Interpsiquis 2021
XXII Congreso Virtual Internacional de Psiquiatría, Psicología y Salud Mental

CLÍNIC BARCELONA Hospital Universitari

PROGRAMACIÓN FETAL Y NEUROIMAGEN

ANA COSTAS CARRERA

Unidad de Esquizofrenia, Instituto Clínic de Neurociencias, Hospital Clínic, Barcelona (España)

El presente trabajo no tiene conflictos de intereses.

ANTECEDENTES

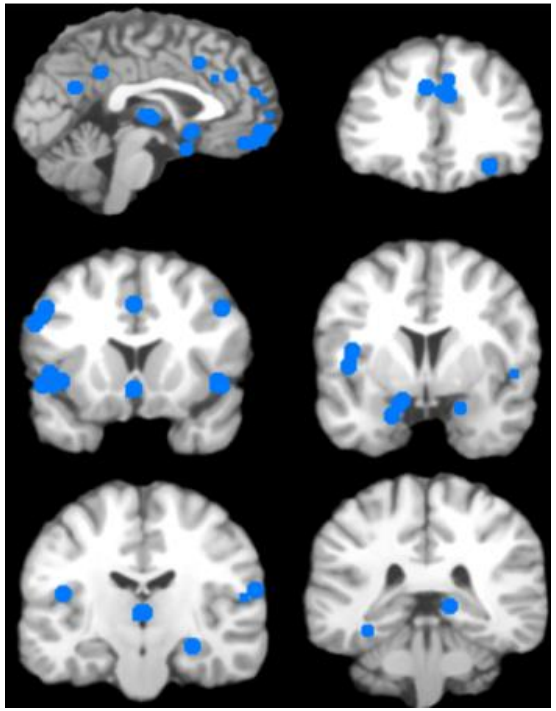
- Posible rol en la alteración de redes neuronales en desarrollo de SCZ. (Kesavan et al., 1999)

- Alteraciones cerebrales encontradas en SCZ (Shepherd et al., 2012) :

Reducción de materia gris en:
- Circunvolución frontal.
- Córtex cingulado.
- Ínsula.
- Tálamo.
- Circunvolución post-central.
- Región temporo-medial.
- Circunvolución parahipocampal.

Reducción de materia blanca en cuerpo calloso.

Incremento de volumen en:
- Ventrículos.
- Cavum septum pellucidum (CSP).



ANTECEDENTES

- La presencia de anomalías cerebrales en SCZ anterior a debut de clínica (Borgwardt et al., 2008; Lappin et al., 2007).

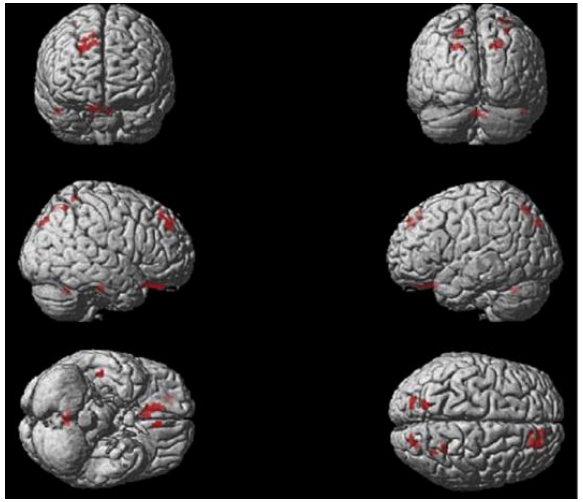
- Pacientes EMAR y PEP ↓ S.G. en circunvolución temporal, ínsula, precuneus y circunvolución posterior-cingulada. (Borgwardt et al., 2008).

