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Background: The N-methyl-D-aspartate receptor (NMDAR) hypofunction model of schizophrenia suggests that dysfunction of these receptors could underlie the brain functional abnormalities characterising these patients. In NMDAR encephalitis (NMDARE), which holds clinical similarities with schizophrenia, autoantibodies target NMDARs, predominantly located in the hippocampal region, leading to disrupted glutamatergic transmission. One study so far has described abnormal connectivity between the medial temporal lobe and posterior default mode network regions in patients with NMDARE (Peer et al., 2017), however no study so far has examined brain functional correlates of schizophrenia and NMDARE comparatively.
Methods: Patients with schizophrenia (N=16) and with NMDARE shortly after clinical stabilisation (N=15) were recruited within a tertiary setting, and compared with age and sex-matched healthy volunteers (N=20). All individuals were scanned with a 3T Siemens scanner including a functional resting state sequence, during which individuals were instructed to view a fixation cross. A seed-based analysis was performed using a spherical seed of 4mm located in the left hippocampus (MNI coordinates x =-32, y=-24, x=-14). Only grey matter voxels were considered to obtain the seed average signal. BOLD signal was preprocessed including slice timing, motion correction, spatial smoothing, and frequency filtering, and regressed taken into account movement parameters (rigid transformation, frame displacement, and DVARS). Statistics was performed between the correlation maps including age and sex as covariates. Family-wise error (FWE) was used to correct for multiple comparisons.
Results: Seed to voxel analyses revealed connectivity between the seed and the bilateral thalamus, parahippocampus, precuneus, posterior cingulate, right hippocampus and lateral temporal regions (threshold Fisher's z > 0.28). We first examined differences in connectivity between both patient groups combined and healthy volunteers, which revealed greater connectivity in patients than in controls between the left hippocampus and the left inferior parietal, postcentral and posterior cingulate gyri (pFWE< 0.05). When examining patient groups individually, patients with schizophrenia continued to exhibit significantly greater connectivity between the left hippocampus and left inferior parietal and postcentral region (pFWE< 0.05) and at near trend level in the posterior cingulate (pFWE= 0.15). NMDARE patients also presented near trend level increased connectivity in the posterior cingulate and postcentral gyri (pFWE= 0.10). There were no differences in functional connectivity of the left hippocampus between patients with schizophrenia and with NMDARE.
Discussion: To our knowledge, this is the first study to compare patients with schizophrenia with patients with NMDARE using measures of brain function. We found that, for both conditions, the left hippocampus showed greater connectivity with areas belonging to the posterior default mode network. Connectivity between these regions has been associated with psychotic symptoms in schizophrenia (Lefebvre et al., 2016). Our findings suggest that this alteration could also underlie neuropsychiatric symptoms in NMDARE, and provides further evidence that NMDAR dysfunction may underpin the pathophysiology of schizophrenia.

