in the review (3551 participants). Antidepressants versus placebo: results for dropouts did not show evidence of difference, 31 studies, 2819 participants, RR 1.03 (Cl 95% 0.93 to 1.14). Looking at Abstinence from cocaine use, even though not statistically significant, the difference shown by the analysis in the three-weeks abstinence rate was in favour of antidepressants (eight studies, 942 participants, RR 1.22 (Cl 95% 0.99 to 1.51)). Considering only studies involving tricyclics, five studies, 367 participants, or only desipramine, four studies, 254 participants, the evidence was in favour of antidepressants. However, selecting only studies with operationally defined diagnostic criteria, statistical significance favouring antidepressants, as well as the trend for significance shown by the full sample, disappeared. Looking at safety issues, the results did not show evidence of differences (number of patients withdrawn for medical reasons, thirteen studies, 1396 participants, RR 1.39 (Cl 95% 0.91 to 2.12)). Subgroup analysis considering length of the trial, associated opioid dependence or associated psychosocial interventions as confounding factors, failed in showing consistent and statistically significant differences in favour of antidepressants. Antidepressants versus other drugs: Comparing antidepressants with dopamine agonists or with anticonvulsants, no evidence of differences was shown on dropouts and on other outcomes (abstinence from cocaine use, adverse events).Authors' conclusions: At the current stage of evidence data do not support the efficacy of antidepressants in the treatment of cocaine abuse/dependence. Partially positive results obtained on secondary outcome measures, such as depression severity, do not seem to be associated with an effect on direct indicators of cocaine abuse/dependence. Antidepressants cannot be considered a mainstay of treatment for unselected cocaine abusers/dependents.

Pelle G. Il Disturbo Obssesivo-Compulsivo nel periodo perinatale: Prevalenza, fenomenologia, eziologia e trattamento. Psicoterapia Cognitiva e Comportamentale. 2014;20(2):161-74.

This work aims to synthesize existing literature on the prevalence, phenomenology, etiology and treatment of perinatal Obsessive-Compulsive Disorder. Even though data on prevalence rates are inconsistent, given the high variability in methodologies used in the various studies, the general pattern of these findings raises the possibility of increased vulnerability to Obsessive-Compulsive Disorder during the perinatal period. More consistent are findings regarding symptom profiles: during pregnancy contamination obsessions regarding the fetus and washing/cleaning compulsions predominate; whereas in the post-partum period obsessional thoughts concerning harming the infant accompanied by avoidance of the infant and checking behaviors predominate. A discussion of widely accepted etiological models is also provided. Although preliminary, data on the

effectiveness of medications and cognitive-behavioral therapy are described. Finally, attention is paid to strategies for screening and diagnosis, the identification of risk factors and the development and implementation of specific prevention programs. (PsycINFO Database Record (c) 2014 APA, all rights reserved) (journal abstract).

Penzel F. Obsessive-compulsive disorders: A complete guide to getting well and staying well, Oxford University Press, New York, NY; 2000.

Discusses the spectrum of obsessive-compulsive disorders (OCDs), from the classic form characterized by the intrusive, repetitive, and often unpleasant thoughts, to body dysmorphic disorder ("imagined ugliness"), trichotillomania (compulsive hair pulling), compulsive skin picking, and nail biting. The author takes the reader through each step of the most effective behavioral therapies, detailing how progress is made and how to avoid relapse. He also offers a discussion of medication—how medication is used as part of the overall treatment, its effect on pregnancy, how to choose the best medicine, and how to know if it is working. Also, the author discusses the treatment of children with these disorders, offers advice for the families of sufferers, and lists sources of help and information (including the latest sites on the Internet). The book includes an appendix that features symptom checklists for each of the OC spectrum disorders, the Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) diagnostic descriptions, a reading list, and a glossary.(jacket) This book takes the view that classic OCD itself is only a part of a family of neurobiological disorders, ranging from symptoms of compulsiveness at one end of the scale, to disorders of impulse control at the other. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (introduction)

Quirk KC, Einarson TR. Sexual dysfunction and clomipramine. Can J Psychiatry. 1982;27(3):228-31.

Three cases of orgasmic inhibition by clomipramine are reported, one in a male and two in females. All were depressed patients with obsessive-compulsive features. Orgasmic dysfunction manifested shortly after beginning clomipramine therapy despite a return of libido as the depression lifted. Two of these patients switched to desipramine which led to a resolution of sexual dysfunction while maintaining the patient's depression free. The third patient manipulated dosage times to diminish the orgasmic problem. Strong anticholinergic and/or anti-adrenergic properties of clomipramine are suspected to underlie the development of this problem.

Rabinowitz I, Baruch Y, et al. High-dose escitalopram for the treatment of obsessive-compulsive disorder. Int Clin Psychopharmacol. 2008;23(1):49-53.

The aim of this study was to evaluate the efficacy and tolerability of high-dose escitalopram in patients suffering from obsessive-compulsive disorder (OCD). In an open-label, 16-week prospective study, patients with OCD received escitalopram at a dose of 20 mg/day for 3 weeks, after a 1-week titration at 10 mg/day. Patients who did not achieve a > or =25% reduction from baseline in the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) score during these 4 weeks were continued on higher doses of escitalopram (maximum 50 mg/day) for 12 weeks. The primary efficacy measure of OCD symptoms was change from baseline in the Y-BOCS score. Overall, 67 patients (33 women, 34 men) with a mean Y-BOCS score of 29.6 entered the study. After 4 weeks of standard-dose escitalopram treatment, one patient discontinued owing to pregnancy, and two patients achieved a reduction in Y-BOCS > or =25%. Consequently, 64 patients were eligible to receive high-dose escitalopram (mean dose, 33.8 mg/day at endpoint). At endpoint, high-dose escitalopram had significantly improved the OCD symptoms (Y-BOCS score) and all the other efficacy measures (P<0.001), compared with baseline. Escitalopram was also well tolerated, with no discontinuations during the 12-week high-dose phase. The only reported adverse drug reactions were dry mouth (n=8, 12.1%) and decreased sexual desire (n=21, 31.8%). Preliminary investigation shows that high-dose escitalopram is an efficacious and well tolerated treatment for patients suffering from severe OCD. Randomized, blinded studies are needed to reinforce these findings.

Ray PC, Tas DA, et al. Periodic fever and hyperimmunoglobulin D syndrome in a boy with pediatric autoimmune neuropsychiatric disorders associated with group A - -hemolytic streptococcus. Journal of Child and Adolescent Psychopharmacology. 2013;23(4):302-4.

Present a case report with concurrent hyperimmunoglobulin D syndrome (HIDS) and obsessive-compulsive disorder (OCD) comorbid with attention-deficit/hyperactivity disorder (ADHD) combined type, speech disorder (stuttering), and Tourette's disorder (TD). The patient was born prematurely following 28 weeks of gestation because of early membrane rupture; he weighed 750 g and was hospitalized for 1.5 months. During the mental status examination, the patient seemed younger than 9 years old, and was small for his age. There were no dysmorphic features. Eye contact was

normal, but he exhibited avoidant behaviors. In the rheumatology-immunology department, the patient was also given the diagnosis of HIDS because of fever associated with chills, sore throat, cervical lymphadenopathy, abdominal pain and mevalonate kinase (MVK) gene mutation. Sertraline 25 mg/day was started then titrated up to 50 mg/day to treat obsessive-compulsive symptoms. After 2 months of sertraline treatment the patient's compulsive cleaning, checking, and sniffing symptoms partially decreased. In addition, although there was no severe recurrence of OCD symptoms, checking and cleaning compulsions and motor tics were observed more severely after the fever attacks, and there were subthreshold cleaning obsessions at 8-month follow-up. The presented case highlights that the similar pathophysiologic mechanisms for pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) and HIDS may have substantial overlap. (PsycINFO Database Record (c) 2013 APA, all rights reserved)

Rees JC. Obsessive-compulsive disorder and gut microbiota dysregulation. Med Hypotheses. 2014;82(2):163-6.

Obsessive-compulsive disorder (OCD) is a debilitating disorder for which the cause is not known, and treatment options are modestly beneficial. A hypothesis is presented wherein the root cause of OCD is proposed to be a dysfunction of the gut microbiome constituency resulting in a susceptibility to obsessional thinking. Both stress and antibiotics are proposed as mechanisms by which gut microbiota are altered preceding the onset of OCD symptomology. In this light, pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) leading to episodic OCD is explained not by group A beta-hemolytic streptococcal infections, but rather by prophylactic antibiotics that are administered as treatment. Further, stressful life events known to trigger OCD, such as pregnancy, are recast to show the possibility of altering gut microbiota prior to onset of OCD symptoms. Suggested treatment for OCD would be the directed, specie-specific (re)introduction of beneficial bacteria modifying the gut microbiome, thereby ameliorating OCD symptoms. Special considerations should be contemplated when considering efficacy of treatment, particularly the unhealthy coping strategies often observed in patients with chronic OCD that may need addressing in conjunction with microbiome remediation.