- En PEP:

- ↓Volumen hipocampal

- ↑ Volumen ventricular

(Adriano et al., 2012)

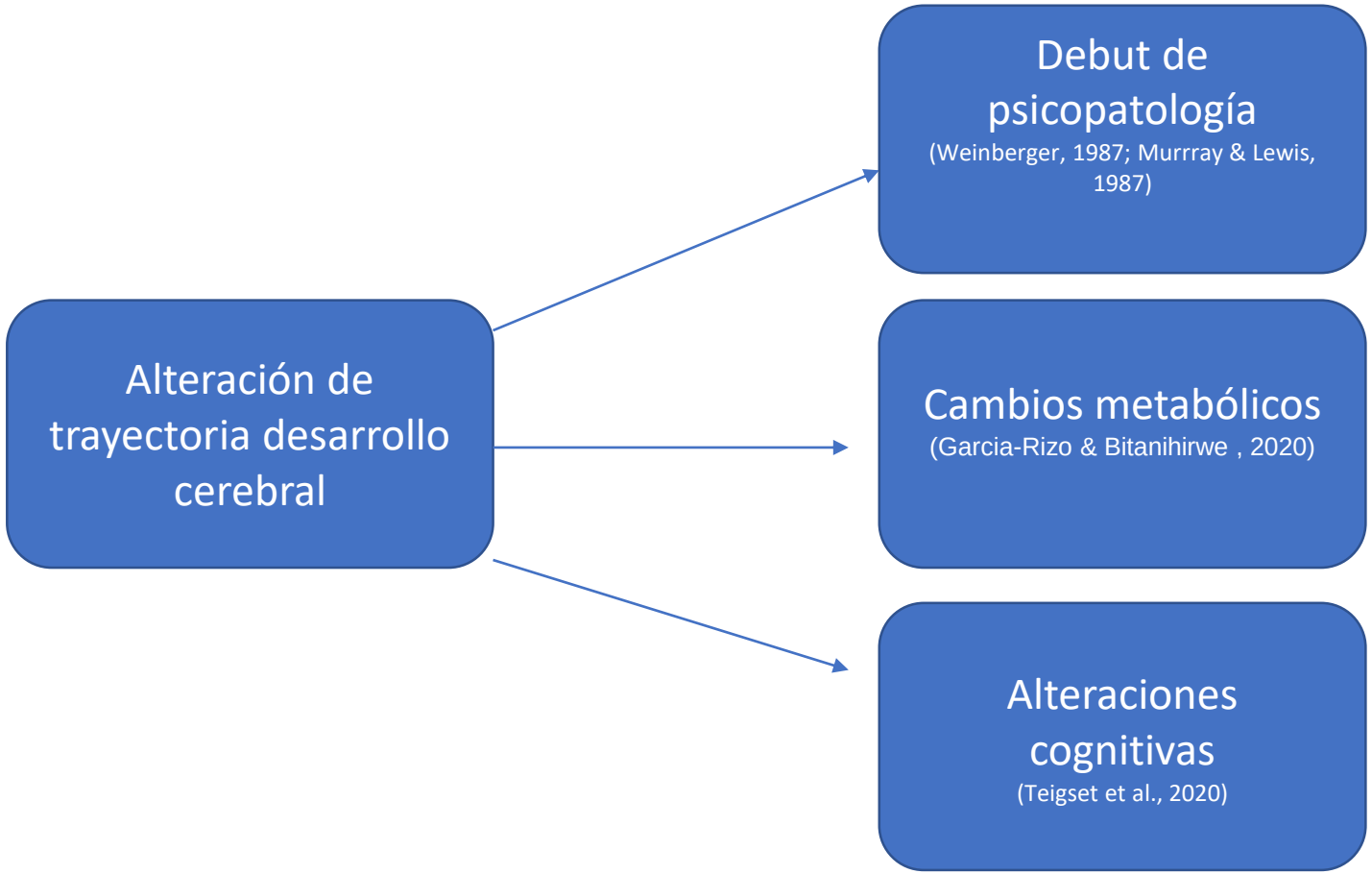


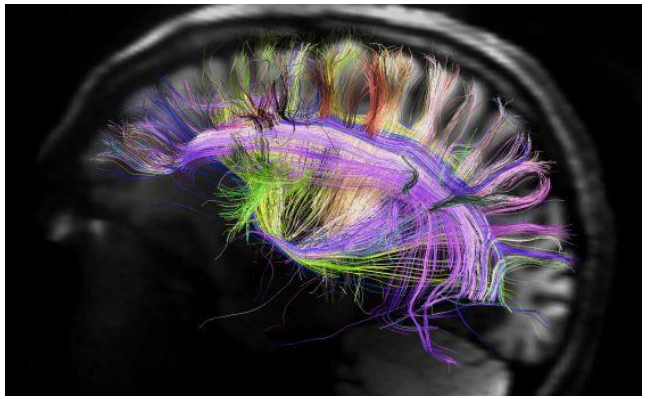
ANTECEDENTES

- Hipótesis del neurodesarrollo en SCZ: G x A.
- Las C.O. uno de los F.R. más estudiados. (Cannon et al., 2002; Smith et al., 2015)
- La exposición a C.O. incrementa riesgo de SCZ (OR: 2.0-3.0), especialmente en 2º trimestre. (Hultmann et al., 1999; Schmitt et al., 2014; Rees et al., 2008)
- F.R. más altos para cesárea emergencia, desprendimiento placenta y bajo peso al nacer.
- Posible factor común en todos ellos -> HIPOXIA

ANTECEDENTES

- Posible relación entre C.O. y Esquizofrenia:

