

The Outgroup Intolerance Hypothesis for Schizophrenia

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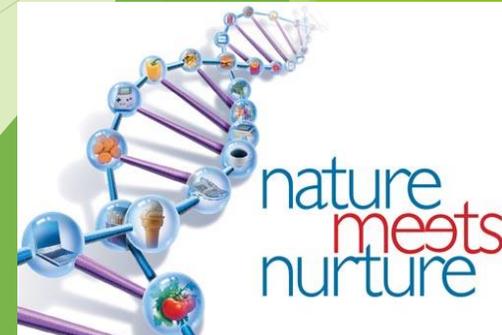
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Gene-environmental models



Gene-environmental models

- ▶ The genes for psychosis are seen as ‘normal genes’ that play a role in development and that ‘a spectrum of genetic vulnerability exists in the population, which in the context of a **toxic social environment** is expressed as a continuum of psychosis’ (Burns, 2009).
- ▶ The ‘toxic social environment’ has been linked to being male, immigrant, living in urban setting and in an area of low ethnic density
- ▶ The Outgroup Intolerance Hypothesis is an attempt to explore the evolutionary roots of that toxic social environment



A REFORMULATION OF THE SOCIAL BRAIN THEORY FOR SCHIZOPHRENIA

the case for out-group intolerance

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EDITORIAL

Can the new epidemiology of schizophrenia help elucidate its causation?

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The Outgroup Intolerance Hypothesis (OIH) (Abed & Abbas, 2011)

- ▶ During more than 99% of human evolutionary history, our ancestors lived as hunter gatherers in close-knit groups
- ▶ The social brain evolved to deal with the demands of living in such social conditions, surrounded by kin and with a clear delineation between ingroup and outgroup members

The Outgroup Intolerance Hypothesis (OIH) (Abed & Abbas, 2011)

- ▶ In the post-neolithic with settled living, new social systems emerged, resulting in a blurring of the demarcation between ingroup and outgroup members (this reached its peak with the advent of cities)
- ▶ This has led to a **mismatch** between the design of the social brain and the novel social environment
- ▶ The novel social environment can exert a detrimental effect on the development and functioning of the social brain primarily in the domain of inter-group regulation.
- ▶ The **stress caused by this mismatch** is what leads to schizophrenia in genetically vulnerable individuals

The Hypothesised Nature of the Environmental Stressor

- ▶ Excessive contact with non-kin or outgroup members during critical stages of development; or
- ▶ Inadequate (or poor quality) contact with kin or ingroup members during critical stages of development; or
- ▶ Some combination of both of the above.

The Hypothesised Nature of the Vulnerability

- ▶ Oversensitivity to the existence of strangers in the social environment, or
- ▶ An impairment in the ability to re-categorise or re-designate outgroup individuals as ingroup members
- ▶ Or some combination of both

Evidence for the OIH

- ▶ Xenophobia and the ingroup-outgroup distinction
- ▶ Evidence that schizophrenia is a social brain disorder
- ▶ Epidemiological evidence
- ▶ Evidence from psychopathology
- ▶ Evidence from Oxytocin studies
- ▶ Other evidence

Schizophrenia As a Disorder of the Social Brain

- ▶ Bleuler's 3 A's points to profound social handicap
- ▶ Loss of connectedness with the social surroundings is a cardinal feature (Brune)
- ▶ Impaired social competence

(Green et al., 2005; Brune et al., 2011)

Schizophrenia As a Disorder of the Social Brain II

Deficits in social cognition:

-Impairments in mental state attribution and empathy

Brune, 2005; Bora et al., 2006; Shamay-Tsoory et al., 2007; Ba et al., 2008; Green & Leitman, 2008; Derntl et al., 2009; Sergi et al., 2009; Fett et al., 2013)

-Recognition of emotional facial expressions

Hooker and Park, 2002; Kohler et al., 2003; Tsoi et al., 2008; Derntl et al., 2009; Huang et al., 2011