Reid A. OCD critical variables in CBT OCD. Advances in psychology research (Vol 96). Nova Biomedical Books, Hauppauge, NY; 2013; p. 245-67.

Cognitive-Behavioral Therapy (CBT) has been empirically validated as an effective first-line treatment for both pediatric and adult Obsessive-Compulsive Disorder (OCD). However, OCD is a highly heterogeneous disorder, causing many treatment refractory cases that leave clinicians baffled. This chapter reviews the past ten years of research on several of the most challenging OCD presentations, including OCD with poor insight, high family accommodation, comorbid oppositional defiant disorder, scrupulosity, and post-partum onset. Each of these presentations are discussed in terms of identifying characteristics, treatment augmentation, and case examples. Research supporting innovative assessment for these OCD presentations is outlined as well. CBT is a highly adaptable treatment approach. This chapter aims to summarize past findings and facilitate future research that will guide clinicians in adapting CBT for treatment refractory OCD, thus improving overall treatment outcome. (PsycINFO Database Record (c) 2015 APA, all rights reserved) (chapter)

Reid A, McNamara J, et al. Critical variables in cognitive-behavioral therapy for pediatric and adult obsessive-compulsive disorders. Advances in psychology research (Vol. 93). Nova Science Publishers, Hauppauge, NY; 2012; p. 29-51.

Cognitive-Behavioral Therapy (CBT) has been empirically validated as an effective first-line treatment for both pediatric and adult Obsessive-Compulsive Disorder (OCD). However, OCD is a highly heterogeneous disorder, causing many treatment refractory cases that leave clinicians baffled. This chapter reviews the past ten years of research on several of the most challenging OCD presentations, including OCD with poor insight, high family accommodation, comorbid oppositional defiant disorder, scrupulosity, and post-partum onset. Each of these presentations are discussed in terms of identifying characteristics, treatment augmentation and case examples. Research supporting innovative assessment for these OCD presentations is outlined as well. CBT is a highly adaptable treatment approach. This chapter aims to summarize past findings and facilitate future research that will guide clinicians in adapting CBT for treatment refractory OCD, thus improving overall treatment outcome. (PsycINFO Database Record (c) 2015 APA, all rights reserved) (chapter)

Roller CG. Sexually compulsive/addictive behaviors in women: a women's healthcare issue. J Midwifery Womens Health. 2007;52(5):486-91.

Sexually compulsive/addictive behavior is a pattern of sexual behaviors that cause distress and/or impairment of social functioning. It is marked by obsessive thoughts, compulsive behaviors, and the individual's inability to stop the behaviors despite negative consequences. Women experiencing sexually compulsive/addictive behavior are preoccupied with sex not as a response to desire but rather as a behavior that serves the purpose of anxiety reduction. Sexually compulsive/addictive behavior is associated with several health consequences, including sexually transmitted infections, unwanted pregnancies, abortions, and violence. It is important for providers to understand the addiction process, assessment, diagnosis, and interventions for these women.

Rose EA, Porcerelli JH, et al. Pica: common but commonly missed. J Am Board Fam Pract. 2000;13(5):353-8.

BACKGROUND: Pica is the compulsive eating of nonnutritive substances and can have serious medical implications. Although it has been described since antiquity, there has been no single agreed-upon explanation of the cause of such behavior. METHODS: Databases from MEDLINE and PSYCH-Lit were searched from 1964 to the present to find relevant sources of information using the key words "pica," "obsessive-compulsive disorder," "iron-deficiency anemia," and "nutrition." RESULTS AND CONCLUSIONS: Pica is observed most commonly in areas of low socioeconomic status and is more common in women (especially pregnant women) and in children. To our knowledge, the prevalence of pica is not known. Numerous complications of the disorder have been described, including iron-deficiency anemia, lead poisoning, and helminthic infestations. Pica is probably a behavior pattern driven by multiple factors. Some recent evidence supports including pica with the obsessive-compulsive spectrum of disorders. Many different treatment regimens have been described, with variable responses. It is important to be aware of this common, but commonly missed, condition.

Ross EJ, Wong S. News from the 2nd world congress on women's mental health. Primary Psychiatry. 2004;11(6):22-6.

Presents news briefs from the second world congress on women's mental health. One of the brief states that antipsychotic augmentation of selective serotonin reuptake inhibitors or serotonin norepinephrine reuptake inhibitors are effective for treatment of post-partum obsessive-compulsive disorder. Another new brief presents a case study reporting efficacy of mirtazapine for treatment of severe morning sickness. Another news deals with the possibility of prenatal depression forecasting post-partum depression in adolescent mothers. Although the risk of depression during pregnancy is generally emphasized during the post-partum period, the results of the study suggest that there is considerable continuity between prenatal and post-partum depression and that symptoms may be lower after giving birth. (PsycINFO Database Record (c) 2012 APA, all rights reserved)

Ross LE, McLean LM. Anxiety disorders during pregnancy and the post-partum period: A systematic review. J Clin Psychiatry. 2006;67(8):1285-98.

OBJECTIVE: The post-partum period is recognized as a time of vulnerability to affective disorders, particularly post-partum depression. In contrast, the prevalence and clinical presentation of anxiety disorders during pregnancy and the post-partum period have received little research attention. In this article, we review the medical literature as it relates to the prevalence and clinical presentation of panic disorder, obsessive-compulsive disorder, posttraumatic stress disorder, and generalized anxiety disorder during pregnancy and the post-partum period. DATA SOURCES: MEDLINE (1966 to July 2005 week 1) and Psych Info (1840 to July 2005 week 1) were searched using combinations of the following search terms: pregnancy, childbirth, post-partum, panic disorder, phobia, obsessive-compulsive disorder, posttraumatic stress disorder, and generalized anxiety disorder. STUDY SELECTION: All relevant papers published in English and reporting original data related to perinatal anxiety disorders were included. DATA EXTRACTION: Studies were examined for data related to the prevalence, presentation, predictors/risk factors, new onset, course, and treatment of anxiety disorders during pregnancy and the post-partum period. DATA SYNTHESIS: Anxiety disorders are common during the perinatal period, with reported rates of obsessive-compulsive disorder and generalized anxiety disorder being higher in post-partum women than in the general population. The perinatal context of anxiety disorders presents unique issues for detection and management. CONCLUSIONS: Future research is needed to estimate the prevalence of perinatal anxiety disorders more precisely, to identify potential implications of maternal anxiety disorders for maternal quality of life and child development, and to determine safe and effective treatment methods.

Rosso G, Bechon E, et al. La paziente con DOC in gravidanza e nel post partum. Rivista di Psichiatria. 2012;47(3):200-4.

Aim: Obsessive-compulsive disorder (OCD) can occur with specific characteristics during the pregnancy/post-partum period. The presence of OCD in a such delicate period in a woman's life can lead to severe suffering of the patient herself, of her relatives and the newborn. The purpose of this article is to offer a comprehensive review of scientific literature concerning the relationship between OCD and pregnancy/post-partum. Methods: Literature was identified by searching in Medline (Medical Literature Analysis and Retrieval System On-line), using the PubMed search engine. The keywords used were "obsessive-compulsive disorder", "pregnancy", "post-partum period", "perinatal period". Results: The last trimester of pregnancy and the. post-partum period is at increased risk of onset of OCD, especially in susceptible individuals. During pregnancy/post-partum, OCD is characterized by typical clinical features: obsessions (aggressive and/or contamination) are more frequent than compulsions (checking and/or washing); further, if untreated, the symptomatology tends to persist and/or recur during any subsequent pregnancies. Discussion: From the literature it appears that the diagnosis of OCD during pregnancy/post-partum should be performed as soon as possible, both to ensure the correct patient and family psychoeducation, and timely access to psychopharmacological treatment and/or psychotherapy. (PsycINFO Database Record (c) 2013 APA, all rights reserved) (journal abstract).

Rosso G, Bechon e, et al. [OCD during pregnancy and post-partum]. Riv Psichiatr. 2012;47(3):200-4.

AIM: Obsessive-compulsive disorder (OCD) can occur with specific characteristics during the pregnancy/post-partum period. The presence of OCD in a such delicate period in a woman's life can lead to severe suffering of the patient herself, of her relatives and the newborn. The purpose of this article is to offer a comprehensive review of scientific literature concerning the relationship between OCD and pregnancy/post-partum. METHODS: Literature was identified by searching in Medline (Medical Literature Analysis and Retrieval System On-line), using the PubMed search engine. The keywords used were "obsessive-compulsive disorder", "pregnancy", "post-partum period", "perinatal period". RESULTS: The last trimester of pregnancy and the post-partum period are at increased risk of onset of OCD, especially in susceptible individuals. During pregnancy/post-partum, OCD is characterized by typical clinical features: obsessions (aggressive and/or contamination) are more frequent than compulsions (checking and/or washing); further, if untreated, the symptomatology tends to persist and/or recur during any subsequent pregnancies. DISCUSSION: From the literature it appears that the diagnosis of OCD during pregnancy/post-partum should be performed as soon as possible, both to ensure the correct patient and family psychoeducation, and timely access to psychopharmacological treatment and/or psychotherapy.