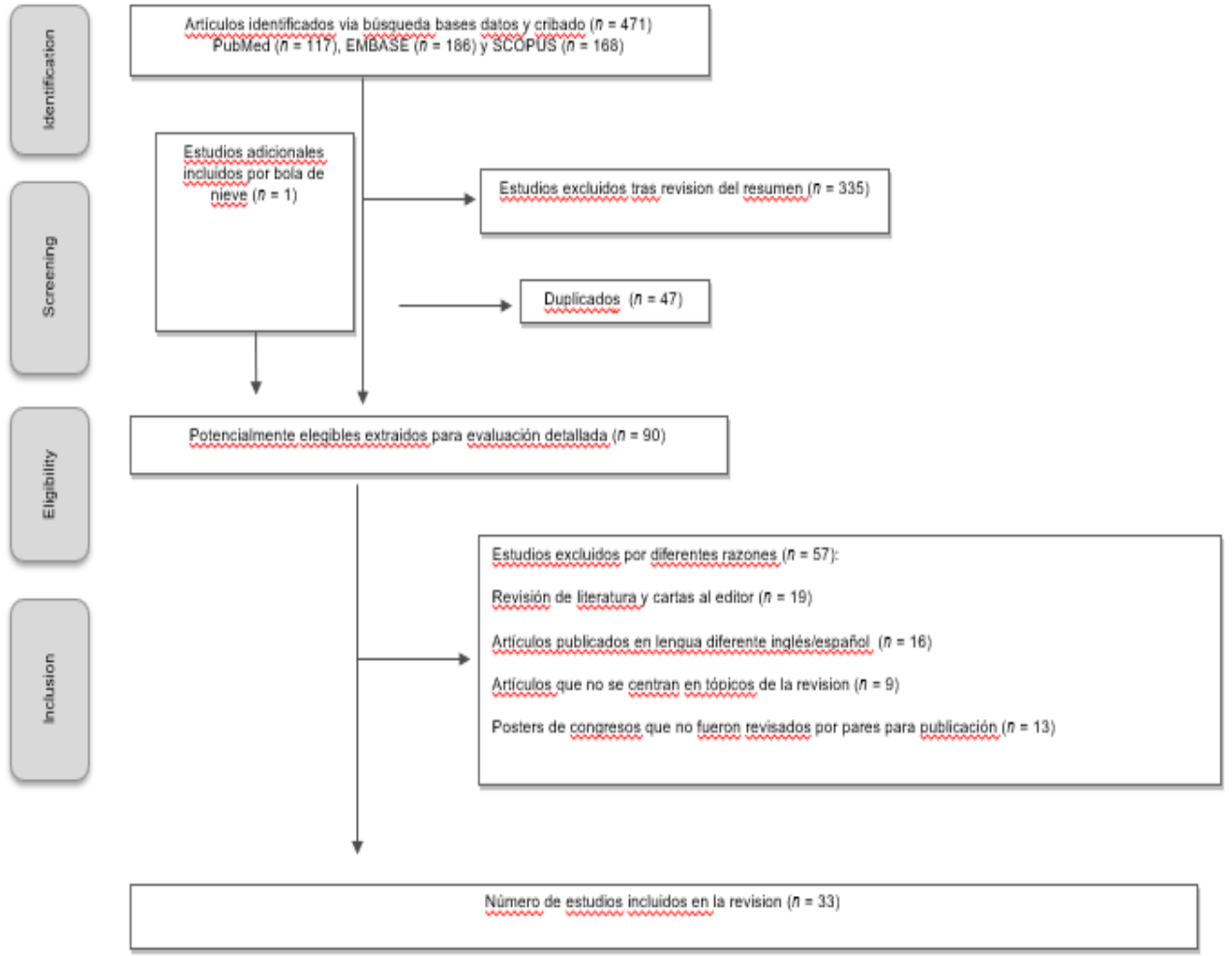




OBJETIVO Y MÉTODOS

- Evidencia actual de la posible relación entre C.O. y alteraciones cerebrales en neuroimagen de pacientes con esquizofrenia y otros trastornos psicóticos.

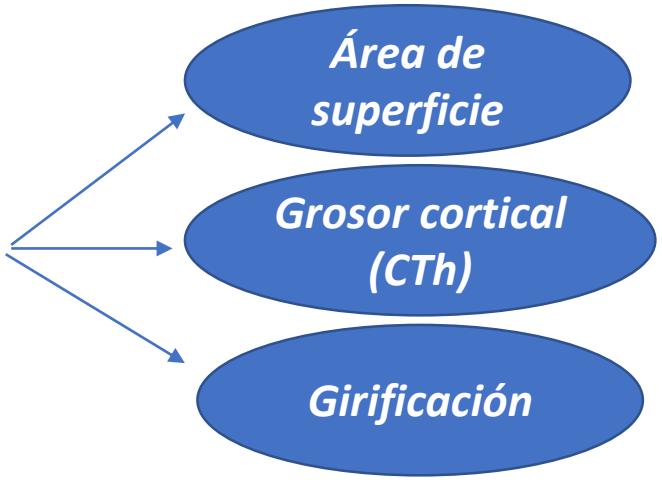
- Revisión bibliográfica: 33 artículos.



MORFOLOGÍA CEREBRAL Y CO

VOLUMEN Y CORTEZA CEREBRAL

- Volumen cortical: compuesto por 3 índices



- Los índices presentan distinto desarrollo madurativo.