S165. GLUTAMATERGIC ABNORMALITIES IN EARLY SCHIZOPHRENIA AND BIPOLAR DISORDER MEASURED USING WHOLE-BRAIN SPECTROSCOPY

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Background: Glutamatergic abnormalities in schizophrenia and bipolar disorder gave been identified using proton magnetic resonance spectroscopy (1H-MRS). Although schizophrenia and bipolar disorder are both known to involve extensive brain networks, most MRS studies have been done using single-voxel techniques. In this study we used whole brain 1H-MRS to examine glutamine-plus-glutamate (Glx) in early schizophrenia and bipolar disorder to examine metabolic abnormalities associated with affective and non-affective psychosis and with exposure to antipsychotic medication.
Methods: Three dimensional 1H-MRS was acquired in young schizophrenia (SCZ, N=36, 24 M, 22.8±3.9 years, 19 antipsychotic-naïve and 17 antipsychotic-treated), bipolar (N=13, 5 antipsychotic-naïve and 8 antipsychotic-treated), schizoaffective-bipolar type (N= 3, 2 antipsychotic-naïve and 1 antipsychotic-treated) subjects, and healthy controls (HC, N=29, 17M, 23±4.4yrs). Glx, N-acetylaspartate, choline, myo-inositol and creatine group contrasts from all individual voxels that met spectral quality were analyzed in common brain space (voxel-wise p-threshold=0.001), followed by cluster-corrected alpha value (p<0.05). Bipolar subjects (N=13) and schizoaffective-bipolar type (N=3) were combined (SBP) (N=16, 11M, 21.9±2.9yrs, 7 antipsychotic naïve and 9 antipsychotic-treated).
Results: SCZ subjects compared to HC had lower Glx in the left superior (STG) and middle temporal gyri (16 voxels, p=0.04) and increased creatine in two clusters involving left temporal, parietal and occipital regions (32, and 18 voxels, p=0.02 and 0.04, respectively). Antipsychotic-treated and naïve SCZ had similar Glx reductions (8/16 vs 10/16 voxels respectively, but p's>0.05). However, creatine was higher in antipsychotic-treated vs HC's in a larger left hemisphere cluster (100 voxels, p=0.01). Also in treated SCZ, choline was increased in left middle frontal gyrus (18 voxels, p=0.04). Finally, in antipsychotic-naive SCZ, NAA was reduced in right frontal gyri (19 voxels, p=0.05) and myo-inositol was reduced in the left cerebellum (34 voxels, p=0.02). SBP subjects had no significant differences from HC in any area of the brain for any of the metabolites at a voxel-wise p-threshold of 0.001. A cluster of reduced Glx was found at in the right cuneus and precuneus (276 voxels, p=0.05) using a less stringent voxel-wise p-threshold of p< 0.05.
Discussion: Data-driven spectroscopic brain examination supports the presence of reductions in Glx in the left STG early in the course of schizophrenia; this was not seen in individuals with bipolar symptoms. A trend toward decreased Glx in the right cuneus and pre-cuneus in bipolar and schizoaffective patients is consistent with previous findings of abnormal function in this area. The left STG may be a critical target for postmortem and neuromodulation studies in schizophrenia studies.

S166. EFFECTIVE CONNECTIVITY OF FRONTOSTRIATAL SYSTEMS IN FIRST-EPISODE PSYCHOSIS

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Background: Neuroimaging studies have found dysconnectivity of frontostriatal circuits across a broad spectrum of psychotic symptoms. However, it is unknown whether dysconnectivity within frontostriatal circuits originates from disrupted bottom-up or top-down control signaling within these systems. Here, we used dynamic causal modelling (DCM) to examine the effective connectivity of frontostriatal systems in first-episode psychosis (FEP).

Methods: A total of 55 FEP patients (26 males; mean [SD] age = 19.24 [2.89]) and 24 healthy controls (15 males; mean [SD] age = 21.83 [1.93]) underwent a resting-state functional magnetic resonance imaging protocol. Biologically plausible connections between eight left hemisphere regions encompassing the dorsal and ventral frontostriatal systems were modelled using spectral DCM. The regions comprise dorsolateral prefrontal cortex, ventromedial prefrontal cortex, anterior hippocampus, amygdala, dorsal caudate, nucleus accumbens, thalamus, and the midbrain. Effective connectivity between groups were assessed using a parametric Bayesian model. Associations between effective connectivity parameters and positive symptoms, measured by the Brief Psychiatric Rating Scale positive subscale, was assessed in the patient group in a separate Bayesian general linear model.
Results: DCM shows evidence for differences in effective connectivity between patients and healthy controls, namely in the bottom-down connections distributed in the frontostriatal system encompassing the hippocampus, amygdala, striatum, and midbrain. Compared to healthy controls, patients also demonstrated increased disinhibition of the midbrain. In patients, positive symptoms are associated with increased top-down connections to the midbrain. Outgoing connection from the midbrain to the nucleus accumbens is also increased in association with positive symptoms.
Discussion: Aberrant top-down connectivity in the frontostriatal system in patients is consistent with top-down dysregulation of dopamine function in FEP, as dopaminergic activity in the midbrain is proposed to be under the control of higher brain areas. In patients, increased self-inhibition of the midbrain, as well as symptom associations in both ingoing and outgoing connections of this region, are congruous with hyperactivity of the midbrain as proposed by the dopamine dysregulation hypothesis. Here, we demonstrate that mathematical models of brain imaging signals can be used to identify the key disruptions driving brain circuit dysfunction, identifying new targets for treatment.

