S8. GRIN1 Promoter Methylation Changes In Blood Of Early-Onset Psychotic Patients And Unaffected Siblings With Childhood Trauma

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ns; 40 mg/day=3.6%, p<0.05; 80 mg/day=4.9%, p<0.01; 120 mg/day=9.3%, p<0.001, PM dosing group: 20 mg/day=-0.4%, ns; 40 mg/day=2.8%, p<0.05: 80 mg/day=0.2%, ns; 160 mg/day=5.8%, p<0.05).
There was no clear dose-dependent trend associated with nausea and RD was similar between AM and PM dosing group (AM dosing group: 20 mg/day=0.2% ns; 40 mg/day=3.8%, p<0.05; 80 mg/day=3.8%, ns; 120 mg/day=6.6%, ns, PM dosing group: 20 mg/day=-1.6%, ns; 40 mg/day=-1.7%, ns; 80 mg/day=5.5%, p<0.01; 160 mg/day=2.8%, ns).
Discussion: The risk of adverse events in the treatment of schizophrenia with lurasidone can vary depending on the timing of administration. In particular, for akathisia and somnolence, the incidence risks were reduced when lurasidone was administered in PM. Unlike with AM administration, the dose-dependence in the risks of these adverse events were not observed in lurasidone PM administration.
The timing of lurasidone administration could be considered in effort to minimize potential adverse events.

S6. SLEEP ENDOPHENOTYPES OF SCHIZOPHRENIA: A HIGH-DENSITY EEG STUDY IN DRUG-NAÏVE, FIRST EPISODE PSYCHOSIS PATIENTS

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Background: Slow waves, the hallmark of the deep nonrapid eye movement sleep electroencephalogram (EEG), are critical for restorative sleep and brain plasticity. They arise from the synchronous depolarization and hyperpolarization of millions of cortical neurons and their proper generation and propagation relies upon the integrity of widespread cortico-thalamic networks. Slow wave abnormalities have been reported in patient with Schizophrenia, although with partially contradictory results, probably related to antipsychotic and sedative medications. Recently, their presence and delineation, have been convincingly shown in first-episode psychosis patients (FEP). However, clear evidence of this biomarker at the onset of the disease, prior to any psychopharmacological intervention, remains limited. Moreover, no attempt has been made to elucidate the prognostic meaning of this finding.
Methods: We collected whole night sleep high–density electroencephalography recordings (64-channel BrainAmp, Brain Products GmbH, Gilching, Germany) in 20 drug-naive FEP patients and 20 healthy control subjects (HC). Several clinical psychometric scales as well as neurocognitive tests were administered to all subjects in order to better define psychopathological status and vulnerability. EEG slow wave activity (SWA, spectral power between 1 and 4 Hz) and several slow wave parameters were computed at each electrode location, including density and amplitude, at each electrode location. Along with a group analysis between FEP and HC, a subgroup analysis was also computed between patients who showed a progression of symptoms to full-blown Schizophrenia (SCZ, n = 10) over the next 12-month follow-up and those who did not (OTH, n = 10).
Results: Sleep macro-architecture was globally preserved in FEP patients. SWA (1–4 Hz) was lower in FEP compared to HC but this difference didn't reach statistical significance. Slow wave density was decreased in FEP compared to HC, with a significance that survived multiple comparison correction over a large fronto-central cluster. Mean amplitude was preserved. At the subgroup analysis, these results were largely driven by the subgroup of patients with a confirmed diagnosis of SCZ at a 12-month follow-up. Indeed, no difference could be found between OTH and HC, while a strong significance was still evident between SCZ and HC.
Discussion: Our data confirm previous findings on reduced slow wave density in FEP, and expand them to acute subjects, before any treatment is prescribed. This is in line with available data on diffuse abnormalities of cortico-cortical and cortico-thalamic networks in these patients. Interestingly, our data also offer preliminary evidence that this deficit is specific for SCZ, as it appears to differentiate patients who developed SCZ from those with other diagnoses at follow-up. Given the traveling properties of slow waves, future research should establish their potential as markers of connectivity in SCZ.

