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

cortico-thalamo-cerebellar circuitry with a blood marker set of elevated of IL-6, TNF-α and CRP (ρ = 0.272; P = 0.002). A depression signature separated ROD from HC individuals via altered GMV in the limbic system with a blood marker set of elevated IL-1ß, IL-2, IL-4, S100B and BDNF (ρ = 0.186; P = 0.021). Only the psychosis staging signature showed a distinct proteomic enrichment regarding innate immune response, abnormal neutrophil function, cellular senescence, and anti-inflammatory drugs (Balanced Accuracy (BAC) = 87.73%; Area Under the Curve (AUC) = 0.94). Childhood trauma differentially predicted psychosis and depression signatures, while past level of functioning, personality and quality of life was predictive of both signatures (BAC = 67.19-78.00%; AUC = 0.71-0.83).

**Image:**

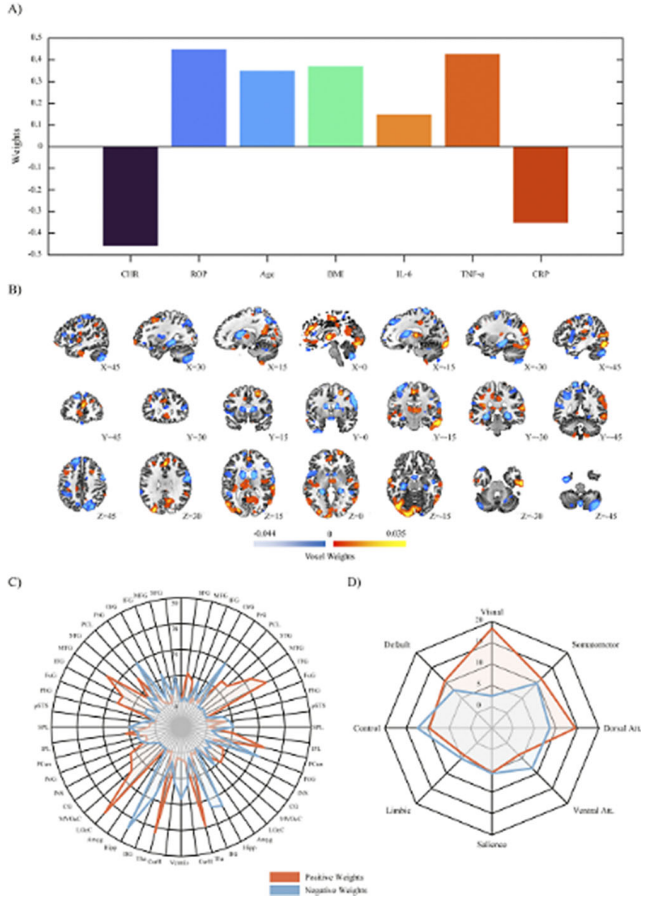



**Image 2:**

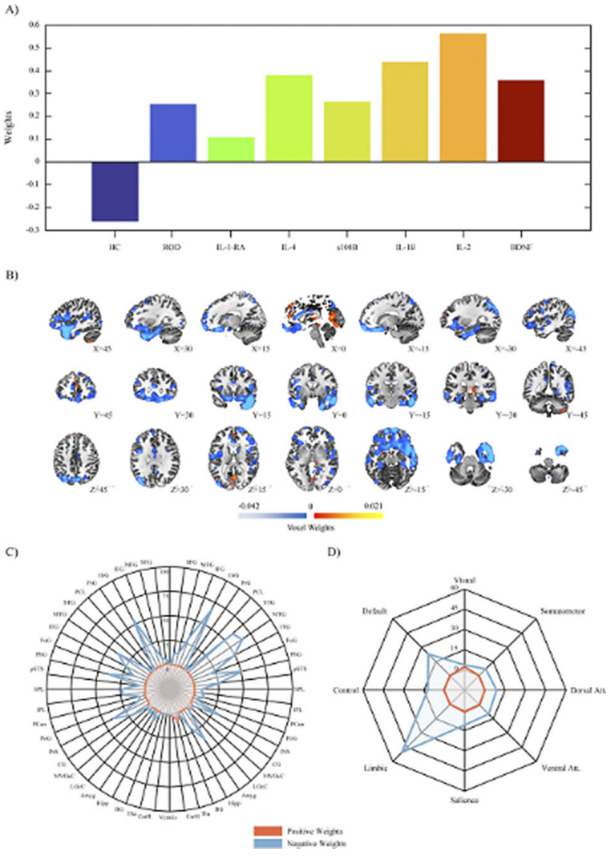
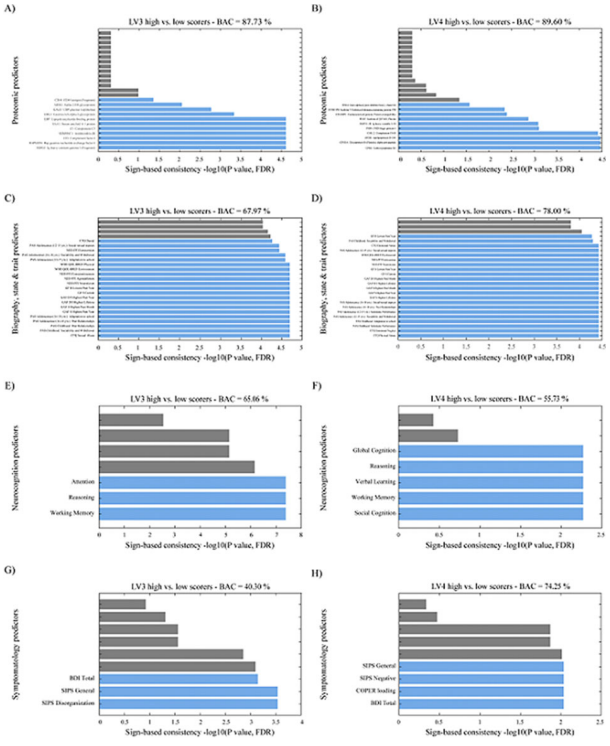