Saccomani L, Vercellino F, et al. [Tic disorders in children and adolescents. Clinical and genetic features, comorbidity]. Minerva Pediatr. 1999;51(4):101-8.

Tic disorders in children and adolescents. Clinical and genetic features, comorbidity. BACKGROUND: Aim of the study is to evaluate the clinical and genetic characteristics of tic disorders, in view of individuating similarities or differences relevant to the prognosis among different nosologically groups. METHODS: A retrospective study of 79 children and adolescents (average age 9.3 years) was performed. The cases were diagnosed according to DSM-IV as: transitory tics (TT) 13 cases; chronic tics (CT) 50 cases; Tourette disease (TD) 16 cases. They were compared to a control group of 18 school age children without any neurological or psychiatric disturbance. The study included: semi-structured interviews focused on natural history of the disturbances, familiarity, presence of perinatal pathology, comorbidity; neurological examination, EEG, psychodiagnostics tests and investigation. RESULTS: Mean age of onset and type of first symptoms are the same in the three groups. Compared to the control group there is a significant increase in: familiarity for tics disturbances in TD; presence of perinatal pathological factors in the three groups of patients; comorbidity for obsessive-compulsive disorder (OCD) in CT and TD, comorbidity with ADHD in CT group. Three clinical cases are reported to exemplify the mixed features in the families and the different responsivity to the pharmacological treatment.

Sanders J, Whitty P, et al. Delusions or obsessions: the same only different? A case reports. Psychopathology. 2006;39(1):45-8.

The phenomenological distinction between delusions and obsessions has been the subject of much debate in psychiatry. Some authors feel these symptoms are distinct nosologically entities, while others argue that they reflect manifestations of the same symptom and are distinguishable based on the level of insight a patient displays. In this report we describe the case history of a lady who presented with an obsessional disorder. The symptom was resistant to standard treatments and sub-

sequently became more delusional in nature. We review the literature in terms of the classification of obsessions and delusions and help clinicians in terms of the diagnosis and treatment of cases where the distinction between these phenomena is not clear and offer alternative means of classifying these symptoms based on insight.

Savaş E, Ozovaci A, et al. Antidepresanla birlikte atipik antipsikotik ekleme tedavisi kullanan ve kullanmayan obsesif kompulsif bozukluk hastalarinda metabolik sendrom sikliği: Naturalistik, tanimlayici bir ön çalişma. Klinik Psikofarmakoloji Bülteni / Bulletin of Clinical Psychopharmacology. 2010;20(4):307-13.

Objective: In this study, we aimed to investigate the frequency of metabolic syndrome (MetS) in patients with obsessive-compulsive disorder (OCD), its relationship with sociodemographic characteristics and its association with use of antidepressants or antidepressants combined with adjunctive atypical antipsychotics. Methods: The study was designed as a naturalistic, descriptive clinical observation and conducted on patients attending the outpatient clinics of the Anxiety Disorders Unit of the Psychiatry Department at Gaziantep University. A total of 40 OCD patients were included between the ages of 18 and 65, who had been diagnosed with OCD prior to the study according to the DSM-IV TR criteria and who had their treatment regimens started before the study was planned. Twenty patients were on antidepressants alone (antidepressant group) and the remaining 20 patients were on atypical antipsychotics together with antidepressants (antipsychotic group). All patients were on their medications for at least the previous three months. We excluded patients who had any other chronic medical diseases, dementia, moderate or severe mental retardation, epilepsy, substance abuse (except cigarette use), pregnancy, and neurological diseases causing organic brain disorders such as head trauma. The Yale-Brown Obsession Compulsion Scale (Y-BOCS) and Clinical Global Impressions (CGI) Scale were used to assess the patients. Heights, body weights, waist circumferences, and blood pressures of the patients were measured. Venous blood samples from the forearm were obtained after overnight fasting to measure blood glucose, high-density lipoprotein (HDL), triglycerides (TG), total cholesterol, and low-density lipoprotein (LDL). We diagnosed MetS according to the Third Adult Treatment Protocol (ATP III), which was defined by The National Cholesterol Education Program (NCEP). Statistical analyses were done by using SPSS 15.0. Descriptive statistics for continuous parameters were shown as mean (+/- standard deviation). For comparison of continuous variables, according to whether they followed a normal distribution, either Student t test or Mann Whitney U test was used. In comparison of discrete variables, Chisquare and Fisher's Exact tests were used. $P < 0.05$ was taken as the significance level of the tests. Results: There was no significant difference between the antidepressant and antipsychotic groups in terms of gender, marital status, employment status, and smoking. MetS was found in 10 patients in total (25%). Six patients were from antidepressant group, 4 patients were from antipsychotic group and the difference between these two groups was not significant in terms of frequency of metabolic syndromes. There was no difference between cases with MetS and without MetS in terms of educational level, occupation, marital status, age, CGI and Y-BOCS scores. In the antipsychotic group, 9 patients were given quetiapine (45%), 6 patients received risperidone (30%), 3 ziprasidone (15%), and 2 patients were on aripiprazole (10%). Conclusion: The frequency of metabolic syndrome was not statistically different between the antidepressant and antipsychotic groups. Although the study was conducted in a relatively small group of patients; it has revealed that atypical antipsychotic augmentation in OCD does not increase the risk of MetS. (PsycINFO Database Record (c) 2013 APA, all rights reserved) (journal abstract).

Serati M, Benatti B, et al. Post-partum obsessive-compulsive disorder associated with 9q33.1 deletion. Australian and New Zealand Journal of Psychiatry. 2015;49(10):943-4.

The letter presents a case report of a 40-year-old woman showing aggressive obsessions, fear of harming her child and related compulsions (avoidance of being alone with her child) was sent to our post-partum psychiatric service. According to DSM-5 criteria, she received an OCD diagnosis, and treatment with fluvoxamine (titrated till 150 mg/day) was prescribed. Due to a partial response, after 4 weeks, risperidone 0.5 mg/day was added. Due to the new-born clinical presentation (bilateral twisted feet, minor facial alterations, muscle hypertonia, pylori stenosis) a genetic evaluation by array-based Comparative Genomic Hybridization (CGH) was performed, in order to detect DNA copy number variations because of amplifications/ duplications or deletions. The analysis reported a deletion of 229 Kb copies of DNA in 9q33.1, involving pregnancy-associated plasma protein A (PAPPA) gene and 3% portion of astrotactin 2 (ASTN2) gene. A 9q33.1 deletion was incidentally found after a post-partum OCD onset, and authors' opinion is that hormonal and immunological changes could have unmasked an OCD genetic predisposition. 9q33.1 deletion involves ASTN2 gene encoding a protein associated to glial guided neuronal migration, a key step in the develop-

ment of cortical regions and a prerequisite for physiological brain neurodevelopment. In the current literature, 9q33.1 deletion, completely or partially involving gene ASTN1/2, have been associated with psychomotor retardation, autism disorders, attention deficit hyperactivity disorder (ADHD), language disorders, anxiety and OCD. (PsycINFO Database Record (c) 2016 APA, all rights reserved)

Shannahoff-Khalsa DS, Beckett LR. Clinical case report: efficacy of yogic techniques in the treatment of obsessive-compulsive disorders. Int J Neurosci. 1996;85(1-2):1-17.

The aim of this study was to investigate the clinical efficacy of yogic techniques in the treatment of eight adults with obsessive-compulsive disorder (OCD). A specific yogic breathing pattern has been prescribed for the treatment of OCD, as well as others for treating generalized anxiety. A year course of therapy was followed. Subjects improved on the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) comparing baseline with three, six, nine, & 12 months results (one-way ANOVA for repeated measures, F (4,12) = 3.343, p < or = .046). Five patients completed the study (Y-BOCS results were 83%, 79%, 65%, 61% improvement, and one at-18%), group mean improvement of +54%. The Symptoms Checklist-90-R showed significant improvement comparing baseline and 12 months using two-tailed T-tests for OCD (t = 13.856, p < .001), anxiety (t = 3.167, p < .051), and global severity indexes (t = 7.314, p = .005). Perceived Stress Scale scores showed significant improvement for the five test periods (one-way ANOVA for repeated measures, F (4,12) = 9.114, p < or = .001). Five patients were well stabilized on fluoxetine prior to the study, three stopped medication after seven months or less, and two significantly reduced it, one by 25% and the other by 50%. These techniques, merit further study under controlled conditions and could help lead to new approaches for the treatment of OCD and perhaps other impulse control and anxiety-related disorders.

Sharma V, Sommerdyk C. Obsessive-compulsive disorder in the post-partum period: diagnosis, differential diagnosis and management. Women's Health (Lond Engl). 2015;11(4):543-52.