S7. INVESTIGATING THE LINK BETWEEN THE PERIPHERAL ENDOCANNABINOID SYSTEM AND CENTRAL GLUTAMATERGIC NEUROTRANSMISSION IN EARLY PSYCHOSIS: A 7T-MRS STUDY

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Background: Meta-analytic evidence showed increased levels of peripheral endocannabinoid metabolites in psychotic illness. Alterations in the endocannabinoid system are believed to compromise glutamate and dopamine transmission, which play a central role in pathophysiological models of psychosis. I will present preliminary data from an ongoing high-field proton magnetic resonance spectroscopy (MRS) study aimed at investigating the association between peripheral levels of endocannabinoid system metabolites and central glutamate metabolism in individuals at their first non-affective psychotic episode (NA-FEP) and healthy controls.
Methods: We expect to recruit 17 NA-FEP and 20 healthy controls by January 2020. Currently, we recruited 12 NA-FEP and 18 healthy controls from two different research facilities (Imperial College London and University of Oxford) as part of a cross-sectional study. Participants underwent MRS scanning at 7-T with voxels placed in right dorsolateral prefrontal cortex (right-DLPFC), anterior cingulate cortex (ACC), and occipital cortex. Neuro-metabolites will be calculated using the unsuppressed water signal as reference. Endocannabinoid metabolites were quantified from serum samples, collected during the same imaging session.
Results: Analyses are ongoing. Based on previous evidence, expected findings are: (i) reduced glutamate levels in the ACC and right-DLPFC of NA-FEP compared to controls; (ii) increased peripheral endocannabinoid metabolites in NA-FEP compared to controls; and (iii) inverse association between peripheral endocannabinoid metabolites and glutamate levels in ACC and right-DLPFC in NA-FEP
Discussion: This study will help clarifying the contribution of peripheral endocannabinoid system to central brain mechanisms of key relevance for psychotic illness. It will also add further evidence on the limited literature on high-resolution characterisation of brain metabolites in early psychosis. Strengths of the study include: (i) use of high-field MRS, which allows the estimation of glutamate-related compounds at higher precision than at lower field strength; (ii) reduced heterogeneity of the clinical sample (only male and NA-FEP). Limitations: small sample size and cross-sectional design.

S8. GRIN1 PROMOTER METHYLATION CHANGES IN BLOOD OF EARLY-ONSET PSYCHOTIC PATIENTS AND UNAFFECTED SIBLINGS WITH CHILDHOOD TRAUMA

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Background: Childhood trauma may lead to impairments in brain development and increases risk at psychiatric disorders. Evidence also suggests that childhood trauma may affect DNA methylation patterns consequently influencing gene expression (Tomassi et al., 2017). Some of this linking may be correlated with N-methyl-d-aspartate receptor (NMDAR) hypofunction, which plays a major role of central aspects of cognitive and negative features of schizophrenia (Lakhan et al., 2013). Specifically, the GRIN1 gene codes the biologically relevant NMDAR subunit involved in the synaptic plasticity which is expressed in a broad of non-neuronal cells (Hogan-Cann et al., 2016). Aims: We investigated DNA methylation in the promoter region of GRIN1 and LINE-1 methylation in first-episode psychosis patients (FEP), their unaffected siblings and community-based controls with and without childhood trauma. We also tested for correlations between GRIN1 methylation and NR1 concentrations in peripheral blood.
Methods: This study is a part of the epidemiological investigation that estimated the incidence of psychosis and the role of environmental and biological factors in psychosis aetiology in the catchment area of Ribeirão Preto, Brazil, from 1st April 2012 to 31st March 2015. The genomic DNA was extracted from blood of 60 FEP patients, 30 of their unaffected siblings and 60 age- and sex-matched community-based controls. Diagnosis and clinical characteristics were assessed using the DSM-IV (First et al., 1997; Del-Ben et al., 2001) and history of childhood trauma was assessed using the Childhood Trauma Questionnaire (Grassi-Oliverira et al., 2006). The genomic DNA was bisulfite converted and pyrosequencing was used to determine methylation levels in three CpGs sites of the GRIN1 gene and of LINE-1, as a measure of global methylation. NR1 plasma concentrations were measured using ELISA (MyBioSource, San Diego, USA). Data were analyzed using General Linear Model with post-hoc Bonferroni correction and Pearson's correlations.
Results: Individuals, independent of groups, who had experienced childhood trauma presented higher levels of GRIN1 methylation than those without trauma (CpG1: p=0.004; CpG3: p=0.009). Moreover, individuals with physical neglect demonstrated GRIN1 hypermethylation in comparison to individuals without trauma (CpG1: p=0.027; CpG3: p=0.006). Specifically, siblings with emotional neglect presented increased GRIN1 methylation levels at CpG1 when compared with FEP patients and controls with emotional neglect (p=0.028; p=0.001, respectively) and in relation to siblings without trauma (p=0.004). Siblings with physical neglect also showed increased GRIN1 methylation levels at CpG1 when compared to FEP patients and controls with physical neglect (p=0.010; p=0.003, respectively) and in relation to siblings without physical neglect (p=0.001). Furthermore, FEP patients with emotional neglect showed increased GRIN1 methylation at CpG3 when compared to FEP patients without emotional neglect (p=0.010). No differences were observed in the LINE-1 methylation between individuals with or without childhood trauma.
Discussion: This is the first study demonstrating the association between DNA methylation in GRIN1 and childhood trauma in FEP patients, their unaffected siblings and community-based controls. In addition, the interaction between DNA methylation changes in GRIN1 and childhood trauma may be a predict factor of susceptibility for siblings. All these findings suggest evidence for NMDAR dysfunction in response to trauma, contributing the understanding of some of the epigenetics mechanisms by which early life stress affects the glutamatergic system.

