F88. MANIPULATION OF THE GUT MICROBIOTA WITH A PREBIOTIC IN SCHIZOPHRENIA: A DOUBLE-BLINDED RANDOMIZED PLACEBO-CONTROLLED CROSS-OVER STUDY

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Background: Neurocognitive impairment is increasingly recognized as a fundamental symptomatology in schizophrenia with more than 80% of patients exhibiting significant deficits, even at first episode of illness. Current pharmacotherapies do not alleviate cognitive symptoms, often cause severe metabolic dysfunction and weight gain that readily become major health concerns. Identifying adjunctive interventions that improve cognition without disrupting therapeutic actions of anti-psychotic medications, and can mitigate the metabolic side-effects of these drugs, would be highly beneficial to patients and improve prognosis. We have recently demonstrated that the manipulation of the rat gut microbiota with a prebiotic (dietary fibre that grows beneficial enteric bacteria) improves cognitive flexibility and prevents olanzapine-mediated weight gain. We therefore aim to explore whether these actions of the prebiotic translate to medicated stable patients with schizophrenia.

Methods: A total of 40 patients with psychosis aged 18–65 will be enrolled in a 24-week maltodextrin-controlled cross-over experimental medicine study. Participants will receive either a 12-week treatment with a prebiotic (active compound) followed by a 12-week maltodextrin supplement (placebo), or in the reverse order. The order of supplements that participants receive is randomized. The primary outcome is to examine the influence of prebiotic supplementation on neurocognitive functioning, which is measured using a tablet-based neuropsychometric test battery. We will also examine the impact on clinical metabolic measures such as total weight and visceral adiposity. The concentration of immune-related serum proteins as well as neuroendocrine hormones will be evaluated. All measurements will take place at baseline, at 12-week cross-over, and at the end of the 24-week study. A within-subjects repeated measures analysis will be performed, and co-variates (gender, weight, medication) identified. This trial is registered with ClinicalTrials.gov, identifier number NCT01353046.

Results: We have currently screened 36 patients, of whom 30 were eligible for the study (67% male). At baseline, the average age of all recruited was 36.41 ± 11.42. The overall cognitive score was -2.03 ± 0.53 where the subtests included verbal memory (29.09 ± 8.75), digit sequencing (15.41 ± 2.77), token motor (55.74 ± 24.14), semantic fluency (8.83 ± 3.46), letter fluency (11.39 ± 3.65), symbol coding (35.61 ± 9.22) and tower of London (15.1 ± 4.06). There was no difference in overall cognitive between male (14.29 ± 2.46) and female (17.22 ± 2.30) patients. However, long-term associative learning as measured by the digit sequencing subtest appeared to show a significant difference between male (14.29 ± 2.46) and female (17.22 ± 2.33; p=0.008) participants. No significant differences between clinical metabolic measures were observed in baseline BMI (32.25 ± 6.79) and abdominal obesity as measured by hip-to-waist ratio (0.94 ± 0.11). The serum concentrations of immune and endocrine markers will also be presented.

Discussion: This investigation, to our knowledge, is the first clinical study to provide mediated schizophrenia patients with a prebiotic, as a potential means of improving cognition and managing secondary metabolic dysfunction. Although a potential link between commensal enteric bacteria and schizophrenia have been suggested, earlier work with probiotics (live cultures) did not support this association. However, since the current study uses a prebiotic that proliferates multiple species of gut bacteria, it will provide more robust data that will support, or refute, the validity of manipulating the gut microbiome in the treatment of schizophrenia.

F89. COGNITIVE IMPAIRMENT WORSENING ACROSS AFFECTIVE TO PSYCHOSIS SPECTRUM: A COHORT STUDY OF UNIPOLAR/BIPOLAR DEPRESSION AND BIPOLAR SCHIZOAFFECTIVE DISORDERS

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Background: Bipolar (BPD), schizoaffective bipolar (SAM) and major depressive disorders (MDD) reveal large heterogeneity in terms of symptom expression, course and treatment response. This heterogeneity could be the source of a large variance of cognitive performance observed in these subjects. The aim of the present analyses was to compare the cognitive performance of patients with BPD, SAM, MDD and medical controls with adjustment for a comprehensive array of potential confounders. To go a step further we will simultaneously test the effects of multiple clinical characteristics including lifetime history and duration of psychotic symptoms, manic/hypomanic and depressive episodes, age of onset of disorder, current GAF score, time since remission of the last episode and presence of a depressive episode at the time of the assessment on the cognitive performance.

Methods: Data stemmed from the Lausanne-Geneva Family and High-Risk study. Patients with BPD (n=62), SAM (n=22) and MDD (n=51) were interviewed every three years over a mean duration of follow-up of 12 years. All patients were assessed clinically with the semi-structured Diagnostic Interview for Genetic Studies (DIGS). The cognitive assessment was made with the MATRICS and the Victoria Stroop Test.

Results: The global cognitive index (excluding Stroop result) shows that SAM subgroup had the lowest global score with 40.6 (SD=8.5), BPD 47.4 (SD=7.8) and MDD 49.7 (SD=8.7). A multiple linear regression accounting for several confounders such as comorbid psychiatric disorders and medication confirms that only SAM and BPD are statistically different from controls (p<0.001 and p<0.01 respectively). MDD did not differ from controls (p>0.05). Overall, patients with BPD or SAM but not with MDD showed poorer cognitive performance than controls in terms of the global score and speed of processing, verbal learning, working memory, visual learning, attention/vigilance and inhibition.

Discussion: Our data confirm cognitive impairment in patients with BPD or SAM compared to controls after adjustment for a comprehensive array of potential confounder variables. We were able to evaluate the specificity of cognitive performance of psychotic, manic and depressive dimensions of the major mood disorders within the same sample. Furthermore, these data stress that the presence of the “schizo dimension” concomitant to mania and depression contributes to worsening the cognitive performance in an additive manner.

F90. SOCIAL INFERENCE AND BELIEFS DIFFER IN INDIVIDUALS WITH SUBCLINICAL PERSECUTOR DELUSIONAL TENDENCIES

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Background: It has long been suspected that abnormalities in social inference (e.g., about the intentions of others) play a key role for persecutory...
difficulties. Impaired executive function is a core cognitive deficit in schizophrenia, and this dysfunction is likely to predict poor treatment outcomes (e.g., treatment adherence and relapse rate). Therefore, the treatment of schizophrenia should be focused on improving executive function. Several studies have investigated the relationship between executive functions and treatment responses in schizophrenia. In this study, we aimed to investigate the relationship between executive functions and treatment responses in schizophrenia patients using a meta-analysis approach.

Methods: A systematic literature search was conducted to identify relevant studies. Only randomized controlled trials (RCTs) with schizophrenia patients and a measure of executive function were included. The primary outcome was treatment response, defined as improvement in symptom severity or remission. The secondary outcome was the duration of response.

Results: A total of 13 RCTs were included in the meta-analysis. The pooled analysis showed a significant positive correlation between executive function and treatment response (standardized mean difference = 0.32, 95% CI = 0.15 to 0.49, p < 0.001). The duration of response was also significantly longer in patients with better executive function (weighted mean difference = 1.2 months, 95% CI = 0.6 to 1.8 months, p < 0.001).

Conclusion: This meta-analysis suggests a positive relationship between executive function and treatment response in schizophrenia. These findings support the importance of targeting executive function in the management of schizophrenia. Future studies should focus on developing interventions that improve executive function and investigate their impact on treatment outcomes.