- Índice de Girificación más relacionado con etapas pre/perinatales. (Smith et al., 2015).

MORFOLOGÍA CEREBRAL Y CO

VOLUMEN Y CORTEZA CEREBRAL

- Asociación entre CTh y F.R. ambiental en SCZ (Haukvik et al., 2014; Neilson et al., 2017).

- F.R. ambientales asociados con ↓ CTh temporal, mientras que F.R. genético con ↓ CTh global. (Neilson et al., 2017)

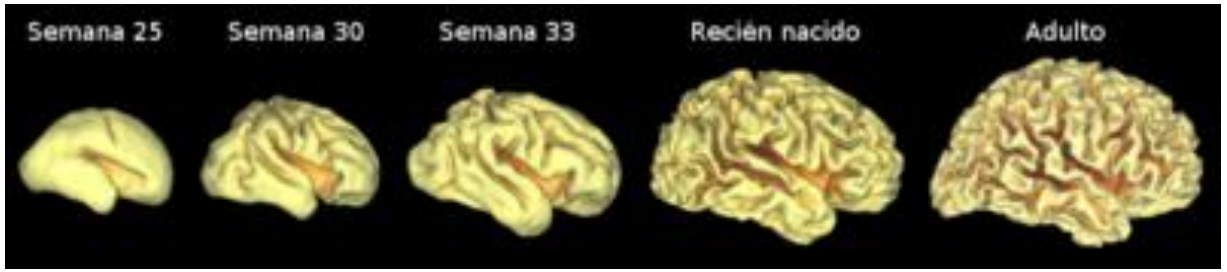
- CTh -> índice poco fiable de C.O. debido a ↑sensibilidad a otros F.R. ambientales.

