

Synopsis no.: S2.43

Preliminary title:

The impact of psycho-social stress factors on measures of attenuated psychosis (schizotypy/psychotic like experiences)

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Publication category: 2

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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

Several environmental factors that increase the risk for psychotic disorders (e.g. childhood trauma, migration, urbanicity, social defeat), could be conceptualized as markers of early, prolonged or current psycho-social stress.

The diathesis-stress model of psychosis (Walker et al, 2008; Pruessner et al, 2017) posits that an enhanced response to stress plays an important role in the onset, exacerbation and relapse of schizophrenia. The stress sensitization mechanism (i.e. an increased stress response to an event as a consequence of a previous exposure to similar events) is hypothesized to play an important role in the risk for psychosis (Collip et al, 2008). According to this model, early, severe or prolonged stress (e.g. childhood trauma) might lead to a dysregulated (i.e. excessive) stress response through sensitization and, as such, explain both the role of early and current stress for increased psychosis risk.

Several studies brought support to this model showing for example an interaction of childhood trauma and later adversity in the development of psychotic symptoms (Lataster et al, 2012) or that exposure to childhood trauma increases stress reactivity (Veling et al. 2016) and stress sensitivity in psychotic subjects (Lardinois et al, 2011)

A limitation of studies in psychotic subjects, is the fact that the disease itself and factors associated with it (hospitalization, discrimination, treatment, substance abuse etc.) have the potential to cause significant stress and/or modify stress response.

The continuum theory suggests that isolated symptoms or pathological traits in attenuated form (e.g. psychotic like experiences, schizotypal traits) exist at various degrees in different individuals from the general population (Verdoux & van Os 2002). The theory also posits that these attenuated traits/symptoms have an origin/etiology similar to the full-blown pathology (Barrantes-Vidal et al, 2015).

Studying attenuated, continuous measures of psychopathology in the general population has several advantages the most notable being that it reduces the risk for misclassification (inherent to the dichotomous approach) (Urbano Blackford, 2017), benefits from the stability of personality traits over time (Venables and Raine 2015) and from the absence of some of the confounding factors present in clinical populations of schizophrenic patients (see above).

Beyond this theoretical interest, the study of risk factors associated with schizotypy or psychotic experiences is worth in itself as they have been associated with psychiatric comorbidity (anxiety, depression – Lewandowski et al, 2006), handicap (Pulay et al, 2009) and altered quality of life (Cohen and Davis, 2009).

To date, there are few studies that investigated the link between psycho-social stress and schizotypy measures: childhood trauma (Velikonja et al., 2015 for a review), migration (Tortelli et al, submitted) life events (Kocsis-Bogár et al, 2013) Furthermore, at our knowledge, there are no studies published on the link between schizotypy measures and discrimination or social defeat.

Finally, no study specifically analyzed, in relation with attenuated psychosis measures, the potential ExE interactions suggested by the sensitization theory.

Objectives:

To answer these limitations, we propose to study, in a large and diverse (age, gender, country of origin) sample:

1. the association of schizotypy/ attenuated psychosis measures with environmental factors related to stress [early stress (childhood trauma), prolonged stress (discrimination, social defeat) and current stress (life events)] and the characteristics of such stress factors (duration, time of exposure etc.) that influence the association;
2. the ExE interaction predicted by the sensitization theory (e.g. an increase in the effect of current stress in subjects with antecedent exposures to early and/or prolonged stress)

2. Hypotheses

The main hypotheses we intend to test are:

- schizotypy/attenuated psychosis is associated with environmental factors related to stress;
- the degree of association will depend on stress factors characteristics;
- there is a significant interaction between early/ prolonged stress and current stress;

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 (see explanatory variables below) are available.
Two samples will be available and analysed: controls and siblings

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 analyses that are the focus of another synopsis (S.2.23).

3.4. Explanatory variables and potential confounders

Environmental factors:

- early stress (CTQ, CECA)
- prolonged stress (Discrimination, social defeat - BCSS)
- current stress (LTE)

Potential confounders

- mainly demographic data (age, gender, ethnicity etc.)

3.5. Statistical analyses

Generalized linear models will be used (as implemented in R) to assess the role of stress on schizotypy/attenuated psychosis measures.

Structural Equation Modelling will be used to propose a global picture of the relationship between the different stress measures and schizotypy/attenuated psychosis measures

The biologic synergism (between previous stress exposure and current stress) will be assessed based on the model developed by Daroch (1997)

Data needed for the study:

For each subject (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.) - see above

Plan for statistical analysis (overall strategy):

- The first analyses will test the role of each stress-related factor on schizotypy scores and the characteristics that influence the degree of association (type of stress, duration, age at occurrence)
- The interaction between the factors associated with an increase in schizotypy (according to the sensitization theory) will be tested afterwards.

Other analyses/methods:

Involvement of external Parties (non EU-GEI):

No

IPR check:

Timeframe:

- The analyses will be done as soon as data for the environmental factors are available (checked/ cleaned) and the data for the schizotypy measures defined (S2. 23)

- According to the publication rules of EU-GEI a first version of the manuscript(s) will be available in the 6 months following availability of data.

Additional comments:

The present proposal expands and specifies a previous, more general, proposal (synopsis S2. 24)

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