microstructural white matter abnormalities in the emergence of neuropsychiatric symptoms.

M156. CORTICAL NEUROANATOMICAL SIGNATURE OF SCHIZOTYPY IN 2,695 INDIVIDUALS ASSESSED IN A WORLDWIDE ENIGMA STUDY

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Background: Cortical neuroanatomical abnormalities have been reported along a continuum between individuals with chronic schizophrenia, first-episode psychosis, clinical high risk for psychosis, and healthy individuals self-reporting subclinical psychotic-like experiences (or schizotypy). Recently, the Schizophrenia Working Group within the ENIGMA (Enhancing Neuro Imaging Genetics through Meta Analysis) consortium provided meta-analytic evidence for robust cortical thickness abnormalities in schizophrenia, while also indicating that these abnormalities are influenced by illness severity and treatment with antipsychotic medications. In this context, schizotypy research allows the investigation of cortical neuroanatomy associated with the expression of subclinical psychotic-like symptoms without the potential influence of a psychotic illness, its severity, or the use of antipsychotics. This study presents the first large-scale imaging meta-analysis of cortical thickness in schizotypy using standardized methods from 23 datasets worldwide.

Methods: Cortical thickness and surface area were assessed in MRI scans of 2,695 healthy individuals (mean [range] age of 29.1 [17–55.8], 46.3% male) who had also completed validated self-report schizotypy questionnaires. Each site processed their local T1-weighted MRI scans using FreeSurfer and, following the protocol outlined in the ENIGMA Schizophrenia Working Group study, extracted cortical thickness for 70 Desikan-Killiany (DK) atlas regions (34 regions per hemisphere + left and right hemisphere mean thickness). At each site, partial correlation analyses were performed between regional cortical thickness by ROI and total schizotypy scores in R, predicting the left, right and mean cortical thickness, adjusting for sex, age and site. Random-effects meta-analyses of partial correlation effect sizes for each of the DK atlas regions were performed using R's metafor package. False discovery rate (pFDR < .05) was used to control for multiple comparisons.

Results: We found significant positive associations between subclinical psychotic-like experiences and mean cortical thickness of the medial orbitofrontal cortex (r = .077; pFDR = .006) and the frontal pole (r = .073; pFDR = .006). When assessed separately by hemisphere, meta-analysis revealed a significant positive association between subclinical psychotic-like experiences and cortical thickness of the left medial orbitofrontal cortex (r = .066; pFDR = .044), and at trend-level with the right medial orbitofrontal cortex (r = .062; pFDR = .053) and the left frontal pole (r = .062; pFDR = .053). No significant associations were observed for surface area.

Discussion: Worldwide cooperative analyses of large-scale brain imaging data support a profile of cortical thickness abnormalities involving prefrontal cortical regions positively related to schizotypy in healthy individuals. These findings are not secondary to potential influences of disease chronicity or antipsychotic medication on the neuroanatomical correlates of psychotic-like experiences. The directionality of the observed meta-analytical effects in schizotypy is opposite to those previously reported in patients with schizophrenia (i.e., thinner cortex). The present findings of increased thickness may indicate early microstructural deficits (e.g. in myelination) that contribute to vulnerability for psychosis. Alternatively, these may reflect mechanisms of resilience associated with the expression of subclinical manifestations of psychotic symptoms in otherwise healthy individuals.

M157. A MULTICENTRE STUDY OF 1H-MRS BRAIN GLUTAMATE LEVELS IN SCHIZOPHRENIA; INVESTIGATING THE EFFECT OF ANTIPSYCHOTIC MEDICATION, SYMPTOM SEVERITY AND AGE

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Background: Proton Magnetic Resonance Spectroscopy (1H-MRS) studies indicate that altered brain glutamate signalling contributes to the pathophysiology of schizophrenia and treatment response. However it is unclear whether clinical and demographic factors affect glutamate levels in the brain. Here we aim to determine the effects of age, antipsychotic medication, symptom severity and duration of illness on levels of glutamatergic metabolites and creatine, in a large multicentre dataset of patients with schizophrenia and healthy volunteers.

Methods: Authors of 1H-MRS studies in schizophrenia were contacted between January 2014 and August 2017 and asked to provide individual glutamate, Glx, glutamine and creatine values alongside demographic and clinical data. Forty-five 1H-MRS studies contributed data to the multicentre dataset, and data was available from 1194 healthy volunteers and 1526 patients with schizophrenia and those at high risk of developing psychosis.
Results: Age was associated with reduced glutamate levels in the medial frontal cortex, but the effect of aging was not accelerated in patients compared to healthy volunteers. Higher glutamate and Glx in the medial frontal and temporal lobes were associated with more severe symptoms, whereas Glx in subcortical regions, specifically the thalamus and striatum, did not relate to symptom severity. In the medial frontal cortex and striatum, exposure to antipsychotic medication was associated with lower levels of glutamatergic metabolites. Duration of illness was not associated with glutamatergic metabolites. Lastly, creatine in the medial frontal cortex and thalamus increased with age.
Discussion: These data suggest that future 1H-MRS studies should control for the effects of age, symptom severity, and antipsychotic medication exposure. Caution is needed when using creatine as a reference to scale metabolites.

