O2.2. EVALUATION OF THE RELATIONSHIP BETWEEN GLUTAMATE AND BRAIN CONNECTIVITY IN ANTIPSYCHOTIC-NAÏVE FIRST EPISODE PATIENTS – A COMBINED MAGNETIC RESONANCE SPECTROSCOPY AND RESTING STATE FUNCTIONAL CONNECTIVITY MRI STUDY

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Background: Schizophrenia is thought to be a disorder of brain dysconnectivity. An imbalance between cortical excitation/inhibition is also implicated, but the link between these abnormalities remains unclear. The present study used resting state functional connectivity MRI (rs-fMRI) and magnetic resonance spectroscopy (MRS) to investigate how measurements of glutamate + glutamine (Glx) in the anterior cingulate cortex (ACC) relate to rs-fMRI in medication-naïve first episode psychosis (FEP) subjects compared to healthy controls (HC). Based on our previous findings, we hypothesized that in HC would show correlations between Glx and rs-fMRI in the salience and default mode network, but these relationships would be altered in FEP.

Methods: Data from 53 HC (age = 24.70 ±6.23, 34M/19F) and 60 FEP (age = 24.08 ±6.29, 38M/22F) were analyzed. To obtain MRS data, a voxel was placed in the ACC (PRESS, TR/TE = 2000/80ms). Metabolite concentrations were quantified with respect to internal water using the AMARES algorithm in jMRUI. rs-fMRI data were processed using a standard preprocessing pipeline in the CONN toolbox. BOLD signal from a priori brain regions of interest from posterior cingulate cortex (default mode network, DMN), anterior cingulate cortex (salience network, SN), and right posterior parietal cortex (central executive network, CEN) were extracted and correlated with the rest of the brain to measure functional connectivity (FC). Group analyses were performed on Glx, FC, and Glx-FC interactions while controlling for age, gender, and motion when applicable. FC and Glx-FC analyses were performed using small volume correction (p<0.01, threshold-free cluster enhancement corrected (TFCE)).

Results: No significant between-group differences were found in Glx concentration in the ACC [F(1, 108) = 0.34, p = 0.56], but reduced FC was found on each network in FEP compared to HC (pTFCE corrected). Group Glx-FC interactions were found in the form of positive correlations between Glx and FC in DMN and SN in the HC group, but not in FEP; and negative correlations in CEN in HC, but not in FEP.

Discussion: While we did not find significant group differences in ACC Glx measurements, ACC Glx modulated FC differentially in FEP and HC. Positive correlations between Glx and FC were found in the SN and DMN, suggesting long range modulation of the two networks in HC, but not in FEP. Additionally, negative correlations between Glx and FC were found in CEN in HC, but not in FEP. Overall, these results suggest that even in the absence of group differences in Glx concentration, the long-range modulation of these 3 networks by ACC Glx is altered in FEP.

O2.3. ABNORMAL BRAIN AGING IN YOUTH WITH SUBCLINICAL PSYCHOSIS AND OBSESSIVE-COMPULSIVE SYMPTOMS

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Background: Psychiatric symptoms in childhood and adolescence have been associated with both delayed and accelerated patterns of grey matter development. This suggests that deviation in brain structure from a normative range of variation for a given age might be important in the emergence of psychopathology. Distinct from chronological age, brain age refers to the age of an individual that is inferred from a normative model of brain structure for individuals of the same age and sex. We predicted brain age from a common set of grey matter features and examined whether the difference between an individual’s chronological and brain age was associated with the severity of psychopathology in children and adolescents.

Methods: Participants included 1313 youths (49.8% male) aged 8-21 who underwent structural imaging as part of the Philadelphia Neurodevelopmental Cohort. Independent Component Analysis was used to obtain 7 psychopathology dimensions representing Conduct, Anxiety, Obsessive-Compulsive, Attention, Depression, Bipolar, and Psychosis symptoms and an overall measure of severity (General Psychopathology). Using 10-fold cross-validation, support vector machine regression was trained in 402 typically developing youth to predict individual age based on a feature space comprising 111 grey matter features. This yielded a brain age prediction for each individual. Brain age gap was calculated for each individual by subtracting chronological age from predicted brain age. The general linear model was used to test for an association between brain age gap and each of the 8 dimensions of psychopathology in a test sample of 911 youth. The regional specificity and spatial pattern of brain age gap was also investigated. Error control across the 8 models was achieved with a false discovery rate of 5%.

Results: Brain age gap was significantly associated with dimensions characterizing obsessive-compulsive (t=2.5, p=0.01), psychosis (t=3.16, p=0.0016) and general psychopathology (t=4.08, p<0.0001). For all three dimensions, brain age gap was positively associated with symptom severity, indicating that individuals with a brain that was predicted to be ‘older’ than expectations set by youth of the same chronological age and sex tended to have higher symptom scores. Findings were confirmed with a categorical approach, whereby higher brain age gap was observed in youth with a lifetime endorsement of psychosis (t=2.35, p=0.02) and obsessive-compulsive (t=2.35, p=0.02) symptoms, in comparison to typically developing individuals.

Discussion: We found that the brain was ‘older’ in youth experiencing higher subclinical symptoms of psychosis, obsession-compulsion, and general psychopathology, compared to normally developing youth of the same chronological age. Our results suggest that deviations in normative brain age patterns in youth may contribute to the manifestation of specific psychiatric symptoms of subclinical severity that cut across psychopathology dimensions.

O2.4. FUNCTIONAL CONNECTOME-WIDE ASSOCIATIONS OF SCHIZOPHRENIA POLYGENIC RISK

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Background: The relationships between schizophrenia polygenic risk and connectome-wide brain connectivity remain unclear. In particular, it is unknown whether and how schizophrenia polygenic risk would influence functional connectivity both at the connectome level and in a state-independent way. In this study, we used multi-paradigm fMRI data from two independent cohorts to investigate these questions.

Methods: The discovery sample included 625 healthy Caucasian participants (age 28.86 ± 3.63 years, 302 males) acquired from the Human Connectome Project (HCP). All subjects completed fMRI scans for a battery of eight paradigms and had imputed genetic data available. Following the procedures in our prior studies, we constructed whole-brain connectivity matrices for each paradigm in each individual. From these derived