MORFOLOGÍA CEREBRAL Y CO

VOLUMEN Y CORTEZA CEREBRAL

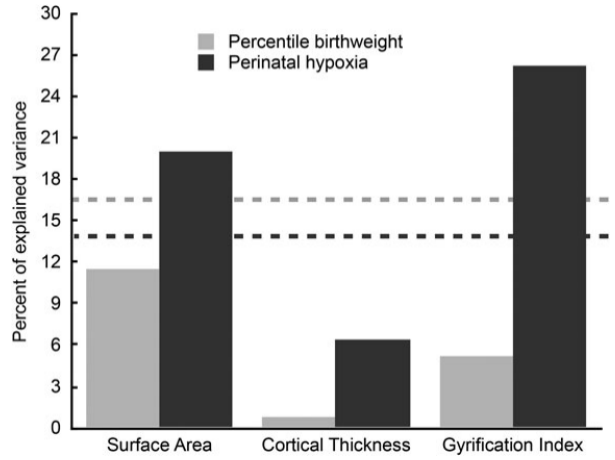
- Menor área de superficie asociada a C.O. (bajo P.N.), pero no diferencias entre SCZ y controles (Haukvik et al., 2013).

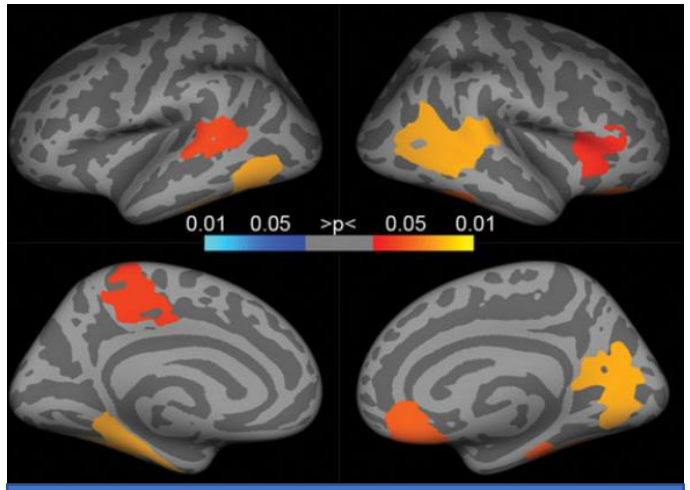
- ↓Girificación en SCZ asociada a peor respuesta a tto., desorganización y ↑signos neurológicos leves. (Palaniyappan et al. 2013b; Gay et al. 2013).



MORFOLOGÍA CEREBRAL Y CO

- Superficie cortical y girificación asociados a C.O. en SCZ, mientras que CTh no. (Smith et al., 2015)





Coloreadas las áreas de menor girificación en grupo con hipoxia perinatal (espectro amarillo)

Conclusión:

No suficiente evidencia de relación entre C.O. y volumen cortical en SCZ.

MORFOLOGÍA CEREBRAL Y CO

RATIO VENTRÍCULO/CEREBRO (VBR)

- *Efecto difuso adicional (add-on effect)* de las C.O. que conduce a cambios estructurales asociados a SCZ.

- Mientras que C.O. ↑ VBR, la carga genética provocaba cambios en regiones concretas (frontales/temporales). (Falkai et al., 2003)

- Estudio comparativo en SCZ con/sin A.F. psicosis: pacientes sin AF tenían mayor dilatación ventricular -> posible influencia de C.O. (DeQuardo et al., 1997)

MORFOLOGÍA CEREBRAL Y CO

RATIO VENTRÍCULO/CEREBRO (VBR)

- Pacientes con C.O. tenían ↑ dilatación ventricular y ensanchamiento surcos corticales (Lewis et al., 1988)

- La severidad de C.O. asociada a ↑ VBR en SCZ (Bersani et al., 2009; McDonald et al., 2002)

- A mayor carga genética, mayor ensanchamiento ventricular ante exposición de C.O. (McDonald et al., 2002 DeLisi et al., 1986).

MORFOLOGÍA CEREBRAL Y CO

RATIO VENTRÍCULO/CEREBRO (VBR)

- C.O. -> *"insultos neurológicos"* que descompensan desde esquizotipia a esquizofrenia (Schulsinger et al., 1984)

Conclusión:

- **Posible relación entre C.O. e incremento de VBR en SCZ, especialmente en pacientes con riesgo genético.**

MORFOLOGÍA CEREBRAL Y CO

HIPOCAMPO

- Reducción de estructuras límbicas bilaterales en SCZ. (DeLisi et al., 1988).