Childbirth can trigger or exacerbate a variety of psychiatric disorders, but the extant literature has focused primarily on mood disorders. Obsessive-compulsive disorder (OCD) after childbirth can occur alone or in combination with other psychiatric disorders such as major depressive disorder. Due to the general lack of awareness of the relationship between childbirth and OCD among clinicians as well as patients, the disorder may be underdiagnosed or misdiagnosed as major depressive disorder. This article describes the prevalence, clinical features, common psychiatric comorbidities, differential diagnosis and potential consequences of underdiagnosis or misdiagnosis. Using case vignettes strategies for its detection and clinical management are suggested. Finally, areas in need of further research are proposed.

Sichel DA, Cohen LS, et al. Post-partum obsessive compulsive disorder: a case series. J Clin Psychiatry. 1993;54(4):156-9.

BACKGROUND: The puerperium has typically been a period of risk for the development of psychiatric illness. Although post-partum depressive illness has been discussed extensively in the literature, obsessive compulsive disorder during pregnancy and puerperium has received little attention. METHOD: Fifteen women with new-onset obsessive compulsive symptoms during the puerperium were retrospectively evaluated by chart review; all met DSM-III-R criteria for obsessive compulsive disorder. Distinctive features of their clinical presentation, pharmacotherapy received, and status at 1-year follow-up were recorded. RESULTS: Patients were noted to have a characteristic constellation of symptoms comprised of disabling intrusive obsessional thoughts to harm their babies. Obsessive rituals were not observed in any of the patients described. Patients frequently developed secondary depression and appeared to be exquisitely responsive to serotonin selective reuptake inhibitors. CONCLUSION: The puerperium may be a period of risk for development of new-onset obsessive compulsive disorder. Clinicians caring for puerperal women need to be aware of the impact of these symptoms on maternal and fetal well-being.

Sichel DA, Cohen LS, et al. Post-partum onset of obsessive-compulsive disorder. Psychosomatics. 1993;34(3):277-9.

Sockalingam S, Zemans M. Clinical case rounds in child and adolescent psychiatry: Compulsive hoarding associated with abortion. Journal of the Canadian Academy of Child and Adolescent Psychiatry / Journal de l'Académie canadienne de psychiatrie de l'enfant et de l'adolescent. 2007;16(4):177-9.

The patient was a 15 years old Caucasian female, 7 weeks pregnant when she presented to our outpatient clinic for increased irritability. Her current stressors were her pregnancy and subsequent ter-

mination of her relationship with her 16 years old boyfriend. The patient had a medical abortion at 9 weeks gestation and was re-assessed 8 weeks after this procedure. Within 1 week of her abortion, she developed progressive hoarding behavior's, involving garbage, water bottles and dirty plates, and was eventually unable to sleep in her bedroom due to the collected items. A trial of fluoxetine was initiated at 10 mg per day in conjunction with cognitive-behavioral therapy. Due to her persistent symptoms, her fluoxetine dose was gradually titrated to 50 mg/day and risperidone 0.5 mg at night was added at week 18 to treat residual OCD symptoms and irritability. Her irritability was not suggestive of akathisia or mania. After 22 weeks of CBT and pharmacotherapy treatment, her CY-BOCS and BDI scores decreased to 16 and 14 respectively. She completed a 14-session course of CBT and was maintained on fluoxetine 60 mg and risperidone 0.5 mg per day. After 12-months of treatment, the patient no longer met the criteria for OCD (CY-BOCS = 0), although she had residual depressive symptoms (PsycINFO Database Record (c) 2012 APA, all rights reserved).

Soreni N. Commentary on compulsive hoarding associated with abortion. Journal of the Canadian Academy of Child and Adolescent Psychiatry / Journal de l'Académie canadienne de psychiatrie de l'enfant et de l'adolescent. 2007;16(4):179.

Comments on an article by Sockalingam et al. (see record 2007-18877-007). The authors report a case of an adolescent onset of obsessive compulsive (OC) and depressive symptoms following medical termination of pregnancy at 9 weeks gestation. In addition, the authors describe successful implementation of standardized, evidence based multimodal treatment approaches. This case highlights the complex task of understanding the relationship between clinical symptoms, etiology and physiology of OC symptoms. Thus, the present case report successfully raises the issue of studying physiological correlates of specific OCD symptoms during childhood and adolescence. (PsycINFO Database Record (c) 2012 APA, all rights reserved)

Speisman BB, Storch EA, et al. Post-partum obsessive-compulsive disorder. J Obstet Gynecol Neonatal Nurs. 2011;40(6):680-90.

OBJECTIVE: To synthesize the extant literature on the prevalence, phenomenology, etiology and treatment of post-partum obsessive-compulsive disorder (OCD). A discussion of differential diagnosis between post-partum OCD and other post-partum psychiatric conditions (e.g., depression, psychosis) and none post-partum-onset OCD is provided. DATA SOURCES, STUDY SELECTION AND DATA EXTRACTION: All studies addressing post-partum OCD between the years 1950 and 2011 were reviewed. Data from all pertinent studies was explored as it related to post-partum OCD. DATA SYNTHESIS: Studies were organized based on their empirical technique (e.g., retrospective, prospective), population studied (e.g., clinical OCD, nonclinical populations, males), and etiological or treatment theory (e.g., cognitive-behavioral). CONCLUSION: The prevalence, phenomenology, etiology, and treatment of post-partum OCD are reviewed. The limited data on treatment approaches and outcomes for post-partum OCD are highlighted with a discussion of the role of nurses in the prevention and identification of post-partum OCD.

Speisman BB, Storch EA, et al. Post-partum obsessive-compulsive disorder. Journal of Obstetric, Gynecologic, & Neonatal Nursing: Clinical Scholarship for the Care of Women, Childbearing Families, & Newborns. 2011;40(6):680-90.

Objective: To synthesize the extant literature on the prevalence, phenomenology, etiology and treatment of post-partum obsessive-compulsive disorder (OCD). A discussion of differential diagnosis between post-partum OCD and other post-partum psychiatric conditions (e.g., depression, psychosis) and none post-partum-onset OCD is provided. Data Sources, Study Selection and Data extraction: All studies addressing post-partum OCD between the years 1950 and 2011 were reviewed. Data from all pertinent studies was explored as it related to post-partum OCD. Data Synthesis: Studies were organized based on their empirical technique (e.g., retrospective, prospective), population studied (e.g., clinical OCD, nonclinical populations, males), and etiological or treatment theory (e.g., cognitive-behavioral). Conclusion: The prevalence, phenomenology, etiology, and treatment of post-partum OCD are reviewed. The limited data on treatment approaches and outcomes for post-partum OCD are highlighted with a discussion of the role of nurses in the prevention and identification of post-partum OCD. (PsycINFO Database Record (c) 2016 APA, all rights reserved) (journal abstract).

Storch E, Murphy T, et al. D-cycloserine augmentation of cognitive-behavioral therapy in pediatric obsessive-compulsive disorder: A preliminary study. Neuropsychopharmacology. 2010;35:S275-6. DOI: 10.1038/npp.2010.217.

Background: The N-methyl-D-aspartate (NMDA) receptor is critically involved in fear extinction, and the NMDA partial agonist D-cycloserine (DCS) has been shown to enhance extinction of learned fear in animal studies. Studies in human adults have shown efficacy of DCS augmentation of exposure therapy in acrophobia, social phobia, and panic disorder. Among adults with OCD, Wilhelm et al. (2008) showed medium between-group effect sizes in favor of DCS and Kushner et al. (2007) showed significantly more rapid reduction in obsession-related fear ratings. We examined the potential benefit and safety of DCS versus placebo augmentation of CBT in pediatric OCD patients, to our knowledge the first clinical study of DCS in youth with OCD. Methods: Thirty youth with a principal diagnosis of OCD were recruited across two study sites between February 2007-December 2009. Participant characteristics are presented in Table 1. After obtaining written consent and assent, participants completed study measures, were administered a physical examination, had lab values assayed (CBC, metabolic panel, urine toxicology, and pregnancy test [for post-pubescent females]) and were randomized in a double blinded fashion to CBT + DCS or CBT + Placebo. Assessments were conducted at pre-treatment, after session 6, and within one-week posttreatment. All participants received ten 60 min CBT sessions. As a dosage of 0.7 mg/kg was found to be effective in adult studies, two dosing levels were used based upon weight: children between 25-45 kg took 25 mg (0.56-1.0 mg/kg/day); and children between 46-90 kg took 50 mg (0.56-1.08 mg/kg/day) one hour before sessions 4-10. Measures included the CY-BOCS, ADIS-IV-P, CGI-Severity (CGI-S), Multidimensional Anxiety Scale for Children (MASC) and the Children's Depression Inventory-Short Form. Data were analyzed with separate 2 (site: Florida, MGH) by 2 (condition: CBT + DCS, CBT + Placebo) by 3 (time: pre-treatment, mid-treatment, post-treatment; Dependent variables: CGI-Severity, CY-BOCS Total Score) or 2 (site) by 2 (condition) by 2 (time: pre-treatment, post-treatment; Dependent variables: ADISCSR for OCD, MASC, CDI-Short Form) fixed-effects linear regression with time as the repeated measure. Cohen's d was used to examine the magnitude of treatment effect. Results: There were no site differences across baseline demographics or clinical characteristics. Pre-treatment scale scores did not significantly differ as a function of group assignment (Table 2). For CGI-Severity ratings, we identified significant main effects for time ($F(2,27) = 86.8$; $p<.001$, $d=3.5$) and group ($F(1,28) = 6.4$; $p=.02$, $d=0.97$). The group by time interaction was not statistically significant ($F(2,27) = 1.5$; $p=.22$); the effect size was moderate in favor of the CBT + DCS arm ($d=0.47$) with a 57% versus 41% symptom reduction. Using the CY-BOCS, a significant time main effect ($F(2,27) = 118.4$; $p<.001$, $d=4.1$) was identified. Although neither the main effect for group ($F(1,28)=3.1$; $p=.09$) nor the group by time interaction ($F(2,27)=.69$; $p=.51$) met statistical significance, their effect sizes were moderate ($d=0.66$) and small ($d=0.31$), respectively. The average CY-BOCS reduction for the CBT + DCS arm was 72% versus a 58% symptom reduction for those randomized to CBT + Placebo. Using the ADIS-CSR, a main effect of time ($F(1,28) = 87.6$; $p<.001$, $d=3.5$) was identified. There was no significant group or group by time interaction for MASC or CDI-Short Form scores (Table 2). No participant reported adverse effects related to DCS or placebo. CBC, LFTs, electrolytes and BUN, creatinine all were normal at enrollment and after treatment with DCS. Discussion: Children randomized to DCS augmentation of CBT showed moderate treatment effects relative to a placebo control on several symptom severity indices. D-cycloserine was well-tolerated: no significant DCS-related adverse effects took place, and lab values did not change in treated youth. Despite several limitations, these preliminary data support study of 1) a fully powered trial applying DCS to CBT in pediatric OCD; 2) other pediatric anxiety disorders for which CBT is indicated; and 3) efficacy of DCS on alternative outcomes (e.g., participant attrition, treatment durability).

