

Synopsis for EU-GEI Publication

Synopsis no.: S.2.28
Preliminary title: Exploring the interplay between genetic distance and sociocultural factors in understanding the increased risk of psychotic disorders in ethnic minority groups.
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Publication category: Peer reviewed publication
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Work Packages involved: WP2
Partners involved from whom candidate co-authors (<i>additional to working and writing group</i>) should be nominated: Jean-Paul Selten
Objectives (scientific background, hypothesis, methods, and expected results): <u>Background</u> Rates of psychotic disorders are consistently higher in ethnic minority groups ¹ but different ethnic groups appear to be affected in different host countries, such as those of Moroccan ancestry in the Netherlands ² , and Black African and Black Caribbean groups in the UK ³ . This risk appears to be specific to individuals who have migrated to Western countries as rates in the general population in for instance Jamaica ⁴ and Surinam ⁵ appear to be similar to rates in the general population in Western Europe. Furthermore, within the same ethnic groups, first, second and even third generations can have differential risks ⁶ . A sociological exploration of this is available in synopsis 2.29, where I propose to look at the role of social and cultural distance as well as psychosocial disempowerment in explaining higher rates of psychotic disorders in minority groups. However, their role vis-à-vis genetic risk factors is not well-understood. The explicit purpose of the EU-GEI study was to investigate the interaction between genetic and environmental determinants of psychotic disorders, in order to elucidate the pathogenic processes underlying these disorders. Heritability of schizophrenia is high, and concordance between identical twins is almost 50%. Yet, no single 'schizophrenia gene' has been identified, but rather 108 schizophrenia-related loci, each of them with a very small effect size ^{7,8} . The search for a genetic explanation of schizophrenia is further complicated by the limitation that genome wide association studies (GWAS) have reduced validity in non-white samples (it is not very predictive of case-status). So, including a polygenic risk score computed using GWAS as an indicator of genetic risk would introduce a differential bias in examining the higher risk of disorder in ethnic minorities. Fortunately, in order to investigate the role of the social environment, it is possible to map genetic distance via principal component analysis in relation to African and Asian ancestry. We can therefore expand on the idea outlined in synopsis 2.29 that social and cultural distance from the majority

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population increases the risk of developing a psychotic disorder via increased psychosocial disempowerment by examining if this operates in tandem with increased genetic distance. We expect that markers of social and cultural distance will be stronger predictors of the excess risk in minorities than genetic distance. This would provide further strong evidence that the excess risk amongst minority groups arises from social constructs to which people are exposed.

Aims

The broad aim of the work outlined in this synopsis is therefore to deconstruct the effects of genetic, cultural and social distance, and to examine their interplay in explaining the higher rates of psychosis in ethnic minority groups.

This is done by testing the following hypotheses:

1. There is a positive relationship between genetic and cultural distance as well as between genetic and social distance.
2. Increased genetic, cultural and social distance are associated with an increased risk of developing a psychotic disorder.
3. Social and cultural distance will explain the excess risk in ethnic minority groups, with little or no additional effect of genetic distance.
4. Amongst people who self-identify in the majority white ethnic group, there will be no association between genetic distance and psychosis risk

Methods

The following variables will be included (for a list of precise data items, see below):

Outcome variable: case/control/sibling status

Predictor variables: ethnic minority status, cultural distance, and psychosocial disempowerment/

- Ethnic minority status
- Cultural distance is closely correlated with linguistic distance⁹, and we will use language trees to approximate this.
- Social distance will consist of socio-economic status, years of education and social isolation.
- Psychosocial disempowerment will be measured using self-perceived discrimination, and generalised neighbourhood trust as well as perceptions of ethnic diversity and cooperation in the neighbourhood.
- Genetic distance is measured via principal component analysis, looking at African and Asian ancestry. This variable will be used to approximate ethnic minority status when this can't be derived on the basis of sociodemographic information.

Confounding will be appropriately allowed for by including age, sex, childhood trauma, cannabis use, family history of psychosis and other mental illness, and paternal age.

Expected results

The expected results can be found in the aims of the study.

Data needed for the study:

A summary of the data items needed for this study can be found in the table below.

	<i>Description</i>	<i>EU-GEI variables</i>	
Outcome	Case/control/sibling status	Mrc1_socde01a	Subject status
Predictors	OPCRIT diagnosis	Icd10_dichot_b	ICD10 dichotomised diagnoses
	Ethnic minority status	Mrc1_socde03	Ethnicity, all sites
		Mrc1_socde04	Ethnicity, site-specific

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	Mrc1_socde05	Place of birth
	Mrc1_socde08	Fathers place of birth
	Mrc1_socde10	Mothers place of birth
Religious affiliation	Mrc2, question 12	What is your religious affiliation?
	Mrc2, question 13	How often do you attend services
Cultural distance	Mrc1_socde12	First language
	Mrc1_socde13	Language other, specify
	Mrc2 – question 14	Fluency in majority language
Social distance	Mrc1_socde21	Social class subject C 10 class model
	Mrc1_socde22	Social class subject M 10 class model
	Mrc1_socde36	Social class subject C 5 class model
	Mrc1_socde37	Social class subject M 5 class model
	Mrc2, question 8	What is the highest level of education you have achieved?
	Mrc2, question 9	How many years have you been in education?
	??	Social isolation
Genetic distance	PCA1	African ancestry
	PCA2	Asian ancestry
Psychosocial disempowerment	??	Discrimination questionnaire
	Soenast08a	I trust my neighbours
	Soenast06a	Most people are White British
	Soenast06b	People come from many different backgrounds
	Soenast06c	People from different ethnic groups generally get on well with each other
	Soenast06d	People from minority ethnic groups often suffer physical or verbal abuse
Confounders	Mrc1_socdebd	Birth date
Age	Mrc1_socde02	Age
	Nos_dup002	Date of first contact (cases only)
Sex	Mrc1_socde01	Sex
Family history of psychosis		
Family history of other mental illness		
Cannabis use		
Childhood trauma	Ctq001 – ct2025	Childhood trauma questionnaire
Paternal age	Mrc1_socde32	Fathers age at birth
Plan for statistical analysis (overall strategy):		
Demographic data will be cleaned in cooperation with Charlotte Gayer-Anderson and Marta di Forti (IoPPN), and genetic data will be gathered in cooperation with Alexander Richards (Cardiff University)		
Univariate associations will be tested using univariate logistic regression. This will subsequently be		

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expanded into a multivariate model, and into a regression model allowing for mediating effects.

Methods will be further developed in cooperation with James Kirkbride, Peter Jones and Alex Richards.

Other analyses/methods:

Involvement of external Parties (non EU-GEI):

IPR check:

Timeframe:

We aim to have all the data cleaned and variables created by 1 January 2017, and to have the analyses completed by 1 April. An initial draft of results will be available by 1 July.

Additional comments:

This synopsis is part of a PhD-project looking at an explanatory framework for higher rates of psychotic disorders in minorities using EU-GEI data, under supervision of James Kirkbride and Peter Jones.

Bibliography

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