- Reducción de hipocampo izquierdo asociado a SCZ y mayor prevalencia en pacientes con C.O., posible explicación -> hipoxia. (Stefanis et al., 1999)

- Estudios de gemelos MZG: Relación entre menor volumen hipocampal en SCZ con C.O. (McNeil et al., 2000)

MORFOLOGÍA CEREBRAL Y CO

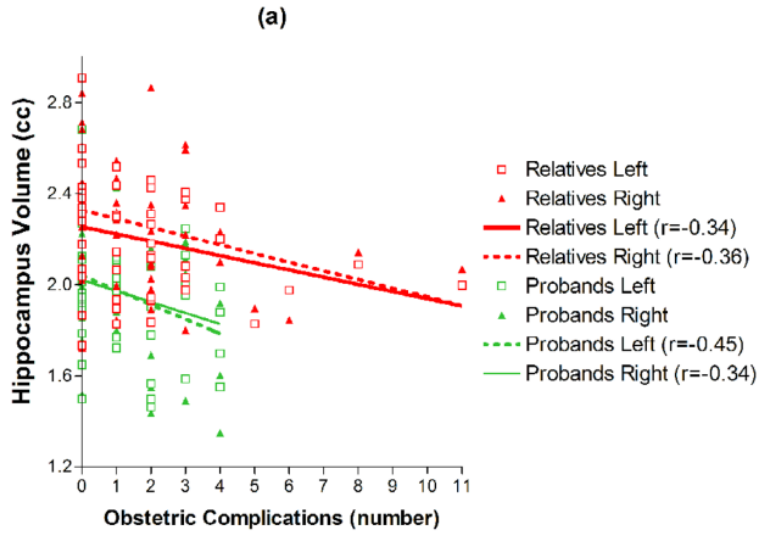
HIPOCAMPO

- Posible asociación entre reducción volumen hipocampal y ↑C.O.

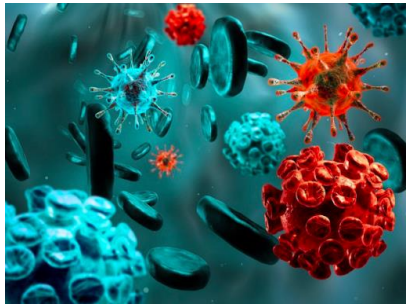
- Gradiente tamaño: A más C.O. mayor reducción volumen hipocampal
(Ho & Magnanota, 2010).

Conclusión:

- Posible relación entre C.O. y volumen hipocampo. Son necesarios más estudios.



RELACIÓN ENTRE CO Y SCZ



INFECCIÓN INTRAUTERINA

- Mayoría de virus no penetran placenta.
- Mecanismos de acción -> cascada de citoquinas materna altera neurodesarrollo.
- Infección prenatal asociada a mayor longitud del cavum septum pellucidum (CSP) y mayor riesgo de SCZ (Brown et al., 2009).
- IL-8 asociado a dilatación ventricular y disminución de corteza entorrinal izquierda y cíngulo posterior derecho en SCZ pero no controles (Ellman et al., 2010)

RELACIÓN ENTRE CO Y SCZ

HAMBRUNA GESTACIONAL

- Reducción de volumen cerebral en SCZ expuestos a hambruna.

- Efecto de interacción entre SCZ y hambruna gestacional en reducción de volumen cerebral. (Hulshoff et al., 2000)

CRECIMIENTO FETAL E HIPOXIA

- Hipoxia perinatal asociada a menor área de superficie y girificación cortical.

- Retraso en crecimiento intrauterino asociado a menor superficie cortical.

- Cuando se producen de forma simultánea, tienen un efecto aditivo en el cerebro.

(Smith et al., 2015)

MODELO G X A

- G x A: Efecto sinérgico de la interacción entre genes y ambiente en el origen de la psicosis. (Van Os et al., 2008).

