Synopsis for EU-GEI WP5 Publication

Synopsis no.: S5.9

Preliminary title: MRC Fellowship: Trajectory of Brain Structure and Function before and after the Onset of Psychosis: a Longitudinal Multicentre Study

Contact info for the person(s) proposing the synopsis

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Publication category: 5
Subprojects, involving one or more Work Packages and one or more Parties, arising from work done in relation to the project, wich is not part of the projects Do Woe Work Packagesm as descrbed in Annex I to the Contract, but using products generated by activities with the project. For example samples, data from the database ect.

Working and writing group: Matthew Kempton, Steve Williams, Philip McGuire and other parties contributing longitudinal MRI data from WP5

Work Packages involved: WP5

EU-GEI Partners involved from whom candidate co-authors (*additional to working and writing group*) should be nominated: IoP and other interested centres contributing longitudinal MRI data

Objectives (scientific background, hypothesis, methods, and expected results):
The is an MRC funded Fellowship of Matthew Kempton to collected new longitudinal MRI and fMRI data from WP5 subjects who have been scanned at baseline as part of the EU-GEI study.

The overall objective is to use neuroimaging to measure the trajectory of changes in the structure and function of the brain before and after the onset of psychosis.

The main specific objectives are:
1) To measure the volume of the hippocampus, insula and lateral ventricles at multiple time-points before and after the onset of psychosis.
2a) To measure changes in resting state connectivity before and after the onset of psychosis
2b) To measure hippocampal-striatal functional connectivity before psychosis occurs.
3) To determine if assessing the trajectory of these changes using machine learning can be used to predict which individuals will develop psychosis

Hypotheses
A) i) The onset of psychosis is associated with a decrease in the volume of the hippocampus and insula, and an increase in the volume of the lateral ventricles, compared to the baseline scan.
ii) These volumetric changes predate the first episode of psychosis, occurring while the individual is still within the prodromal phase.
iii) The onset of psychosis is associated with an increase in functional connectivity between the hippocampus and striatum.
iv) In subjects at high risk, assessing the longitudinal trajectory of MRI changes using machine learning can be used to predict which individuals will later develop psychosis.
B) i) The trajectory of longitudinal MRI changes in those who develop psychosis will be paralleled by the trajectory of changes in the severity of symptoms, and impairments in cognitive and global

functioning.
ii) Combining MRI and non-imaging measures in the machine learning algorithm will improve the accuracy of predicting which subjects will develop psychosis.

Data needed for the study: (please list the EU-GEI WP5 instruments):
-Baseline Structural MRI data from EU-GEI (Longitudinal data from MRC Fellowship)
-Transition status
-Follow-up GAF scales
-Follow-up cognitive measures (these will be in relation to MRI data only)
-Basic demographics eg age, gender, years of education

Plan for statistical analysis (overall strategy):

The focus will be on follow-up MRI data funded by the MRC fellowship
Structural MRI: DARTEL and FreeSurfer analysis with an ROI approach focussing on regions identified in the hypothesis. A longitudinal processing pipeline in FreeSurfer has recently been developed will be used to optimise the processing steps. A mixed model regression analysis, which allows the use of data with different numbers of observations per subject and irregular intervals will be implemented to obtain the best fit for the trajectory of volume change in ARMS-T, ARMS-NT and controls.

One of the challenges in translating findings from neuroimaging research into clinical practice is that the former are generally mean differences between groups, while the clinician needs a tool that can use the imaging data from an individual patient. The use of SVM (support vector machines) is an approach that has the potential to overcome this as the algorithm classifies each subject as belonging to a 'transition to psychosis' or 'non-transition' group. Gray matter difference images between the baseline and second scan along with functional connectivity maps at the second scan will be analysed using PROBID, an SVM toolbox developed at our centre. PROBID splits the data into training and test data and implements the computational steps required to train the network, outputting the accuracy of the classification and discriminating maps highlighting which brain regions are important in the classification. The SVM algorithm will be used to determine if it can correctly identify which ARMS subjects will transition to psychosis based on their gray matter difference and functional connectivity images. In a second analysis, symptom, cognitive and global functioning measures will be added to determine whether this improves the sensitivity and specificity estimates.

Other analyses/methods:
N/A

Involvement of external Parties (non EU-GEI):
It is expected that there will be collaboration external parties whom have expertise in longitudinal structural MRI analyses but these collaborators are unlikely to have access to the data

IPR check (Intellectual property rights):
N/A

Timeframe:
Start date: Longitudinal MRI data is currently being collected from a sample of centres with WP5
End of data collection: This is expected after the end of EU-GEI approx. spring 2017
Analysis: 6 months
Write up: 3 months

Additional comments:
N/A