Swanson M, Epperly T. Vomiting, abdominal pain, compulsive bathing--Dx? J Fam Pract. 2014;63(5):257-9.

Szajer K, Karakula H, et al. [Psychopharmacotherapy of anxiety, obsessive-compulsive and sleep disorders during pregnancy and lactation]. Psychiatr Pol. 2005;39(3):519-26.

The aim of the third part of our work, associated with psychopharmacotherapy during pregnancy and lactation is to present guidelines of expert--groups concerning the current rules of treating anxiety, obsessive-compulsive and sleep disorders and actual data about spreading of these disorders, pre- and perinatal effects of drugs used and the classification of them according to FDA and the safety of these medications for the breast fed newborn.

Szajer K, Karakuła H, et al. Psychofarmakoterapia zaburzeń lękowych, obsesyjno--kompulsyjnych oraz snu w okresie ciąży i laktacji. Psychiatria Polska. 2005;39(3):519-26.

The aim of the third part of our work, associated with psychopharmacotherapy during pregnancy and lactation is to present guidelines of expert-groups concerning the current rules of treating anxiety, obsessive-compulsive and sleep disorders and actual data about spreading of these disorders, pre- and perinatal effects of drugs used and the classification of them according to FDA and the safety of these medications for the breast fed newborn. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract).

Teissedre F, Chabrol H. A study of the Edinburgh Postnatal Depression Scale (EPDS) on 859 mothers: detection of mothers at risk for post-partum depression. Encephale. 2004;30:376-81.

The post-partum is a high-risk period for the occurrence of anxious and depressive episodes. Indeed, during the first few days after delivery, mothers can present post-partum blues symptomatology: fatigue, anxiety, disordered sleeping and a changing mood. Post-partum depression is characterized by a changing mood, anxiety, irritability, depression, panic and obsessional phenomena. It occurs in approximately 10 to 20% mothers. The exact prevalence depending on the criteria used for detection. The first symptoms usually appear between the fourth- and sixth-week post-partum. However, post-partum depression can start from the moment of birth or may result from depression evolving continuously since pregnancy. We can add that the intensity of post-partum blues is a risk factor that can perturb maternal development. So, it is important for health professionals to dispose of predictive tools. This study is a validation of the French version of the EPDS. The aims of the study were to evaluate the post-partum depression predictive value at 3 days post-partum and to determine a cut-off score for major depression. Subjects participating in this study were met in 3 obstetrical clinics in, or in the vicinity of, Toulouse. Mothers with psychological problems, under treatment for psychological problems or mothers whose babies present serious health problems were excluded from the study. The EPDS was presented to 859 mothers (mean age=30.3; SD=4.5) met at one of the clinics at 3 days post-partum (period 1). They had an EPDS mean score of 6.4 (SD=4.6); 258 (30%) mothers had an EPDS score 9. 82.6% of these mothers experienced a natural childbirth and 17.3% a caesarean section; 51.5% gave birth to their first child, 36.2% to their second child and 12.3% to their third or more. All subjects were given a second EPDS with written instructions to complete the scale during the period 4 to 6 weeks post-partum and return it for analysis (period 2). Between the 4 to 6 weeks post-partum period, 722 mothers replied again to the EPDS. 131 mothers had an EPDS score 11 (mean age=30.3; SD=4.8). They had an EPDS mean score of 13.6 (SD=3.3). Mothers with probable depression were interviewed and assessed, using the Mini (Mini Neuropsychiatric Interview, Lecrubier et al. 1997), the SIGH-D (Structured Interview Guide for the Hamilton Depression Scale) and the BDI (Beck Depression Inventory) in order to diagnose a major depressive episode. They had a HDRS mean score of 13.7 (SD=5.1) and a BDI mean score of 13.6 (SD=5). At 3 days post-partum, we observed that 258 mothers (30%) had an EPDS scores 9 and 164 mothers (19%) had an EPDS scores 11. Between 4- and 6-weeks post-partum, we observed 18.1% of post-partum depression (EPDS 11) and 16.8% (EPDS 12) of major post-partum depression. The analysis of the sensitivity and the specificity at 3 days post-partum provides a cut-off score of 9 (Sensibility: 0.88) (Specificity: 0.50) as predictive of post-partum depression, for this cut-off score, the type I error is low (5.8%) but the type II error is more higher (18.9%). The analysis of the sensitivity and the specificity between 4- and 6-weeks post-partum provides a cut-off score of 12 (Sensibility: 0.91) (Sensibility: 0.74) for the detection of major post-partum depression. Factor analysis shows at 3 days post-partum that the internal structure of the scale is composed of two subscales. The first factor F1 "anxiety" accounts 28% of the variance and the second factor F2 "depression" accounts 20% of the variance. Between 4- and 6-weeks post-partum, factor analysis suggests a unidimensional model in the evaluation of post-partum depression which is better than two factor model. This factor accounts 40% of the variance. The scale has a good predictive value, and we can observe a significant correlation with the EPDS periods 1 and 2 ($r=0.56$; $p<0.05$). This result shows that the depressive mothers mood intensity predicts a future depressive risk. Furthermore, correlations between EPDS and BDI ($r=0.68$; $p<0.05$) and EPDS and HDRS ($r=0.67$; $p<0.05$) show a good convergent validity. The reliability study confirms the good internal consistency of the EPDS, at 3 days post-partum and in the post-partum depression -symptomatology evaluation (Cronbach's Alpha>0.80). In conclusion, this scale demonstrates good validity and is fast and easy use in obstetrical services, allowing early detection of women who risk developing post-partum depression and, in the first week of post-partum, of mothers who suffer from a major post-partum depression. The use of the EPDS for an early screening of the risk of postnatal depression which is essential considering the consequences that postnatal depression can have on the development of the infant, on the quality of the relationship within the couple and on other

social relationships. Mothers at risk for postnatal depression should be controlled and surveyed by the health professionals in obstetrical clinics.

Timpano KR, Abramowitz JS, et al. Efficacy of a prevention program for post-partum obsessive-compulsive symptoms. J Psychiatr Res. 2011;45(11):1511-7.

Obsessive-Compulsive Disorder (OCD) has emerged as a common and impairing post-partum condition. Prospective studies have identified psychological vulnerabilities for the emergence of post-partum obsessive-compulsive symptoms (OCS), including general anxiety symptoms, pre-existing OCS, and specific cognitive distortions. The identification of these factors makes feasible the development of prevention programs that could reduce the impact of post-partum OCS. The present investigation examined a cognitive-behavioral prevention program using a randomized, double blind, controlled trial. Expecting mothers in their 2nd or 3rd trimester with an empirically established, malleable risk factor for post-partum OCS received either the prevention program (N=38) or a credible control program (N=33), both of which were incorporated into traditional childbirth education classes. Results revealed that at 1 month, 3 months, and 6 months post-partum, the prevention program was associated with significantly lower levels of obsessions and compulsions than was the control condition (all p's<0.05). Group differences remained significant even after controlling for baseline OCS and depression symptoms. Those in the prevention condition also reported decreasing levels of cognitive distortions, in contrast to the control condition (p's<0.05). Results support the potential utility of incorporating a CBT-based OCS prevention program into childbirth education classes.