- Gradiente de alteración cerebral en SCZ: interacción C.O. + R.G. (riesgo genético). (Cannon et al., 1993; Schmitt et al., 2014)

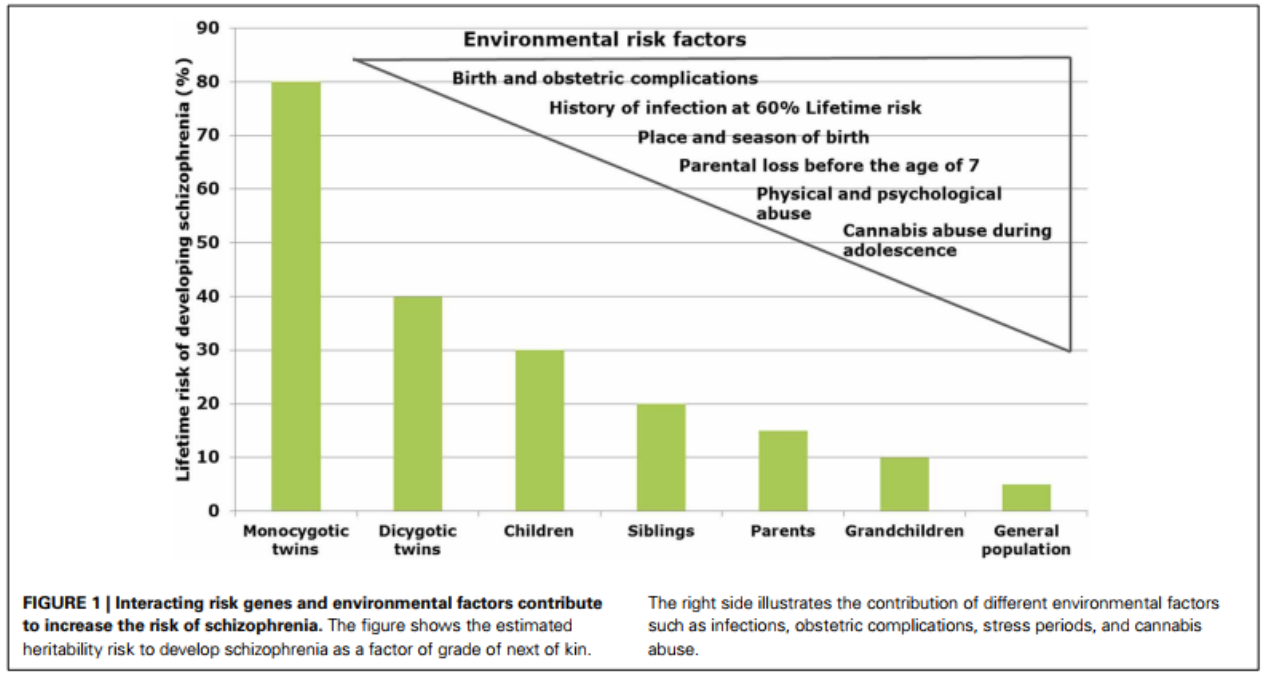


FIGURE 1 | Interacting risk genes and environmental factors contribute to increase the risk of schizophrenia. The figure shows the estimated heritability risk to develop schizophrenia as a factor of grade of next of kin. The right side illustrates the contribution of different environmental factors such as infections, obstetric complications, stress periods, and cannabis abuse.

MODELO G X A

- Correlación negativa con volumen de S.G. cerebral y C.O. en U-HRP. (Gilbert et al., 2003)

- Pacientes con riesgo genético ↑ riesgo de alteración cerebral ante C.O. (Mcdonald et al.,2002)

- Familiares de pacientes con SCZ mayor riesgo de presenter C.O. (Sugranyes et al., 2017)

CONCLUSIONES

I. Evidencia de relación entre C.O. y VBR y regiones límbicas en SCZ.

II. No hay evidencia sobre relación entre C.O. y corteza cerebral y girificación.

III. Escasa evidencia sobre subtipos de C.O. y especificidad de las alteraciones cerebrales en SCZ, pero hipoxia parece ser mediador importante.

