

## Synopsis for EU-GEI WP5 Publication

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| <b>Synopsis no.: S5.7</b>   |
| <b>Preliminary title: Stress Sensitivity and Brain Structure in the At-Risk Mental State</b>  |
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| <b>Publication category: 3</b><br>Publications from a single work package involving only some parties (or in some cases only one party) in the Work Package   |
| <b>Working and writing group:</b> Maria Calem, Matthew Kempton, Ulrich Reininghaus, Craig Morgan, Philip McGuire, Lucia Valmaggia and EU-GEI ESM collaborators - Inez Myin-Germeys, Barnaby Nelson, Eva Velthorst   |
| <b>Work Packages involved:</b> WP5  |
| <b>EU-GEI Partners involved from whom candidate co-authors (<i>additional to working and writing group</i>) should be nominated:</b><br>Amsterdam and Melbourne WP5 authors   |
| <b>Objectives (scientific background, hypothesis, methods, and expected results):</b><br><br>My PhD, which was summarised in a separate EU-GEI WP5 synopsis, is on the neuroanatomical changes associated with both early life stress (childhood adversity) and recent stress (stressful life events) in ARMS. It will also investigate whether there is an interactive effect of these two forms of stress on neuroanatomy.<br><br>This synopsis proposes to extend the PhD project to include a publication on brain structure and stress sensitivity, as measured by the Experience Sampling Method (ESM). There would also be potential to explore a moderating effect of childhood adversity on the relationship between brain structure and stress sensitivity.<br><br>Using ESM data, stress sensitivity will be conceptualized as an increase in negative affect and intensity of psychotic-like experiences in response to daily hassles (i.e. perceived unpleasant events that occur in the flow of daily life).<br><br>In terms of neuroimaging data, this study will focus on region-of-interest analysis of four brain structures: the hypothalamus and pituitary gland, which are part of the hypothalamic-pituitary-adrenal(HPA)-axis, and the hippocampus and amygdala, which affect its activity.<br><br><b>Hypotheses:</b><br><br>The association between daily hassles and increased a) negative affect and b) intensity of psychotic-like experiences will be stronger in ARMS participants with greater pituitary volume and smaller hippocampal, amygdala and hypothalamus volume.<br><br>Childhood adversity will moderate this relationship between brain structure and stress sensitivity, in that people with a history of childhood adversity and with greater neuroanatomical differences will report |

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increased a) negative affect and b) intensity of psychotic-like experiences in response to daily hassles.

### Data needed for the study: (please list the EU-GEI WP5 instruments)

Data to be used is from ARMS cases from London, Amsterdam and Melbourne.

- Baseline structural MRI data
- ESM data
- List Of Threatening Experiences
- Childhood Experiences of Care and Abuse Questionnaire (CECA-Q)
- Childhood Trauma Questionnaire (CTQ)
- Bullying Questionnaire

### Plan for statistical analysis (overall strategy):

Multilevel linear regression analysis will be carried out in Stata with ESM measurements (level 1) nested in subjects (level 2).

In terms of ESM data, the independent variable will be event stress, and the dependent variables (to be modeled separately) will be negative affect and intensity of psychotic-like experiences. First, separate analyses will be carried out for each brain structure (hippocampus, amygdala, hypothalamus and pituitary), and then with volume and a stress x volume interaction term entered as independent variables. Interaction terms will be evaluated using likelihood ratio tests.

Stratified analyses will be carried out to quantify differences in stress sensitivity and brain structure volumes in people with and without a history of childhood adversity. Presence of childhood adversity (CA) and relevant interaction terms will also be entered as independent variables to assess whether stress reactivity is associated with brain structure volume (stress x volume interaction) and whether CA moderates the relationship between brain structure volume and stress reactivity (stress x volume x CA interaction). Interaction terms will be evaluated using likelihood ratio tests.

**Other analyses/methods:** N/A

### Involvement of external Parties (non EU-GEI):

None.

**IPR check (Intellectual property rights):** N/A

### Timeframe:

This work is to be included in my PhD, which is due to be submitted by July 2017. The publication of the MRI + ESM + childhood adversity analysis may be delayed so that those who are interested in ESM and childhood adversity can publish their paper first.

**Additional comments:** N/A