Evidence from Epidemiology

- ▶ Gender: Male: female risk ratio = 1.4:1
- ▶ The incidence of schizophrenia is not uniform across the world
- ▶ Variation across countries has ranged from 55 fold (Torrey, 1987) to 13-fold (Goldner et al, 2002)
 - ▶ The evidence points to lower incidence in traditional societies and higher incidence in westernised/industrial/urbanised societies
- ▶ Increased risk associated with
 - ▶ Migration
 - ▶ Urbanisation
 - ▶ Ethnic minority status

Migration

- ▶ Meta –analysis of studies between 1977-2003 showed a mean weighted relative risk of schizophrenia of:
 - ▶ 2.7 for 1st generation immigrants
 - ▶ 3.3 for 2nd generation immigrants
 - ▶ 4.8 for black immigrants

Cantor-Graae & Selton, 2005

- ▶ Meta analysis of 21 studies found incidence rate ratios (IRR) of
 - 2.3 for First Generation Immigrants
 - 2.1 for Second generation immigrants.

Bourque et al 2011

- ▶ However, the risk of psychosis is cancelled out if the migration involves a move from a situation of social exclusion to social inclusion **van Os, 2012**

Urbanicity

- ▶ A meta-analysis of 10 studies showed a pooled effect size of 1.7
Krabbendam and van Os 2005
- ▶ “The relationship may be causal as it explains about 30% of schizophrenia incidence”
- ▶ The effect is consistent across cultures and shows a dose-response relationship

Ethnic Minority Status

- ▶ Increased risk in ethnic minorities (Halpern, 1993; Boydell et al, 2001).
- ▶ Increased risk in ethnic minorities is inversely proportional to their population density in a given locality (Boydell et al, 2001)
- ▶ Greater risk in more visible minorities (van Os, 2012)
- ▶ High levels of own-group ethnic density is a protective factor for psychoses in a range of studies (Das-Munshi et al, 2012; Shaw et al 2012)

- ▶ **Migration**
- ▶ **Urbanisation**
- ▶ **Ethnic minority status**
- ▶ **Low ethnic density (own-group)**

▶ All are associated with greater exposure to outgroup members

Age of onset

- ▶ Late adolescence and early adulthood
- ▶ The age for departure from family, independence and more exposure to outgroup influences

Evidence from Psychopathology

- ▶ Hypervigilance and overattribution of malicious intentions to others suggest that the mechanisms involved in the evaluation of social threats are overactive (Brune, 2008).
- ▶ A large proportion of the positive symptoms relate to the theme of **threat** (persecutory delusions, 3rd person hallucinations and some of the other 1st rank symptoms).
- ▶ Majority of auditory hallucinations are of male voices (Nayani & David, 2006)
- ▶ Negative symptoms may be considered as a form of withdrawal from threatening social contact.
- ▶ Hence the majority (but not all) of the symptoms are consistent with schizophrenia being a dysregulation in the systems governing the relationship with outgroup members.

Evidence from studies of Oxytocin

- ▶ OXT has been implicated in promoting ingroup loyalty, altruism, solidarity (De Dreu et al, 2010 & 2011).
- ▶ OXT is claimed to modulate the regulation of cooperation and conflict among humans through:
 - 1.Enabling the categorization of others into ingroup or outgroup.
 - 2.Enabling the development of trust.
 - 3.Upregulating neural circuitries involved in empathy and concern for others(De Dreu, 2012)

Oxytocin in Schizophrenia

- ▶ **Altered baseline levels of oxytocin in CSF and plasma** Goldman et al., 2008; Keri et al., 2009; Rubin et al., 2010
- ▶ **Variations in Oxytocin receptor genes were linked to schizophrenia** Souza et al., 2010; Montag et al., 2012,; Teltsh., et al, 2012
- ▶ **OT has potential as a novel antipsychotic**
Feifel et al., 2010; Rubin et al., 2010; Pedersen et al., 2011
- ▶ **Clozapine increases the level of oxytocin**
Uvnas-Moberg et al 1992