IV. Modelo G x A: C.O. interaccionaría con R.G. en desarrollo de SCZ.

V. Son necesarios más estudios para concluir como afectan las C.O. en el cerebro y su relación con la SCZ.

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Review

Biological Psychiatry: CNNI

Obstetric Complications and Brain Imaging in Schizophrenia: A Systematic Review

Ana Costas-Carrera, Clemente Garcia-Rizo, Byron Bitanihirwe, and Rafael Penadés

ABSTRACT

Schizophrenia is a complex disorder in which clinical symptomatology typically reflects underlying brain abnormalities that coalign with multiple physical health comorbidities. The pathogenesis of schizophrenia involves the interplay between genetic and environmental factors, with obstetric complications widely described as key players in elevating the risk of psychosis. In this regard, understanding the anatomical and functional alterations associated with obstetric complications may help to elucidate potential mechanisms through which birth complications could contribute to schizophrenia pathogenesis. We conducted a systematic review of the extant literature describing brain abnormalities and obstetric complications in patients with schizophrenia and related disorders in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines. A total of 471 studies were retrieved and screened, and 33 studies met inclusion criteria for our review. Studies varied considerably in their methods, with 11 studies employing computed tomography, 1 using magnetic resonance spectroscopy, and 21 using magnetic resonance imaging. The scientific quality of the included studies was assessed and documented. Obstetric complications increase the risk of provoking brain abnormalities. These abnormalities range from decreased gray matter volume and abnormal brain–ventricle ratios to a reduction of volume in limbic regions—which relate to what is commonly observed in schizophrenia. However, current evidence from neuroimaging studies remains scant in relation to establishing obstetric complications as an independent risk factor for schizophrenia.

Keywords: Brain imaging, Developmental origins of health and disease, Neuroanatomy, Obstetric complications, Schizophrenia, Systematic review

https://doi.org/10.1016/j.bpsc.2020.07.018

Schizophrenia is a severe mental illness characterized by diverse clinical symptoms along with excess medical comorbidity and premature mortality (1,2). The complex nature of this mental illness reflects a gene and environment (G×E) interaction, with environmental factors that occur during the early perinatal period elevating the clinical risk of developing schizophrenia. Obstetric complications (OCs) are one of the most widely studied environmental risk factors for schizophrenia (3–6) and have been posited to play a role in the dysfunctional neural networks observed in schizophrenia (7). A substantial body of evidence exists linking OCs such as asphyxia, bleeding, emergency caesarian section, and fetal abnormalities (e.g., low birth weight) to schizophrenia. Indeed, the effect size—or odds ratio—of exposure to OCs on subsequent development of schizophrenia has been estimated to lie between 2.0 and 3.0, with the largest effects caused by emergency caesarian section, placental abruption, and low birth weight (3,8,9).

A common factor across all these complications might be perinatal hypoxia (10), with the hippocampus and basal ganglia being particularly susceptible to hypoxia-ischemia in neonates (11). Perinatal asphyxia is related to bilateral hippocampus atrophy (12), neuronal death, and cerebral white matter damage, with more profound effects in mid gestation rather than late gestation (13). In patients, fetal hypoxia has been linked to increased ventricular size and reduced cortical gray matter (4,14,15), but the results are not consistent (16).

Brain abnormalities are also considered to represent the neurobiological basis of schizophrenia (17). Some structural (18) and functional (19) brain abnormalities have been reported using neuroimaging methods, with certain associated neuroanatomical changes even appearing before the onset of the disease (20,21). Thus, reduced gray matter volumes in neocortical prefrontal and temporal regions, anterior cingulate cortex, insula, hippocampus, and parahippocampal gyrus have been described (22). Decreased hippocampal volumes and increased volume of ventricles have been noted in patients with first-episode psychosis, suggesting that these abnormalities have a neurodevelopmental origin (23). In addition, brain connectivity studies have found impairments in different networks, including the frontostriatothalamic circuit, in this disorder (24).

An essential point that still remains unsolved is to determine how these brain abnormalities are related to the onset and progression of schizophrenia. Currently, little is known about how psychotic symptoms and brain abnormalities are interlinked. A tentative solution to improve our understanding of this relationship is to consider the involvement of

ISSN: 2451-9022

ACostas@clinic.cat

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