Results: We found that the clustering coefficient of brain functional network in schizophrenia increased (p = 0.032, beta = 0.000194 at the minimum network sparsity 35% in which all the nodes were fully connected), whereas the global efficiency decreased (p = 0.005, beta = -0.000022), as the progression of schizophrenia. Although the main effect of social anhedonia in predicting both the clustering efficient and the global efficiency were not significant, its interaction with the duration of illness was significant (p = 0.021, beta = 0.000038 for the clustering coefficient; p = 0.023, beta = -0.000063 for the global efficiency).

Discussion: With the development of schizophrenia, the increase of clustering coefficient and decrease of global efficiency of functional brain network may reflect the pathophysiology of schizophrenia since the onset of illness. Social anhedonia plays as a mediator between the altered topological profile of brain network and the progression of schizophrenia.

S148. DIFFERENTIAL NEURAL REWARD MECHANISMS IN TREATMENT RESPONSIVE AND TREATMENT RESISTANT SCHIZOPHRENIA

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Background: The significant proportion of schizophrenia patients refractory to treatment targeting the dopamine system suggests that more than one mechanism may cause psychotic symptoms. Reinforcement learning tasks have frequently been employed in schizophrenia to assess dopaminergic functioning and reward processing, but studies have not directly compared groups of treatment-refractory and non-refractory patients.

Methods: In the current functional magnetic resonance imaging study 21 patients with treatment resistant schizophrenia (TRS), 21 patients with non-treatment resistant schizophrenia (NTR), and 24 healthy controls (HC) performed a probabilistic reinforcement learning task, utilising emotionally valenced face stimuli which elicit a social bias toward happy faces. Behavior was characterized with a reinforcement learning model. Trial-wise reward prediction error (RPE) signaling and the differential impact of emotional bias on these reward signals were compared between groups.

Results: Patients showed impaired reinforcement learning relative to controls, while all groups demonstrated an emotional bias favouring selection of happy faces. The pattern of RPE signaling was similar in HC and TRS groups, whereas NTR patients showed significant attenuation of RPE-related activation. The TRS patients differed from the NTR patients in the relationship between emotional bias and subcortical RPE signal during negative feedback.

Discussion: TRS can be dissociated from NTR on the basis of a different neural mechanism underlying their symptoms. The data support the hypothesis that a favourable response to antipsychotic treatment may be contingent on dopaminergic dysfunction, characterized by aberrant RPE signaling, whereas treatment resistance may be characterized by an abnormality in distinct cognitive mechanisms interacting with this response.

S149. EFFECTS OF INTRANASAL OXYTOCIN ON RESTING CEREBRAL BLOOD FLOW IN PEOPLE AT ULTRA-HIGH RISK FOR PSYCHOSIS

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Background: Recent research suggests that individuals at ultra-high risk for psychosis (UHR) show altered resting cerebral blood flow (rCBF) in key regions linked to psychosis pathophysiology: the hippocampus, midbrain, and basal ganglia. Greater perturbations in basal ganglia rCBF were correlated with positive psychotic symptoms, while remission from the UHR state was associated with a longitudinal normalization of hippocampal rCBF. Oxytocin -a neuropeptide with potential anxiolytic and prosocial properties- is currently under investigation as a novel therapeutic for a number of neuropsychiatric disorders. Previous work conducted in healthy males demonstrated that a single acute dose of intranasal oxytocin had marked effects on rCBF across all of the aforementioned regions (hippocampus, basal ganglia, midbrain), as well as the amygdala, anterior cingulate cortex and cerebellum - regions where neurofunctional alterations have been previously reported in UHR groups. Despite these findings, no studies have yet examined the effects of intranasal oxytocin on resting perfusion in UHR individuals.

Methods: In a double-blind, placebo-controlled, crossover design, 30 UHR males underwent two MRI scans at 3 Tesla, once after 40IU intranasal oxytocin and once after matched placebo (one-week wash-out). Arterial spin labeling (ASL) was used to measure rCBF starting approximately 22 minutes post-intranasal administration. The severity of attenuated psychotic symptoms was assessed using the Comprehensive Assessment of At-Risk Mental States (CAARMS). Measures of social cognition, emotional processing and level of functioning were also acquired. We hypothesized that relative to placebo, a single acute dose of intranasal oxytocin would modulate rCBF in the hippocampus, basal ganglia and midbrain, and that this effect would be greater in those with more severe baseline deficits in social and emotional functioning.

Results: Data analysis is currently ongoing and the results will be presented at the conference.

Discussion: These results will provide physiological evidence for a potential first-in-class intervention for UHR patients. Given the current lack of evidence for effective treatments in this patient group, better understanding of the neural correlates of the high-risk state and the physiological basis for the effects of novel therapeutics is desperately warranted.

S150. DOPAMINE SYNTHESIS CAPACITY IN ANTIPSYCHOTIC NAIVE FIRST EPISODE PSYCHOTIC PATIENTS

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Background: Insufficient response to antipsychotics constitutes a challenge in the treatment of patients suffering from schizophrenia. Treatment resistances have been linked to a normal striatal dopamine system. We aim to stratify antipsychotic-naive first-episode patients based on striatal dopamine synthesis capacity (DSC) measured with positron emission tomography (PET). We hypothesize that patients who respond to treatment have an increased DSC at baseline compared to non-responders and healthy controls (HC).

Methods: The current data have been collected as part of a multimodal first episode study. Patients are examined before and after 6 weeks treatment with flexible doses of Aripiprazole. PET: Dynamic scans are performed in an integrated PET-CT scanner using the tracer 3,4-dihydroxy-6-[18F]fluoro-L-phenylalanine (18F-FDOPA). Duration of scanning is two times one hour, with half an hour break.

Discussion: The significant proportion of schizophrenia patients refractory to treatment targeting the dopamine system suggests that more than one mechanism may cause psychotic symptoms. Reinforcement learning tasks have frequently been employed in schizophrenia to assess dopaminergic functioning and reward processing, but studies have not directly compared groups of treatment-refractory and non-refractory patients.