Timpano KR, Abramowitz JS, et al. Efficacy of a prevention program for post-partum obsessive-compulsive symptoms. Journal of psychiatric research. 2011;45:1511-7. DOI: 10.1016/j.jpsychires.2011.06.015.

Obsessive-Compulsive Disorder (OCD) has emerged as a common and impairing post-partum condition. Prospective studies have identified psychological vulnerabilities for the emergence of post-partum obsessive-compulsive symptoms (OCS), including general anxiety symptoms, pre-existing OCS, and specific cognitive distortions. The identification of these factors makes feasible the development of prevention programs that could reduce the impact of post-partum OCS. The present investigation examined a cognitive-behavioral prevention program using a randomized, double blind, controlled trial. Expecting mothers in their 2nd or 3rd trimester with an empirically established, malleable risk factor for post-partum OCS received either the prevention program (N=38) or a credible control program (N=33), both of which were incorporated into traditional childbirth education classes. Results revealed that at 1 month, 3 months, and 6 months post-partum, the prevention program was associated with significantly lower levels of obsessions and compulsions than was the control condition (all p's<0.05). Group differences remained significant even after controlling for baseline OCS and depression symptoms. Those in the prevention condition also reported decreasing levels of cognitive distortions, in contrast to the control condition (p's<0.05). Results support the potential utility of incorporating a CBT-based OCS prevention program into childbirth education classes.

Uguz F, Gezginc K, et al. Course of obsessive-compulsive disorder during early post-partum period: A prospective analysis of 16 cases. Comprehensive Psychiatry. 2007;48(6):558-61.

Objective: The aim of the current study was to prospectively examine a course of obsessive-compulsive disorder (OCD) during the early post-partum period. Method: The study data were collected from 16 pregnant women with a diagnosis of OCD according to the Structured Clinical Interview for DSM-IV (SCID-I). Obsessive-compulsive disorder symptoms were assessed by the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) before and after childbirth. Psychopharmacologic or psychotherapeutic treatments were not administered over the study period. Results: Scores of the mean Y-BOCS-total and Y-BOCS-obsession were significantly reduced from the basal levels to 6 weeks postnatally. No significant difference was found in terms of Y-BOCS-compulsion between 2 interviews. During the study period, whereas the Y-BOCS-total scores were decreased by at least 25% in 8 (50.0%) of 16 patients, only 1 (6.2%) of 16 patients experienced at least a 25% increase in the same scores. Conclusion: The results from a small patient group suggest that some patients may experience a marked improvement in preexisting OCD symptoms after childbirth. (PsycINFO Database Record (c) 2016 APA, all rights reserved) (journal abstract).

Uguz F, Kaya N, et al. One-year follow-up of post-partum-onset obsessive-compulsive disorder: a case series. Prog Neuropsychopharmacol Biol Psychiatry. 2008;32(4):1091-2.

Underhill K, Montgomery P, et al. Abstinence-plus programs for HIV infection prevention in high-income countries. Cochrane Database of Systematic Reviews. 2008. DOI: 10.1002/14651858.CD007006.

Background: Abstinence-plus interventions promote sexual abstinence as the best means of preventing acquisition of HIV, but also encourage safer-sex strategies (e.g. condom use) for sexually active participants. Objectives: To assess the effects of abstinence-plus programs for HIV prevention in high-income countries. Search methods: We searched 30 electronic databases (CENTRAL, PubMed, EMBASE, AIDSLINE, PsycINFO) ending February 2007. Cross-referencing, hand-searching, and contacting experts yielded additional citations. Selection criteria: We included randomized and quasi-randomized controlled trials evaluating abstinence-plus interventions in high-income countries (as defined by the World Bank). Interventions were any efforts that encouraged sexual abstinence as the best means of HIV prevention, but also promoted safer sex. Results were self-reported biological outcomes, behavioral outcomes, and HIV knowledge. Data collection and analysis: Three reviewers independently appraised 20070 citations and 325 full-text papers for inclusion and methodological quality; 39 evaluations were included. Due to heterogeneity and data unavailability, we presented the results of individual studies instead of a meta-analysis. Main results: Studies enrolled 37724 North American youth; participants were ethnically diverse. Programs took place in schools (10), community facilities (24), both schools and community facilities (2), healthcare facilities (2), and family homes (1). Median final follow-up occurred 12 months after baseline. Results showed no evidence that abstinence-plus programs can affect self-reported sexually transmitted infection (STI) incidence, and limited evidence that programs can reduce self-reported pregnancy incidence. Results for behavioral outcomes were promising; 23 of 39 evaluations found a significantly protective intervention effect for at least one behavioral outcome. Consistently favorable program effects were found for HIV knowledge. No adverse effects were observed. Several evaluations found that one version of an abstinence-plus program was more effective than another, suggesting that more research into intervention mechanisms is warranted. Methodological strengths included large samples and statistical controls for baseline values. Weaknesses included under-utilization of relevant outcomes, self-report bias, and analyses neglecting attrition and clustered randomization. Authors' conclusions: Many abstinence-plus programs appear to reduce short-term and long-term HIV risk behavior among youth in high-income countries. Evidence for program effects on biological measures is limited. Evaluations consistently show no adverse program effects for any outcomes, including the incidence and frequency of sexual activity. Trials comparing abstinence-only, abstinence-plus, and safer-sex interventions are needed.

Vulink NC, Denys D, et al. Female hormones affect symptom severity in obsessive-compulsive disorder. Int Clin Psychopharmacol. 2006;21(3):171-5.

There is circumstantial evidence that reproductive events can influence symptom severity of obsessive-compulsive disorder (OCD). We sent self-report questionnaires to 350 female outpatients with OCD to examine the relationship between the menstrual cycle, pregnancy, menopause, hormonal contraceptives, selective serotonin reuptake inhibitors and symptom severity of OCD. Yale-Brown Obsessive-Compulsive Scale scores were used at three serial time points during the menstrual cycle to assess symptom severity. One hundred and one out of 350 questionnaires (29%) were returned and completed. Forty-nine patients reported an exacerbation of OCD symptoms during the premenstrual period, nine during the menopause and 17 patients during pregnancy, whereas 11 patients mentioned improvement of OCD symptoms during pregnancy. Premenstrual dysphoric disorder could only partly explain a premenstrual exacerbation of OCD symptoms. Exacerbation of OCD could be related to reproductive events in a considerable number of patients, especially the pre-menstruum. Because reproductive cycle events influence the symptom severity of OCD, the menstrual cycle should be considered when assessing the severity of OCD symptoms during pharmacological studies.

Wariki Windy MV, Ota E, et al. Behavioral interventions to reduce the transmission of HIV infection among sex workers and their clients in low- and middle-income countries. Cochrane Database of Systematic Reviews. 2012. DOI: 10.1002/14651858.CD005272.pub3.

Background: Various interventions have been adopted to reduce HIV transmission among sex workers and their clients, but the effectiveness of these strategies has yet to be investigated using meta-analytic techniques. Objectives: To evaluate the effectiveness of behavioral interventions to reduce the transmission of HIV infection among sex workers and their clients in low- and middle-

income countries. Search methods: The Cochrane Central Register of Controlled Trials (CENTRAL), the Cochrane HIV/AIDS group specialized register, the Cochrane Database of Systematic Reviews, MEDLINE, PsycINFO, Sociological Abstracts, CINAHL, Dissertation Abstract International (DAI), EMBASE, LILACS, BIOSIS, SciSearch, INDMED, ProQuest, and various South Asian abstracting databases were included in the database list. The publication sites of the World Health Organization, the US Centers for Disease Control and Prevention, and other international research and non-governmental organizations also appeared in the database list. Selection criteria: Randomized controlled trials (RCTs) and quasi-RCTs examining the effects on HIV transmission risk of different behavioral interventions or comparing behavioral interventions with no intervention, where described any one of the outcome measures, such as HIV incidence and prevalence, STI incidence and prevalence, change in self-reported of condom use, and other HIV-related outcome. Data collection and analysis: Two authors independently assessed trials, extracted data and assessed the risk bias. Heterogeneity amongst trials was also tested. Main results: A total of 13 trials with 8,698 participants were included. Primary outcomes (HIV and STI prevalence and incidence) were reported in seven trials. Of these, HIV incidence was reported in only three trials. After a 6-month follow-up assessment, there was no evidence that social cognitive behavioral intervention was effective in reducing HIV incidence (RR 0.12, 95% CI 0.01 to 2.22). However, there was a reduction in HIV incidence at 3-month follow-up assessment of promotion of female and male condom (RR 0.07, 95% CI 0.00 to 1.38). Social cognitive interventions and promotion of female and male condom use were significantly reduced STIs incidence (RR 0.57, 95% CI 0.34 to 0.96) and (RR 0.63, 95% CI 0.45 to 0.88), respectively. Secondary outcomes were identified in 13 trials. Meta-analyses showed evidence that interventions to promote the use of female and male condoms do reduce non-condom use (RR 0.83, 95% CI 0.65 to 1.05) compared to promotion of male condoms alone, and that social cognitive interventions reduced drug use among sex workers (RR 0.65, 95% CI 0.36 to 1.16) compared to standard care. Authors' conclusions: Available evidence nevertheless suggests that compared with standard care or no intervention, behavioral interventions are effective in reducing HIV and the incidence of STIs amongst female sex workers (FSWs). Given the benefits of social cognitive theory and the promotion of condom use in reducing HIV/STI and the public health need to control transmission amongst FSWs, there is a clear finding in favour of behavioral interventions. However, it should be recognized that there is a lack of information about most other outcomes and target populations, and that all the trials were conducted in low- and middle-income countries.