S167. THE EFFECT OF THE CATECHOL-O-METHYLTRANSFERASE VAL153MET POLYMORPHISM ON TEMPORAL INTERHEMISPHERIC CONNECTIVITY AND LANGUAGE COMPREHENSION IN PATIENTS WITH SCHIZOPHRENIA

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Background: Difficulties in language comprehension is the major psychopathology in schizophrenia. The catechol-O-methyltransferase (COMT) Val153Met polymorphism, a candidate gene related to the pathogenesis of schizophrenia, is associated with higher cognitive abilities including language comprehension. At the brain level, this function is known to be supported by reciprocal communication via transcallosal projections between the temporal regions. This study investigated the effect of the COMT Val153Met polymorphism on white matter (WM) integrity of the tapetum, which connects the bilateral temporal lobes, and language comprehension in patients with schizophrenia.
Methods: Ninety patients with schizophrenia participated in this study. The COMT Val153Met polymorphism was analyzed, and the genotype groups were divided into Val-allele homozygotes and Met-allele carriers (45 participants in each group). Diffusion tensor imaging (DTI) data were acquired from all participants. Fractional anisotropy (FA) values were extracted from the bilateral tapetum. The levels of language comprehension were measured using verbal comprehension subtests of the Korean version of WAIS.
Results: Val-allele homozygotes showed higher FAs in left tapetum than Met-allele carriers (mean ± SD: val-allele homozygotes = 0.809 ± 0.059, Met-allele carriers = 0.777 ± 0.079; t = 2.16, p = 0.034). The right tapetum FAs were not different between two groups. (mean ± SD: val-allele homozygotes = 0.772 ± 0.065, Met-allele carriers = 0.748 ± 0.061; t = 1.83, p = 0.071). Although the sum of verbal comprehension subtest scores did not differ between two groups, only Val-allele homozygotes showed a negative correlation between the sum scores and left tapetum FAs (val-allele homozygotes: r = -0.426, p = 0.021, Met-allele carriers: r = -0.193, p = 0.275).
Discussion: This study suggests that the COMT Val153Met polymorphism may be associated with structural changes in interhemispheric WM tracts connecting the temporal regions. Furthermore, COMT-associated WM changes may contribute to individual variations in language comprehension of patients with schizophrenia, particularly Val-allele homozygotes. We expect that our findings provide some clues for understanding the interaction between the brain and genes in patients with schizophrenia.

S168. THE ASSOCIATION BETWEEN MMP-9 AND CHOROID PLEXUS VOLUME IN SCHIZOPHRENIA

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Background: Schizophrenia (SCZ) is a severe and chronic brain disorder that affects about 1% of the world population. It is among the most burdensome illnesses with a serious impact on patients, their families and society. To this day, a lot remains unknown about the neuropathological cause and etiology of SCZ.
The prominent two-hit theory postulates that early neurodevelopmental abnormalities interact with a later "second hit" which occurs around symptom onset. Recent research points towards the role of inflammation in pathophysiology of schizophrenia.
Matrix metalloproteinase-9 (MMP-9) was recently suggested as a potential key player in both first and second "hit" in the pathology of SCZ. It is considered to not only regulate brain development and synaptic plasticity, but to also mediate neuroinflammation. A point of interest for interaction with neuroinflammatory pathways is the Choroid Plexus (ChP). MMP-9 has been reported to be upregulated in ChP in SCZ. Since ChP regulates CSF production and permeability of the blood-CSF-barrier, MMP-9 upregulation in ChP might lead to its enlargement, as well as enlargement of the lateral ventricles and increased extracellular water volume, all found previously in SCZ. We investigate, for the first time, the relationship between MMP-9 blood plasma concentration and volume of ChP in patients with SCZ compared to healthy controls (HC).
Methods: We included 66 subjects (25 female = 38%, 41 male = 62%, mean age 32.59 +/- 9.14 years); 32 were patients with SCZ, 34 were HC.
ELISA analysis was performed to measure MMP-9 blood concentrations in patients and HC.
A whole brain, high-resolution three-dimensional T1-weighted magnetization prepared rapid gradient echo (MPRAGE) sequence scan was used to collect 240 sagittal slices, field of view = 224 x 224 mm2, 1 mm3 isotropic voxel, TR = 2.3 s, TE = 2.33 ms, flip angle = 8° on a 3T Siemens Magnetom Prisma.

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