S9. NEUROIMAGING AND NEUROPHYSIOLOGY BIOMARKERS OF SCHIZOTYPAL PERSONALITY DISORDER: A SYSTEMATIC REVIEW

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Background: Schizotypal personality disorder (SPD) is a cluster A personality disorder affecting 1.0% of general population, characterised by disturbances in cognition and reality testing dimensions, affect regulation, and interpersonal function. SPD shares similar but attenuated phenomenological, genetic, and neurobiological abnormalities with schizophrenia (SCZ) and is described as part of the continuum of schizophrenia spectrum disorders. Neuroimaging and neurophysiology are the main non-invasive techniques for the investigation of brain structure and function, so they play a crucial role in psychiatric research and for their applications into clinical practice. The present review aims to systematically identify the major neuroimaging and neurophysiology biomarkers of SPD.
Methods: The present review has been conducted according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement. The protocol was prospectively registered in PROSPERO - International prospective register of systematic reviews. The systematic review was performed to summarise the most comprehensive and updated evidence on functional neuroimaging and neurophysiology findings obtained through different techniques (DW-MRI, DTI, PET, SPECT, fMRI, MRS, EEG) in subjects with SPD.
Results: The search initially yielded 218 records. After study selection and reference screening, the final set comprised 52 studies. Of the 52 studies included in this review, 9 were on DW-MRI and DTI, 11 were on PET and SPECT, 11 were on fMRI and MRS, and 21 were on EEG. Although it was complex to synthesise all the functional abnormalities found in the included studies into a single, unified, pathogenetic pathway, a common theme that emerged was the dysfunction of brain circuits including striatal, frontal, temporal, limbic regions, and their networks. This dysfunction may be the result of a dysregulation along the dopaminergic pathways and lead to deficits or defects in processes that organise a person's cognitive-perceptual evaluation of the environment and the relatedness to him/herself. As for the limitations, a quantitative data synthesis was not planned for this work, therefore no meta-analytical integrations are presented in this review. The results of individual neuroimaging studies, in fact, are not comparable due to small and heterogeneous samples, analytical flexibility, or differences in imaging modalities and behavioral tasks.
Discussion: Brain abnormalities in SPD are similar, but less marked, than those found in SCZ, and they do not mirror each other. In fact, different patterns of functional abnormalities in SPD and SCZ have been found in this systematic review, suggesting the 'presence' of possible compensatory factors, protecting subjects with SPD from frank psychosis and providing diagnostic specificity. Specifically, SPD differentiates from SCZ by showing: (a) milder frontal-striatal-temporal white matter dysconnectivity in DTI studies, (b) lesser frontal and striatal dysfunction and a decreased striatal dopaminergic activity in PET and SPECT studies, respectively, (c) different patterns of dysfunctional activation of frontal-striatal-thalamic circuitry during attentional processing in fMRI studies, and (d) milder alterations in EEG sensory gating and no evidence of alterations in EEG auditory or visual processing.

S10. SCREENING FOR ANTI-NMDAR ANTIBODIES AMONGST PATIENTS WITH FIRST EPISODE PSYCHOSIS

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Background: Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis is an autoimmune limbic encephalitis, where psychiatric symptoms are often dominant in the initial phase. These patients are usually treated in psychiatric wards, due to first episode psychosis (FEP). The antibodies responsible for the symptoms, can be identified from the patients' sera. During