M158. ASSOCIATIONS OF NEUROLOGICAL SOFT SIGNS AND CEREBELLAR-CEREBRAL FUNCTIONAL CONNECTIVITY IN PATIENTS WITH FIRST-EPISODE SCHIZOPHRENIA AND THEIR UNAFFECTED SIBLINGS

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Background: Neurological softs signs (NSS) are defined as subtle neurological abnormalities with manifestations of motor coordination, sensory integration and disinhibition. Evidence has suggested NSS as one of the most promising endophenotypes for schizophrenia spectrum disorders. Moreover, accumulating evidence also suggest that NSS may be associated with specific functional connectivity. The present study aimed to examine the cerebellar-cerebral resting-state functional connectivity (rsFC) of NSS in patients with first-episode schizophrenia (FES) and their unaffected siblings (SB).
Methods: We administered the abridge version of the Cambridge Neurological Inventory (CNI) to 51 FES patients, 20 unaffected SB, and 50 healthy controls (HC) to assess the severity of NSS. All the participants also underwent a resting-state functional magnetic resonance imaging (MRI) scan. Ten regions of interest (ROIs) in the cerebellum were selected to represent cerebellar motor network (MN) and cerebellar executive control network (EN), which corresponded to the "sensorimotor-cognitive" dichotomy of NSS. rsFC between each ROI and the whole brain voxels were constructed, and the linear regression analysis was conducted to examine the cerebellar-cerebral rsFC patterns of NSS in each group.
Results: Regarding the cerebellar MN, there were positive correlations observed between the rsFC of the cerebellar MN with the default mode network (DMN) and NSS in FES patients group (CNI total score and the motor coordination subscale) and the SB group (CNI total score and the motor coordination and sensory integration subscales). The rsFC of the cerebellar MN and the sensorimotor network were significantly and positively correlated with NSS (CNI total score and the motor coordination and sensory integration subscales) in the SB group.
Regarding the cerebellar EN, we found that both the FES and the SB groups exhibited significantly negative correlations between NSS (CNI total score and the motor coordination subscale) and the rsFC of the cerebellar EN with the DMN. Moreover, the rsFC between the cerebellar EN and the sensorimotor network was positively correlated with NSS (CNI total score and the motor coordination and disinhibition subscales) in the SB group.
Discussion: We found inverse correlations between NSS and the rsFC of the cerebellar EN/MN and the DMN in both FES patients and their unaffected SB, suggesting that altered cerebellar-cerebral rsFC between these networks is correlated with the NSS. Moreover, the SB group exhibited a unique correlational pattern that NSS were correlated with the cerebellar-sensorimotor network rsFC, suggesting that such a network connectivity may serve as a potential biomarker for schizophrenia.

M159. PSYCHOTIC-LIKE EXPERIENCES, POLYGENIC RISK SCORES FOR SCHIZOPHRENIA AND STRUCTURAL PROPERTIES OF THE SALIENCE, DEFAULT MODE AND CENTRAL-EXECUTIVE NETWORKS IN HEALTHY PARTICIPANTS FROM UK BIOBANK

Abstract not included.

M160. INVESTIGATING STRUCTURAL CONNECTIVITY CORRELATES OF VERBAL MEMORY DEFICITS AMONG FIRST-EPISODE PSYCHOSIS PATIENTS

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Background: Verbal memory is one of the most affected cognitive domains in patients with schizophrenia and related psychoses. Several studies have found associations between cognitive abilities and white matter fractional anisotropy (FA) in schizophrenia; however, only a few tractography studies have investigated FA relative to verbal memory in patients with a first episode of psychosis (FEP) compared with healthy controls (HC). Although white matter tractography differences have been well established between chronic patients and HC, the direction of findings from FEP studies has been inconsistent. Thus, the present study aims to examine whole-brain white matter differences and its association with verbal memory in individuals with a FEP relative to HC using tractography.
Methods: Diffusion-weighted images were acquired on a 1.5T scanner for patients (n=65) and controls (n=54) at baseline. The Wechsler Memory Scale was used as a measure of verbal memory. Pre-processing was performed on a subject-by-subject basis using MRtrix. Diffusion tractography was generated using a probabilistic anatomically-constrained tractography algorithm, which constrains the reconstruction to specific biological priors. Furthermore, the spherical-deconvolution informed filtering of tractograms (SIFT) tool will be used to ensure the tractogram is biologically meaningful. This results in subject-specific connectomes defining the mean FA between two regions of interest that were defined using the Desikan- Killiany atlas. A linear model was used to test for main effect of group and main effect of verbal memory on white matter tract FA, covarying for age and sex. For both sets of analyses, results were corrected for multiple comparisons using false discovery rate (FDR).
Results: A significant main effect of group on whole-brain average FA was observed, with patients displaying lower average FA compared to healthy controls (Patients=0.291, controls=0.300, $p<0.05$). Whole-brain white matter tract FA analysis revealed that there are widespread differences