S145. ANTIPSYCHOTIC DISCONTINUATION IN FIRST EPISODE PSYCHOSIS: [18F]DOPA AND [11C]RACLOPRIDE PET STUDY

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Background: Recent meta-analysis revealed that elevated presynaptic striatal dopaminergic function is a robust feature of psychosis like schizophrenia. Considering increased dopaminergic capacity in psychotic disorders, it is not surprising that antipsychotic drugs, which primarily block dopaminergic neurotransmission, are mostly effective in the treatment of psychosis. However, it remains obscure what would happen to presynaptic dopaminergic function with antipsychotic treatment. This is an important issue addressing whether the current antipsychotic drugs are correcting the primary dopaminergic abnormality or not. In addition, the issue can give a clue regarding the mechanism of relapse in psychotic disorders.

Methods: We measured presynaptic dopamine capacity using [18F]DOPA PET before and after the antipsychotic discontinuation in first episode psychosis. The binding potentials of [11C]raclopride were also measured after the discontinuation. Healthy controls had [18F]DOPA and [11C]raclopride scans at the corresponding date.

First episode psychosis patients were carefully monitored in the aspects of symptomatic aggravations.

Results: The presynaptic dopamine capacity and the density of dopamine receptors showed significant group effect and the interaction between group and time (p<0.005)

Discussion: Dopaminergic function seems to play a critical role in relapse of first episode psychosis.

S146. EFFECT OF CLOZAPINE ON REGIONAL CEREBRAL BLOOD FLOW IN TREATMENT-RESISTANT SCHIZOPHRENIA

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Background: Approximately one-third of schizophrenia patients will not respond adequately to conventional antipsychotic treatment; termed treatment-resistant schizophrenia (TRS). The only antipsychotic recommended for this group is clozapine, which may have unique efficacy in improving residual symptoms. The biological mechanisms underlying its efficacy are poorly understood. Previous studies have examined the effects of clozapine on regional cerebral blood flow (rCBF) using radiotracer approaches in relatively small samples of patients, showing, in particular, frontal and limbic perfusion changes1,2,3. In this study, we evaluate the effects of clozapine on rCBF, measured with a non-invasive MRI technique - pulsed continuous arterial spin labelling (pCASL) - which does not require radiotracer injection, as part of an ongoing study to identify neuroimaging predictors and mediators of clozapine response.

Methods: Participants ≥18 years of age with TRS were recruited at the Institute of Psychiatry, Psychology & Neuroscience, Kings College London (UK). TRS status was ascertained by the documented failure to respond to at least two different antipsychotic trials of adequate length. Participants were either clozapine-naïve or had not taken clozapine for at least three months prior to the baseline MRI scan. After baseline MRI, clozapine was administered as part of routine clinical care for 12 weeks, after which a second MRI scan was performed. Symptomatic response was defined as a reduction of 20% of the Positive and Negative Syndrome Scale (PANSS) score and non-response was defined as <20% decrease in PANSS score.

pCASL data was acquired on a General Electric 3 Tesla MR-750 MR scanner. Arterial blood was labelled using a long, adiabatic (1.8 seconds) radio frequency pulse. After a post-labeling delay of 2.025s, perfusion images were acquired with a 3D Fast Spin Echo spiral multi-shot readout (TE 32ms/TR = 5500ms; ETL = 64). Cerebral blood flow (CBF) maps were computed with a spatial resolution of 2x2x3mm, in a total acquisition time of less than 6min. CBF maps were pre-processed using the Automatic Software for ASL processing (ASAP) toolbox5. Changes in rCBF after 12 weeks of clozapine were analysed in a full factorial ANOVA design, using SPM 12 (www.fil.ion.ucl.ac.uk/spm). Clusters of significant CBF changes were assessed at p<0.05 after Family-Wise Error correction for cluster extent, using a cluster-forming threshold of T>2.74.

Results: This is an interim analysis of 24 patients who completed both scans. Contrasts were examined at a whole brain, assumption-free voxel-wise analysis, restricted to grey matter and co-varied for global perfusion. Clozapine administration significantly decreased perfusion in the medial frontal gyri. There was also a significant response x time interaction, centred in the left posterior cingulum and extending to the bilateral visual cortex and right precuneus.

Discussion: These interim results indicate that pCASL may be able to identify brain regions in which activity is modulated by clozapine administration as well as areas that may mediate symptomatic improvement. A key question for future analyses will be the degree to which rCBF may predict symptomatic response to clozapine, as the ability to predict a good likelihood of response could enable earlier clozapine initiation.

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S147. ASSOCIATION BETWEEN SOCIAL ANHEDONIA AND TOPOLOGICAL PROFILE OF BRAIN NETWORK IN SCHIZOPHRENIA

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Background: As a refractory negative symptom, social anhedonia is prevalent in people with schizophrenia spectrum disorders. Furthermore, schizophrenia is conclusively correlated with disorganized functional brain network reflected by topological profile. However, studies on the relationship between social anhedonia and topological properties of functional brain network in schizophrenia were limited to a large extent. In the present study we explored the neurofunctional mechanism of social anhedonia in schizophrenia from the perspective of topological profile of functional brain network.

Methods: Six-minute resting-state fMRI images were acquired from 65 patients with schizophrenia in a 3T SIMENS scanner. Topological properties of functional brain network derived from the resting-state fMRI image, including clustering coefficient, global efficiency and small-worldness were calculated. The social anhedonia of each participant was measured with the Chapman Social Anhedonia Scale. Due to the wide-range of duration of illness in patients with schizophrenia, we included the duration of illness, social anhedonia and their interaction into a generalized linear model to predict the three topological properties, with gender, age and education years as covariates.