Warneke L. Re: The influence of gonadal hormones on periodicity of obsessive-compulsive disorder. The Canadian Journal of Psychiatry / La Revue canadienne de psychiatrie. 1996;41(1):60-1.

Three cases illustrate the worsening of obsessive-compulsive disorder (OCD) with pregnancy in females (aged 17–35 years) who previously had good control of the illness with medication and behavioral therapy. The relationship between sex hormones, the endogenous opioid system, and the influence of pregnancy on OCD is discussed. (PsycINFO Database Record (c) 2012 APA, all rights reserved)

Wenzel A. Obsessions and compulsions. Anxiety in childbearing women: Diagnosis and treatment., American Psychological Association, Washington, DC; 2011; p. 55-71.

Scholars in this field have taken two distinct approaches in examining the prevalence of perinatal obsessive–compulsive disorder (OCD). In one approach, clinical samples of women who have been diagnosed with OCD are asked to identify, retrospectively, the circumstances surrounding the onset of their OCD. Researchers then calculate the percentage of women who attribute the onset or exacerbation of their OCD to pregnancy or childbirth. I regard these studies as ones that use clinical samples, as women in these samples are selected because they are seeking psychiatric treatment for their symptoms. In the other approach, samples of women who, presumably, are representative of the population of childbearing women seeking obstetric care at various facilities or recruited from public records are assessed, and the percentage of women with OCD is calculated. I regard these studies as ones that use community samples, as women in these samples are receiving standard obstetric care and are not presenting for concerns specifically related to psychiatric distress. Results from both types of research are described. Although there is a lack of prospective research designed to identify risk factors for perinatal OCD, many scholars have made reasonable speculations about the biological basis of obsessive–compulsive symptoms that emerge specifically in this time period, and other scholars have tested cognitive behavioral aspects of OCD in samples of post-partum women. The current state of the literature on correlates of perinatal OCD is described. (PsycINFO Database Record (c) 2015 APA, all rights reserved) (create)

Wenzel A, Gorman LL, et al. The occurrence of panic and obsessive-compulsive symptoms in women with post-partum dysphoria: A prospective study. Archives of Women's Mental Health. 2001;4(1):5-12.

Objective: This study investigated the prevalence of panic and obsessive-compulsive symptoms in a sample of post-partum women who endorsed high levels of dysphoria on a self-report depression measure. Method: A community-based sample of 788 post-partum women with self-reported depressive symptomatology completed an interview assessing major depression, panic disorder, and obsessive-compulsive disorder. Results: An estimated 11% of the sample reported difficulties with panic attacks, 8% reported difficulties with obsessions, and 9% reported difficulties with compulsions. The most common panic symptoms included heart palpitations, sweating, trembling, and paresthesia. The most common content areas of obsessive-compulsive symptoms were concerns about imminent disaster, compulsive cleaning behavior, and compulsive checking behavior, which were often related to fears concerning the newborn child. Comorbid depression and panic disorder were diagnosed in 1% of this sample, and comorbid depression and obsessive-compulsive disorder was diagnosed in 2.4% of this sample. Conclusion: Post-partum panic and obsessive-compulsive symptoms are common experiences that should be considered in treatment planning for women reporting dysphoria after they give birth. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract).

Wetzler AJ, Elias R, et al. Suicidal ideation versus suicidal obsession: a case report. CNS Spectr. 2007;12(7):553-6.

This case report illustrates the relationship between stress and obsessive-compulsive disorder (OCD) by describing an unusual case of OCD sequelae following a suicide attempt. The patient is a 29-year-old married woman who suffered a major depressive episode without OCD and tried to commit suicide by drinking household cleaner. Following the attempt, violent obsessive thoughts of harming herself and others emerged along with avoidance behavior. After exposure therapy, there was a decrease in her obsessive thoughts, less anxiety, and no avoidance behavior. This report highlights not only the existence of "posttraumatic obsession" but also the importance of accurate interpretation of suicidal preoccupation, leading to the diagnosis of OCD rather than suicidal ideation secondary to depression.

Williams K, Brignell A, et al. Selective serotonin reuptake inhibitors (SSRIs) for autism spectrum disorders (ASD). Cochrane Database of Systematic Reviews. 2013. DOI: 10.1002/14651858.CD004677.pub3.

Background: Autism spectrum disorders (ASD) are characterized by abnormalities in social interaction and communication skills, as well as stereotypic behavior's and restricted activities and interests. Selective serotonin reuptake inhibitors (SSRIs) are prescribed for the treatment of conditions often comorbid with ASD such as depression, anxiety and obsessive-compulsive behaviors. Objectives: To determine if treatment with an SSRI: 1. improves the core features of autism (social interaction, communication and behavioral problems); 2. improves other non-core aspects of behavior or function such as self-injurious behavior; 3. improves the quality of life of adults or children and their careers; 4. has short- and long-term effects on outcome; 5. causes harm. Search methods: We searched the following databases up until March 2013: CENTRAL, Ovid MEDLINE, Embase, CINAHL, PsycINFO, ERIC and Sociological Abstracts. We also searched ClinicalTrials.gov and the International Clinical Trials Registry Platform (ICTRP). This was supplemented by searching reference lists and contacting known experts in the field. Selection criteria: Randomized controlled trials (RCTs) of any dose of oral SSRI compared with placebo, in people with ASD. Data collection and analysis: Two authors independently selected studies for inclusion, extracted data and appraised each study's risk of bias. Main results: Nine RCTs with a total of 320 participants were included. Four SSRIs were evaluated: fluoxetine (three studies), fluvoxamine (two studies), fenfluramine (two studies) and citalopram (two studies). Five studies included only children and four studies included only adults. Varying inclusion criteria were used regarding diagnostic criteria and intelligence quotient of participants. Eighteen different outcome measures were reported. Although more than one study reported data for Clinical Global Impression (CGI) and obsessive-compulsive behavior (OCB), different tool types or components of these outcomes were used in each study. As such, data were unsuitable for meta-analysis, except for one outcome (proportion improvement). One large, high-quality study in children showed no evidence of positive effect of citalopram. Three small studies in adults showed positive outcomes for CGI and OCB; one study showed improvements in aggression, and another in anxiety. Authors' conclusions: There is no evidence of effect of SSRIs in children and emerging evidence of harm. There is limited evidence of the effectiveness of SSRIs in adults from small studies in which risk of bias is unclear.

Williams KE, Koran LM. Obsessive-compulsive disorder in pregnancy, the puerperium, and the premenstrual. J Clin Psychiatry. 1997;58(7):330-4; quiz 335-336.

BACKGROUND: Recent reports suggest that pregnancy and the puerperium may precipitate or exacerbate obsessive-compulsive disorder (OCD). The influence of this illness on other reproductive events, such as the premenstrual, is unknown. We examined retrospectively the relationships of pregnancy, the puerperium, and premenstrual to the course of OCD in 57 women. METHOD: Women outpatients with OCD meeting DSM-III-R criteria completed a standardized telephone interview administered by a psychiatric resident. They were asked retrospectively about the clinical course of their illness premenstrual and during and after pregnancy. RESULTS: Of 72 women eligible for the study, 79% (N = 57) completed the interview. Premenstrual worsening of OCD was described by 24 (42%) of the 57 women, and 12 (21%) described premenstrual dysphoria. Of the 57 women, 38 (67%) had been pregnant at least once; 31 (54%) had delivered at least one child. Pregnancy was associated with the onset of OCD in only 5 (13%) of the 38 women. Of the 29 women with preexisting OCD who became pregnant, 20 (69%) described no change in symptoms during pregnancy, 5 (17%) described worsening, and 4 (14%) described improvement. Post-partum exacerbation of OCD symptoms was reported by 7 (29%) of the 24 women with preexisting OCD who completed full-term pregnancies. Nine (37%) of the 24 women with both preexisting OCD and completed pregnancies also reported post-partum depression. CONCLUSION: The premenstrual and post-partum exacerbation of OCD symptoms in some women suggests that the course of this disorder may, in some cases, be influenced by changes in gonadal hormones. Our finding that women with OCD may be at increased risk for post-partum depression underscores the importance of careful post-partum evaluation of women with OCD to prevent maternal and infant morbidity.

Wisner KL, Perel JM, et al. Serum clomipramine and metabolite levels in four nursing mother-infant pairs. J Clin Psychiatry. 1995;56(1):17-20.