**Image 3:**



**Conclusions:** Psychosis and depression exhibit distinct multi-level signatures evident in early disease stages. Enhanced insight into these signatures could help delineate individual trajectories and potentially new mechanisms for pharmacological treatment.

**Disclosure of Interest:** None Declared

## O0013

## Elevated herpesvirus antibody levels linked to schizophrenia and bipolar disorder

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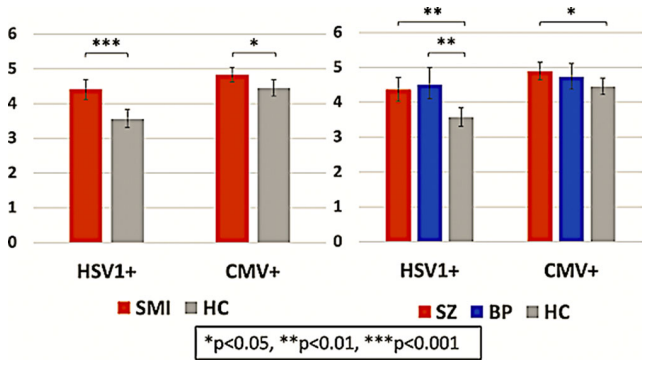
**Introduction:** Previous research has implicated herpes simplex virus 1 (HSV1) and cytomegalovirus (CMV) in severe mental illness (SMI) with conflicting results. Both pathogens have high universal seroprevalence, are neurotropic and after the primary infection typically establish a persistent latent infection with periodic reactivations. Increased immunoglobin G (IgG) concentrations are considered to be attributable to an increased infection severity with more frequent reactivations or host immune system alterations.
**Objectives:** We assessed the HSV1 and CMV IgG concentrations in previously infected (seropositive) patients with SMI and healthy controls (HC). We hypothesized that seropositive patients would show higher IgG concentrations than seropositive HC.
**Methods:** We included 765 patients, 515 with schizophrenia (SZ) and 250 with bipolar disorder (BP), and 541 HC. HSV1 and CMV IgG seropositivity and concentrations were measured with immunoassays. 355 patients, mean age 33 years, 45% females, and 238 HC, mean age 35 years, 44% females, were HSV1 seropositive (HSV1+) while 447 patients, mean age 33 years, 50% females, and 296 HC, mean age 34 years, 47% females, were CMV seropositive (CMV+). In our main analysis among seropositive participants, we investigated the main effect of patient/control status on HSV1 and CMV IgG concentrations.
**Results:** There were no significant differences in CMV or HSV1 seropositivity frequencies between patients with SZ, patients with BP and HC. Among seropositive participants, patients had higher HSV1 ($p<0.001$) and CMV ($p=0.018$) IgG concentrations than HC; stratifying by diagnosis, both patients with SZ ($p=0.001$) and patients with BP ($p=0.001$) had higher HSV1 IgG concentrations than HC, while patients with SZ, but not BP, had higher CMV ($p=0.045$) IgG concentrations than HC (Image). For HSV1, higher IgG concentrations were associated with higher general ($p=0.017$), negative ($p=0.041$) and positive ($p=0.028$) psychotic symptom scores.
**Image:**




**Conclusions:** Seropositive patients with SMI showed higher HSV1 and CMV IgG concentrations than seropositive HC suggesting that patients suffer a more severe infection or exhibit an altered immune response when contracting the pathogens. For HSV1, higher IgG concentrations were linked to more psychotic symptoms.

**Disclosure of Interest:** D. Andreou: None Declared, N. E. Steen: None Declared, K. N. Jørgensen: None Declared, T. Ueland: None Declared, L. Wortinger: None Declared, L. Mørch-Johnsen: None Declared, R. Yolken: None Declared, O. Andreassen Consultant of: Consultant to HealthLytix, Speakers bureau of: Received speaker's honorarium from Lundbeck and Sunovion, I. Agartz Speakers bureau of: Received speaker's honorarium from Lundbeck

## O0014

## Significant beneficial effects of 12-weeks add-on yoga therapy on antipsychotic-stabilized schizophrenia patients through epigenetic modulation: novel findings from a randomized controlled study

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**Introduction:** Complementary and alternative therapy, especially yoga, is emerging as an important treatment modality for various complex disorders. Yoga therapy has reportedly been demonstrated to exhibit clinical benefits in schizophrenia. However, the modulatory effects of yoga therapy on the pathobiological pathways of schizophrenia are inadequately explored. Immune dysregulation is a widely recognized etiopathological construct of schizophrenia. It is not precisely known whether yoga therapy can modulate the expression of immune molecules by regulating gene expression and epigenetic processes in schizophrenia.
**Objectives:** To understand the impact of 12-weeks add-on yoga therapy on the immune-inflammatory pathway in schizophrenia