Objectives: We aimed to develop a new method to assess cognitive performance and simultaneous measurement of psychophysiological signals related to stress and relaxation levels.
Methods: 20 adult patients with mental disorders in a rehabilitation program were recruited along with 21 healthy volunteers. A test protocol was carried out with a purpose-developed computerized psychophysiological device. The protocol consisted of a relaxation period; digitized questionnaires on pathological distress (GHQ) and sense of coherence (SOC); gamified cognitive tasks to assess working memory, attention, and decision-making; and a final relaxation period. Acute stress was assessed by heart rate variability measured by a wireless ECG sensor. The inter-beat interval's root mean square of successive differences (RMSSD) was calculated as an inverse stress measure. Relaxation levels were assessed by the relative power of the alpha frequency band measured by a commercial 4-channel EEG headband. Stress and relaxation levels were compared to the first relaxation period as a baseline.
Results: Patients scored worse than the reference group both regarding distress (d=7, p=0.004) and sense of coherence (d=-8, p=0.047). The cognitive performance of patients was significantly lower (p<0.001) than the reference group for all tasks.
RMSSD at baseline tended to be lower for patients (d=-12.69, p=0.098), reflecting a higher level of physiological stress; 61% of patients started at an elevated stress level compared to 25% of the reference group. In addition, relative alpha levels at baseline were also lower (d=-5.8%, p=0.007) for patients.
Compared to baseline, RMSSD decreased on average to 94% during cognitive assessments in patients and decreased to 91% by the end of the final relaxation. RMSSD decreased to 76% in the reference group and reached a final value of 78% of the baseline. Alpha levels slightly increased among patients during the tasks (103.4%) and then returned close to baseline (99.1%). For the reference group, alpha decreased during the tasks (95.5%) and then slightly increased (97.3%).
Conclusions: Patients displayed heightened distress, reduced sense of coherence, and inferior cognitive scores compared to controls. While starting with higher stress, patients exhibited less elevation in stress during tasks, coupled with alterations in alpha levels, suggesting diminished engagement or focus. Our innovative method could aid in the diagnostics of cognitive performance in mental patients after further measurements for validation.

Disclosure of Interest: None Declared

Precision Psychiatry

O0010

Association between escitalopram dose personalisation based on quantification of drug plasma levels and the outcome of escitalopram treatment

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Introduction: Given the negative impact of anxiety and depression on society and the shortage of new antidepressants, it is of paramount importance to make the best use of available treatment options. Therapeutic drug monitoring (TDM) in escitalopram treatment can potentially be clinically useful, as underexposed patients show reduced efficacy of escitalopram treatment and as adverse drug reactions (ADRs) of escitalopram are dose-dependent.
Objectives: This prospective cohort study aimed to investigate whether escitalopram treatment efficacy or safety are associated with escitalopram dose adjustment based on TDM readouts.
Methods: 89 included patients aged between 15 and 65 years who suffered from depression were enrolled in the study before starting treatment with escitalopram. Patients were assessed one day before starting treatment with the recommended dose of 10 mg/day escitalopram (baseline, visit 0) and at follow-up after four and eight weeks. Dose adjustment at four-week follow-up was based on the measured escitalopram plasma level two weeks after treatment initiation; patients who required dose increase to 15 or 20 mg/day comprised comparator group, patients who did not required dose increase comprised control group, while patients who did not reach optimal exposure at eight-week follow-up were characterized as non-compliers. Treatment efficacy was approximated by the relative change on the Hamilton Depression Rating Scale (HAMD), while safety was approximated based on the changes on the Scandinavian UKU side effect rating scale and ECG readouts. Changes in HAMD, UKU score and QTc interval were compared between groups by one-way ANOVA or chi-square tests.
Results: Compared to baseline, significant reductions in HAMD scores of 36% (95%CI, 30%-43%) and 53% (95%CI, 47%-60%) were observed at four- and eight-week follow-up, respectively; however, there were no significant differences between groups (p > 0.1). In the groups adjusted to 15 and 20 mg, 15/26 and 19/33 patients, respectively, reported adverse effects, compared with 6/17 patients in the control group and 6/13 in the non-complier group (p>0.1). A significant mean QTc prolongation of 6.40 ms (95%CI, 3.27-9.53) was observed between the baseline and eight-week follow-up (p=0.0013), without significant differences in QTc interval prolongation between groups (p > 0.1).
Conclusions: Escitalopram dose adjustment resulted in optimal drug exposure and solid treatment response in the majority of patients; however, no differences in efficacy were found between the patients who required dose adjustments, the ones who did not, and the ones who ultimately did not achieve optimal exposure. In addition, the selective increase of the dose to the patients who did not reach optimal drug exposure on the recommended dose of

10 mg/day did not lead to significant increase in adverse drug reactions and QTc prolongation.

