Further clinical trials are needed to reduce the heterogeneity of the treatment effects and to confirm the potential negative effects of prolactin on cognitive abilities.

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, and often cause severe metabolic dysfunction and weight gain that readily become major health concerns. Identifying adjunctive interventions that improve cognition without disrupting the 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 NCT03153046.

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 (8.33 ± 3.40), 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 medicated 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 PERSECUTORIAL 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
delusions. In this study, we examined the association between subclinical persecutory delusions (PD) and social inference, testing the prediction that proneness to PD is related to altered social inference and beliefs. 

Methods: We included 148 participants who scored on opposite ends of Freeman’s Paranoid Checklist (PCL). High scorers and low scorers were thus assigned to two respective participant groups, which were matched according to age, education in years, and gender. Participants performed a probabilistic advice-taking task with a dynamically changing social context (volatility) under one of two experimental frames. Our design was thus 2x2 factorial (high vs. low delusional tendencies, dispositional vs. situational frame). In the task, participants had to integrate two types of cues simultaneously in order to make informed predictions, namely a social cue (advice provided by an adviser) and a non-social cue (probabilities given via pie-chart). In addition, the experimental frames differentially emphasized possible reasons behind unhelpful advice and either highlighted (i) the adviser’s possible intentions (dispositional frame) or (ii) the rules of the game (situational frame). Task structure was identical across frames. When integrating the framing information, participants were expected to take advice into account more in the situational frame than in the dispositional frame, since the latter induces some mistrust due to highlighting the adviser’s intentions.

Results: The behavioral data showed significant group-by-frame interactions (F=5.7381, p<0.05), indicating that in the situational frame high PCL scorers took advice less into account than low scorers. This reduced adaptation to the frame was particularly visible after the experience of volatility. Additionally, high PCL scorers believed significantly more frequently that incorrect advice was delivered intentionally (F=16.369, p<0.001) and that such malevolent behavior was directed towards them personally (p<0.05). High scorers also reported attributing unhelpful advice more to the adviser (F=8.047, p<0.01) instead of the rules of the game, compared to low scorers. The high scorers in the PCL reported higher negative, positive, and depressive symptoms on the CAPE compared to low scorers (p<0.001) but did not differ regarding cognitive performance in the Brief Neurocognitive Assessment (BNA).

Discussion: Overall, our results suggest that social inference in individuals with subclinical PD tendencies is less sensitive to differences in social context and shaped by negative beliefs about the intentions of others. These findings may help future attempts of identifying at risk mental state individuals and understanding maladaptive behavior in schizophrenia.

F92. COMPARISONS BETWEEN CANNABIS USERS AND NON-USERS PATIENTS WITH FIRST-EPISEDE PSYCHOSIS IN NEUROCOGNITIVE FUNCTIONING: A META-ANALYSIS

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Background: Patients with first episode psychosis (FEP) frequently report cannabis use although its effects on cognitive functioning are still unclear. Several studies suggest a decrease in the executive function, verbal memory and working memory of FEP cannabis users (González-Pinto et al., 2016; Mata et al. 2008) while other studies show improvements in the neurocognitive function of this group (Setién-Suero et al., 2017, Cuhna et al., 2013, Leeson et al., 2012, Yücel et al., 2012; Rodriguez-Sánchez et al., 2010) or even absence of neurocognitive differences between FEP cannabis users and non-users (Burgra et al., 2013). This meta-analysis aims to explore the magnitude of effect of cannabis use on neurocognition in patients with FEP.

Methods: Articles for consideration were identified through extensive literature searches using online databases, which included PubMed, Medline and PsycInfo. The search was limited to English language articles. The used keywords were: “first episode psychosis” OR, “neurocognition and cannabis”, in combination with a number of neuropsychology-related terms including “neurocog” and “neuropsychology”. Given that other substances including alcohol, cocaine, and stimulants are associated with altered cognitive performance, studies in which participants met for polysubstance use disorders, even if there was preferential use towards cannabis, were excluded. Eight studies from 2008 to 2017 met inclusion criteria from a total sample of 16 initial studies. Five hundred and eighteen of these participants were cannabis users with FEP, and 639 were patients with no cannabis use. A total of 58 effect sizes of neuropsychological test variables were categorized into 4 cognitive domains (premorbid IQ, executive functioning, working memory and verbal memory and learning). Age of first cannabis use, duration of cannabis use, percentage of males and age were abstracted and assembled as moderator variables. Standardized mean differences were computed for each cognitive domain between cannabis-using patients and patients with no history of cannabis use. Negative effect sizes would display better cognitive functioning of non-cannabis users. We employed a meta-analytic three level model to combine effect sizes across studies.

Results: Effect sizes were not significantly different from zero in any of the neurocognitive domains when FEP cannabis users and non-users patients were compared [working memory (d= -0.03, SE=0.15, CI = -0.33–0.26, p=0.83), executive function (d= 0.14, SE=0.16, CI = 0.17–0.45, p=0.37), verbal memory and learning (d= 0.04, SE=0.15, CI = 0.25–0.33, p=0.27) and premorbid IQ (d= 0.06, SE=0.09, CI = -0.24–0.12, p=0.50)]. Only one moderator variable resulted significant in the executive function denoting superior performance in FEP cannabis-using patients as they were older.

F91. ASSOCIATION BETWEEN SYMPTOM DIMENSIONS AND EXECUTIVE FUNCTION IN SCHIZOPHRENIA

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Background: Impaired executive function is a core cognitive deficit in schizophrenia and strongly associated with functional outcomes. Understanding the relationship between clinical symptoms and executive function may help the clinician to better manage the cognitive impairment and inform prognosis. The main objective of the present study was to investigate the association between symptom dimensions and executive function in schizophrenia.

Methods: One-hundred and two patients with schizophrenia were recruited from the schizophrenia outpatient clinic from Universidade Federal de São Paulo (PROESQ/UNIFESP). Diagnosis was confirmed through the Structured Clinical Interview for DSM-IV (SCID-I) and dimensional psychopathology was assessed by the Positive and Negative Syndrome Scale (PANSS). The PANSS items were grouped in five factors: positive, negative, disorganized/cognitive, mood/depression and excitement/hostility factors. The task battery included the following tests: Plus–Minus Task, Number–Letter Task, Trail Making Test - Part B, Keep Track Task, Letter Memory Task, Visual Working Memory Test – MTV, Stroop Test, Semantic Generation Task and The Tower of London Test – TOL. All tasks were computerized and assessed by the software Cronos. A single latent variable for executive function was derived through Confirmatory factor analysis and yield good model fits (CFI: 0.997; TLI: 0.996; RMSEA: 0.017; SRMR: 0.041).

Results: When the factors were entered individually, negative (df=121, r=-0.35, p <0.001) and disorganized (df= 121; r=-0.48, p <0.001) factors were significant predictors of EF. In a multivariate regression analysis, including all the factors and correcting for age, gender and duration of illness, only the disorganized factor remained significant (r=-0.21,p<0.001).

Discussion: The disorganized factor was the symptomatic dimension more strongly associated with EF. The potential use of disorganized dimension as indicator of poor executive function and related outcomes, i.e., treatment resistant schizophrenia, should be further investigated.