Synopsis no.: S2.24

Preliminary title:

Environmental and genetic risk factors associated with schizotypy

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Publication category: 1

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Work Packages involved:

WP2

Partners involved from whom candidate co-authors (*additional to working and writing group*) should be nominated:
All partners/sites involved in WP2

Objectives (scientific background, hypothesis, methods, and expected results):

1. Scientific Background/ objectives

1.a. Background

The schizotypy concept has its historical roots in observations, in non-clinical populations, of psychological traits similar to symptoms of schizophrenia but in an attenuated form. Such traits have been observed more frequently in relatives of schizophrenic subjects.

Although schizotypy has been linked at the phenomenological and aetiological level to schizophrenia, to date, the nature of this link is not elucidated. It is not clear, especially at the aetiology level, if schizotypy and schizophrenia are at different points of a continuum with only quantitative differences (i.e. the same risk factors but more of them or more severe associated with schizophrenia) or if there are also qualitative differences (e.g. risk/protection factors specific for one but not the other disorder)

Beyond this theoretical interest, the study of risk factors associated with schizotypy is worth in itself as schizotypy has been associated with psychiatric comorbidity (anxiety, depression – Lewandowski et al, 2009), handicap (Pulay et al, 2009) and altered quality of life (Cohen and Davis, 2009).

For the above-mentioned reasons, numerous studies on risk factors for schizotypy have been conducted to date. However, there are several limitations to these studies.

Most important limitations are:

- a limited number of studies in the general population (most of them in students);

- few studies in large samples;

- very few studies on the role of genetic factors,

- lack of studies on interactions between risk factors (GxE, ExE, GxG);

- lack of studies that tested the association of the risk factors with both schizophrenia and schizotypy (i.e. studies in subjects originating from the same populations and using the same methodology to measure the risk factors)

In the EU-GEI study (WP2) there is a large sample of controls for which measures of schizotypy and detailed data on risk factors - genetic and environmental - are available. At the same time similar data on risk factors are available (and will be analysed in several approved synopses) on a similarly large sample of subjects with schizophrenia, from the same populations as the controls. Thus, data collected in EU-GEI (WP 2) will offer a unique opportunity to answer the present limitations of studies of the aetiology of schizotypy and advance our understanding of the relation between schizotypy and schizophrenia.

1.b. Objectives

A series of studies, that parallel synopses on RF for psychosis, will test the association between schizotypy (SZT) measures and the risk factors (RF) for non-affective psychoses (including ExE, GxG and ExG interactions). All potential RF measured in EU-GEI could be tested in separate analyses in relation with SZT. However, such studies have already been published, sometimes on huge subject samples (e.g. Schubart et al. 2011, studied the link between cannabis and schizotypy on more than 20,000 subjects), thus we propose to focus on interaction studies (based on theoretical, a priori, hypotheses or on the first results of analyses in WP2)[1]

A different set of analyses ("global" analyses) will compare the risk factors' impact on SZT to their impact on non-affective psychoses/schizophrenia. One such global test is already planned in synopsis S2.2[2] in which variation in (mean) values of SZT between centres will be compared with variation in incidence of SZ. A second global analysis is based on a synthesis of the results from the first series of studies (see above). In this analysis we propose to compare the influence of the different (environmental/genetic) risk factors on the two disorders (schizophrenia and schizotypy) i.e. test if all risk factors for schizophrenia increase the scores of schizotypy and if risk factors with higher RR for SZ have higher impact on SZT measures. Finally, one of the goals of WP2 is to develop a translational environmental risk assessment chart, combining into a single scale a measure of environmental liability to schizophrenia spectrum disorders. The capacity of this instrument to predict SZT values would be used as a global test of shared environmental risk between SZT and schizophrenia.

2. Hypotheses

The main hypothesis to be tested is that schizotypy is associated with the same risk factors as schizophrenia/non-affective psychoses.

[1] To analyse/ publish data on the individual RF influence on SZT we propose to do so (after discussion with the working and writing group of the specific synopsis) within the core studies already approved in WP2 (studies on the influence of RF on incidence of psychoses)

[2] Variation in the Incidence of schizophrenia and other psychotic disorders across Europe: findings from the multi-centre EU-GEI study (J. Kirkbride)

3. Methods

3.1. Centres included

All centres participating in WP2

3.2. Subjects included

All subjects for which measures of SZT and of potential RFs are available.
Two samples will be available and analysed: controls and siblings
The main analyses will involve controls; when samples of siblings of sufficient size are available confirmatory analyses of the results in controls will be run in these samples[3].

3.3. Dependent variables (measures of schizotypy)

There are several variables that could be used based on data from the SIS and CAPE and the best variables will be selected based on the analyses from another synopsis (proposed).

3.4. Explanatory variables

All variables (including potential confounders) used to test the relation of putative risk factors with (non-affective) psychoses (in WP2) i.e. environmental and genetic risk factors.

3.5. Statistical analyses

Linear regression or, for categorical data, logistic regression
Correlations.

Data needed for the study:

For each case (from partners): SIS and CAPE data and data on independent variables (putative risk factors)
Data on potential confounding factors e.g. basic demographics (age/ gender etc.)

Plan for statistical analysis (overall strategy):

For the first set of analyses the methods used will follow the methods used to assess the role of risk for schizophrenia/ non-affective psychoses.
For the global analyses measures of correlation (and tests of significance for these correlations) will be used.

Other analyses/methods:

Involvement of external Parties (non EU-GEI):

No

IPR check:

Timeframe:

- Studies could be started as soon as the results of the analyses on the best measures of schizotypy are available (proposal submitted)

[3] it is also probable that similar analyses will be run in the larger samples of sibs available in WP6; in this eventuality it could be more useful to merge the sibs sample from WP2 with the (larger) WP6 sample

- The first set of studies will parallel the similar analyses on RF for schizophrenia

- Global studies will await the publication of results of the main analyses (i.e. analyses of risk factors for psychosis) in WP2.

Additional comments:

Based on this proposal several analyses/ manuscripts could be planned. The interest of a single/ global proposal is to coordinate the different analyses. The writing/working group may eventually split in several groups according to specific interests and analyses.