Disclosure of Interest: None Declared

Psychoneuroimmunology

O0011

Multicausal disruption of complement system activity in schizophrenia: abnormal transcription of C4, complement control proteins and microglia specific genes in brain and blood

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Introduction: The *synaptic pruning* process is based on the joint action of the complement system and microglia. In schizophrenia, accumulating evidence support that abnormal synaptic pruning during adolescence may be due to an altered Complement system activity. While this hypothesis is supported by *C4* overexpression in various brain regions of individuals with schizophrenia, such alterations should be replicated and extended to other brain regions. Moreover, transcriptional studies of genes encoding regulators of the complement system activity (complement control proteins, CCP) and microglia-specific genes are lacking. Furthermore, it remains unknown whether brain and peripheral expression of such genes are related.

Objectives: To explore expression of *C4* as well as 4 CCP encoding genes and 10 microglia-specific genes at the brain and peripheral levels in individuals with schizophrenia as compared to healthy controls.

Methods: We analyzed candidate gene expression from 9 Gene Expression Omnibus datasets obtained from 333 individuals with schizophrenia and 306 healthy controls (HC). We first compared expression of the candidate genes between individuals with schizophrenia and HC in postmortem brain samples from 7 different brain regions. Then, the same comparison was made in 4 different peripheral tissues.

Results: Regarding the complement system, we observed *C4* overexpression in the DLPFC, parietal, temporal cortex and associative striatum of individuals with schizophrenia. We report distinct altered expression patterns of CCP genes in the DLPFC, hippocampus and cerebellum of individuals with schizophrenia. Only *CD46* expression was altered in the blood of individuals with schizophrenia. Regarding microglia, we report an underexpression of several microglia-specific genes in the cerebellum, associative striatum, hippocampus and parietal cortex of individuals with schizophrenia vs. HC. At the peripheral level, we observed a mixed altered expression pattern in the whole blood of individuals with schizophrenia.

Conclusions: Firstly, our results suggest that the CCP-mediated regulatory mechanisms of the Complement system are impaired in the brain of individuals with schizophrenia, potentially contributing to an excessive Complement system activity (CSA). Secondly, our results support the hypothesis of a widespread underexpression of microglia-specific genes in brain tissues of individuals with schizophrenia. Functionally, the observed transcriptional alterations may be related to the synaptic pruning impairment. Alternatively, they may translate a compensatory mechanism for neuroinflammation. In the whole blood, the altered transcriptional pattern may represent a potential peripheral signature of SZ.

Disclosure of Interest: None Declared

O0012

Neuroinflammation in Recent Onset Mental Health Disorders – Developing Multi-level Signatures of Early-stage Depression and Psychosis in Young Adults

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Introduction: An early and comprehensive neurobiological characterization of severe mental disorders could elucidate mechanistic pathways, aid the development of novel therapeutics, and therefore enable timely and targeted intervention in at-risk youth and young adults. Therefore, we present an unsupervised transdiagnostic machine learning approach to investigate shared and distinct patterns of early-stage depressive and psychotic disorders on multiple clinical and neurobiological levels.

Objectives: To derive multi-level neurobiological and clinical signatures of early-stage affective and psychotic disorders in adolescents and young adults.

Methods: From the multicenter prospective European PRONIA cohort, we acquired data from 678 individuals (51% female) comprising young, minimally medicated in- and outpatients with clinical high-risk (CHR) states for psychosis, with recent-onset depression (ROD) or psychosis (ROP), and healthy control (HC) individuals. Within repeated nested cross-validation frameworks, we employed Sparse Partial Least Squares Analysis to detect associations between blood markers and grey matter volume (GMV), followed by support vector machine prediction of these signatures using biographical, clinical, neurocognitive, proteomic, and functional data.

Results: Our results demonstrated a psychosis staging signature separating ROP from CHR individuals via GMV patterns in the