BACKGROUND: Women with post-partum-onset obsessive compulsive disorder may elect treatment with clomipramine. There is minimal information to guide the clinician who must advise breastfeeding women about clomipramine therapy. METHOD: Four clomipramine-treated breastfeeding mother-infant pairs were assessed for serum concentrations of clomipramine, N-desmethylclomipramine, and corresponding 8-hydroxymetabolites. RESULTS: Although the mothers exhibited a wide range of serum concentrations, the parent drug and metabolites were either nondetectable or below the quantifiable limit in the sera of all infants. No adverse clinical effects were observed. CONCLUSION: This report adds to the growing literature that suggests that tricyclic use during breastfeeding rarely results in measurable drug levels in infant sera.

Worley LLM. Review of Understanding post-partum psychosis: A temporary madness. Psychosomatics: Journal of Consultation and Liaison Psychiatry. 2010;51(2):181.

Reviews the book, Understanding Post-partum Psychosis: A Temporary Madness by Teresa M. Twomey and Shoshana Bennett (2009). The authors dedicated women share a strong mission, advocating for women with post-partum disorders by dispelling myth and offering hope for recovery along with accurate information. The book begins with an excellent overview of the differences between post-partum depression (PPP), and post-partum obsessive-compulsive disorder. Next, the author provides an overview of psychological approaches utilized for the treatment of post-partum disorders cautioning that the more severe illness of PPP is a medical emergency requiring referral for a complete medical work up and treatment by a physician with expertise in women's mental health. In summary, this courageous work provides an essential message for women suffering in silence and shame with severe post-partum depression and psychosis, offering them knowledge, respect, and hope. The individual stories in this book serve to remind us that we, as providers, must be well versed in treating this devastating illness–swiftly and compassionately. (PsycINFO Database Record (c) 2013 APA, all rights reserved)

Wu H, Yu D, et al. Morita therapy for anxiety disorders in adults. Cochrane Database of Systematic Reviews. 2015. DOI: 10.1002/14651858.CD008619.pub2.

Background: Morita therapy, first proposed in 1919, is a systematic psychological therapy for anxiety disorders that is based on eastern philosophy. It is mainly used as an alternative therapy for anxiety disorders in Asian countries such as Japan and China. Varying foci of treatment outcomes have been reported. To date, there has been no systematic review to investigate the strength of evidence for Morita therapy in anxiety disorders. Objectives: To assess the effects of Morita therapy compared with pharmacological therapy, other psychological therapy, no intervention or wait list for anxiety disorders in adults. Search methods: We searched The Cochrane Collaboration Depres-

sion, Anxiety and Neurosis Group's Specialized Register (CCDANCTR, which includes relevant randomized controlled trials from MEDLINE (1950 to date), EMBASE (1974 to date) and PsycINFO (1967 to date)), Dissertation Abstracts International (DAI) and four main Chinese medical databases (Chongqing VIP Database, Wanfang Database, China Hospital Knowledge Database, China Biology Medicine disc) as described in the protocol of this review to December 2014. Furthermore, we extended our search in the Cochrane Central Register of Controlled Trials (CENTRAL) and the World Health Organization International Clinical Trials Registry Platform (ICTRP) and the Sagace, a web-based search engine for biomedical databases in Japan. We applied no date or language restrictions. We contacted experts in the field for supplemental data. Selection criteria: We included all relevant randomized controlled trials comparing Morita therapy with any other treatment in the treatment of anxiety disorders. Data collection and analysis: Two authors independently selected studies and extracted data. For homogenous dichotomous data, we calculated fixed-effect risk ratios (RR), 95% confidence intervals (CI) and, where appropriate, numbers needed to treat for an additional beneficial outcome (NNTB) on an intention-to-treat basis. For continuous data, we calculated fixed effect standardized mean differences (SMD) and 95% CI. Main results: We found seven small Chinese studies (449 participants), six of which provided useable data for meta-analysis. No study compared Morita therapy with an inactive control. Unclear randomization methods, lack of blinding and low-quality reporting of outcomes were common in the included studies. We graded the overall risk of bias as high and the quality of the evidence as very low. Two social phobia studies (75 outpatients) directly compared Morita therapy with pharmacological therapy. In this comparison, the pooled RR of global state was 1.85 (95% CI 1.27 to 2.69) and the NNTB was 3 (95% CI 2 to 5), indicating a significant difference between groups favoring Morita therapy in the short term (up to 12 weeks' post-treatment). Data regarding dropouts was insufficient and no description of adverse effects was provided. We graded the quality of the evidence for this comparison as very low, mainly due to high risk of bias in the studies and insufficient information in the results. Four studies (288 inpatients) investigated the effect of Morita therapy plus pharmacological therapy versus pharmacological therapy alone, three studies for the treatment of obsessive-compulsive disorder (OCD) (228 participants) and one study for generalized anxiety disorder (60 participants). One of the OCD studies reported incomplete data of global state while the outcome of global state was missing in the other three studies. There was no significant difference between groups for dropouts for any reason in two OCD studies in the short term (RR 1.76, 95% CI 0.47 to 6.67; I2 = 44%). Information pertaining to drop-outs for adverse effects was unclear. We rated the risk of bias of this comparison as high. We graded the quality of the evidence as very low. Authors' conclusions: The evidence base on Morita therapy for anxiety disorders was limited. All studies included in this review were conducted in China, and the results may not be applicable to Western countries. These included studies were mall, provided insufficient information about dropouts and adverse effects, and contained considerable risk of bias. Therefore, we graded the evidence as very low quality and were unable to draw conclusions on the effectiveness of Morita therapy in the treatment of anxiety disorders. Well-designed future studies that employ adequate allocation concealment, recruit large sample sizes, report dropouts and adverse effects, and report outcomes clearly and consistently are needed to establish the effectiveness of Morita therapy for anxiety disorders.

Yaryura-Tobias JA. Paroxetine. Current treatments of obsessive-compulsive disorder (2nd ed.). American Psychiatric Association, Arlington, VA; 2001; p. 81-91.

This chapter focuses on paroxetine for the treatment of obsessive-compulsive disorder (OCD) and its spectrum. The author discusses pharmacology of paroxetine hydrochloride, the history of its use in OCD, use in pregnancy, side effects, treatment duration and discontinuation and the case example of its use with a 28-yr-old woman. However, the psychiatrist must be knowledgeable about the issues of the diagnosis of OCD or its spectrum in order to implement the optimal treatment strategy. Treatment choices include drug therapy, behavioral therapy, or cognitive therapy. Most clinicians prefer a combined strategy. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (chapter).

Yildirim EA, Hacioglu M, et al. Persistent genital arousal disorder misdiagnosed because of Islamic religious bathing rituals: a report of three cases. J Sex Marital Ther. 2012;38(5):436-44.

Persistent genital arousal disorder is not well known or adequately understood by physicians. The disorder is characterized by a persistent and highly unwanted state of genital arousal and orgasm-like feelings. Ghusl is an ablution in Islamic culture, which is an obligatory ritual wherein the body is washed thoroughly after exposure to religious contaminants such as sexual intercourse, menstruation, and childbirth. Muslim women suffering from the disorder may bathe frequently because of their religious beliefs. The authors summarize the case histories of 3 patients with persistent

genital arousal disorder who were initially misdiagnosed with obsessive-compulsive disorder. All 3 patients presented with complaints of unwanted, persistent orgasms or orgasm-like arousals, and as a result, they performed ghusl several times a day. At previous interviews, the genital arousal was diagnosed as a sexual and somatic obsession, and repeatedly performing ghusl was considered a cleansing compulsion. Physicians' lack of awareness or knowledge of persistent genital arousal disorder, combined with the unwillingness of patients to discuss sexual problems, can lead to a focus on the repetitive bathing, and thus, a misdiagnosis of the problem as obsessive-compulsive disorder. These cases are presented to highlight the possible pitfalls in the diagnosis of persistent genital arousal disorder cases in Islamic countries where ghusl is common.

Zambaldi CF, Cantilino A, et al. Sintomas obsessivo-compulsivos na depressão pós-parto: Relatos de casos. Revista de Psiquiatria do Rio Grande do Sul. 2008;30(2):155-8.

Post-partum depression is the most common affective disorder in the puerperium. There are some symptoms in its clinical presentation, and one might be the higher frequency of obsessions and compulsions. We report six cases identified from the analysis of medical charts of puerperal women receiving care at the Women's Mental Health Program, Hospital das Clínicas, Universiade Federal de Pernambuco, Brazil. All the women were diagnosed with post-partum depression using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) and had associated obsessive-compulsive symptoms. We report time of onset, topics, course and treatment response of these symptoms. Obsessive-compulsive symptoms preceded depressive symptoms in two women and were succeeded in two other women. There was exacerbation of preexisting obsessions and compulsions in two puerperal women. The most frequent topic was aggressive thoughts toward the baby. Improvement in depressive symptoms tended to reduce obsessive-compulsive symptoms. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract).