Synopsis no.: *S5.22*

Preliminary title: The association of polygenetic score and environmental risk score on brain structure in UHR

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Publication category: 3 Publications from a single work package involving only some parties (or in some cases only one party) in the Work Package
Working and writing group: Matthew Kempton, Lucia Valmaggia, Philip McGuire and other interested parties contributing useable data

Work Packages involved: WP5

EU-GEI Partners involved from whom candidate co-authors (*additional to working and writing group*) should be nominated: All centres that have collected usable data to be included in this publication (eg complete MRI, genetic and environmental data which is of a high enough standard to be included in the analysis.

Objectives (scientific background, hypothesis, methods, and expected results): Background: Robust abnormalities in brain structure have been confirmed in psychosis, and some of these abnormalities appear to be present before the onset of the illness. Currently it is not clear if these early abnormalities are associated with genetic risk factors or environmental risk factors. Hypotheses: We hypothesise that polygenic risk score will be associated with localised reductions in cortical thickness in UHR at baseline. In addition a combined environmental risk score will be associated with both distinct and also overlapping reductions in cortical thickness. Finally we hypothesise fhat a limited number of regions will be associated with a polygenetic x environmental risk score (ie an GxE interaction) Methods Polygenetic risk scores would be provided by our colleagues at Cardiff University MRI data would be processed using FreeSurfer using a cortical vertex analysis Polyenvironmental risk score would be calculated building on the work of Stepniak et al (2014). While a significant part of this project would investigate the best way to combine environmental risk factors an initial 'first pass' approach would be to combine z scores from the following key environmental risk factors: Migration, Urbanicity, cannabis use, childhood adversity and recent stressful life events. IN addition to the effects of polyenvironmental risk score we would also like to separately report on the effects of migration and cannabis – which depending on the results may form a separate paper.

Data needed for the study: (please list the EU-GEI WP5 instruments)
-Baseline Structural MRI data from EU-GEI
-Polygenetic Risk Score
-Environmental Risk score which will be calculated from:
Migration,
Urbanisity (both MRC Sociodemographic schedule)
Cannabis use (cannabis experiences questionnaire)
Childhood adversity (CTQ)
Recent stressful life events

The following variables are required not as a main focus of interest but to use as covariates.
-Transition status
-Follow-up GAF scales
-Basic demographics eg age, gender, years of education
-Basic clinical information (e.g basic medication, basic symptoms at baseline, brief substance misuse)

Plan for statistical analysis (overall strategy):
We initial plan to use a multi-regression analysis examining where cortical thickness is associated with polygenic score and polyenvironmental score, controlling for the above covariates including site.
However we will also look at more sophisticated analysis for the environmental risk score which takes into account the expected correlations between environmental risk factors

Other analyses/methods:
N/A

Involvement of external Parties (non EU-GEI):
None

IPR check (Intellectual property rights):
N/A

Timeframe:
Start date: Once baseline MRI data is complete.
Analysis: 4 months
Write up: 3 months

Additional comments:
 N/A