Oxytocin in Schizophrenia

- ▶ OT administration in patients with schizophrenia has shown to improve some of the social cognitive deficits

Keri et al., 2009; Feifel et al., 2010; Rubin et al., 2010; Averbeck et al., 2011; Goldman et al., 2011; Pedersen et al., 2011

- ▶ In a recent study: oxytocin was shown to improve patients' accuracy in recognition of kinship

Fischer-Shofty, Brüne, et al 2013

- ▶ OT increased empathy to pain in outgroup members in controls but not in schizophrenic patients

- ▶ Abu-Akel et al, 2014

Other evidence

- ▶ Improved prognosis in developing countries despite poor MH services

(Jablensky et al. 1992; Sartorius et al. 1986; WHO 1973).

- ▶ Absence of reports of schizophrenia in true hunter-gatherers (uncontaminated by contact from settled human communities) (Anecdotal)

Is Schizophrenia A Dysfunction of the Cultural Brain?

Predictions

- ▶ **Prediction 1:** There will be a gradient of prevalence for schizophrenia in societies world-wide depending on the degree to which a given society departs from the conditions of the EEA. Hence the greater the probability of living in large groups with many strangers (outgroup members) the higher the incidence/prevalence of the disorder and vice versa.
- ▶ **Prediction 2:** There will be a gradient for the prognosis of schizophrenia that follows similar principles as in Prediction 1. Some evidence in favour of this already exists (Jablensky et al. 1992; Sartorius et al. 1986; WHO 1973).
- ▶ **Prediction 3:** Patients with schizophrenia will show more sensitivity to outgroup individuals than the average person. This prediction extends to first degree relatives.
- ▶ **Prediction 4:** Members of the majority (host) population who live in neighbourhoods with high density immigrant populations will be at increased risk of schizophrenia. This may partly explain the increased incidence of schizophrenia in urban settings.

Predictions cont.

- ▶ **Prediction 5:** Members of an immigrant population with greater numbers of immigrant kin in the host country will experience reduced risk of schizophrenia compared to those with few or no immigrant kin.
- ▶ **Prediction 6:** Families who are less culturally assimilated (whether assimilated in the host community or within their own immigrant group) confer a greater risk of schizophrenia upon their children than those who are highly assimilated. This factor may interact with the kinship circle available to the family which may ameliorate the effects of lack of assimilation.
- ▶ **Prediction 7:** Step-parentage during critical stages of development may be a risk factor for schizophrenia (especially short term step-parentage e.g. less than 2 years.)
- ▶ **Prediction 8:** The use of Oxytocin at an early stage of schizophrenia (within 6 months of onset) may permanently correct the deficit where the threshold for designating others as ingroup members may be set too high leading to an excess of outgroup designations.

Limitations

- ▶ OIH is a theory of ultimate causation that does not explain the proximate mechanisms causing the disorder (Specifically does not explain how the stress of outgroup intolerance causes the neuropathological changes in the brain).
- ▶ OIH cannot account for the role of a range of other environmental risk factors such as cannabis use in the causation of schizophrenia

Conclusion

The Outgroup Intolerance Hypothesis contends that:

1. Schizophrenia is a relatively novel human phenomenon that has only arisen since humans became settled and after the frequent exposure to outgroup individuals became common.
2. Schizophrenia is essentially caused by **social factors that interact with a genetic vulnerability**
3. The toxic element in the environment is the existence of (perceived) strangers that produces an exaggerated persistent threat response in some individuals and this leads to aberrant development of the social brain.
4. The hypothesis can explain a range of features of schizophrenia that have remained inexplicable thus far .

**Essentially, all models are wrong
but some are useful.**

George E.P. Box