Eye movement dysfunctions represent well-established endophenotypes for psychiatric disorders. They include impairments of sensorimotor processing, deficits of sustained pursuit maintenance under top-down control, and inhibition errors during antisaccades. How these endophenotypes may be related to genetic variations is not well understood.

**Methods:** 849 participants (schizophrenia N = 230, schizoaffective disorder N = 155, psychotic bipolar disorder N = 206, and healthy controls N = 258) of the Bipolar-Schizophrenia Network on Intermediate Phenotypes (B-SNIP) study were characterized for initial eye acceleration (measure of sensorimotor processing), sustained pursuit maintenance gain (measure of cognitive control), and antisaccade error rate (measure of inhibitory control). A mixed modeling GWAS approach (EMMAX) was used including ~4.3 million genotypes assessed with the PsychChip and 1000 Genomes imputation. Eye movement measures were modeled as quantitative trait phenotypes in relation to genetic data while controlling for genetically derived ancestry measures, age, and sex. Proband and controls were grouped together for primary analyses stratified by the top two genetically derived ancestry groups with follow-up studies in proband or control categories.

**Results:** The most robust associations with sensorimotor processing were identified with SNPs in IPO8 (ch12) across participants (P = 8 × 10^{-11}). In participants of predominantly African ancestry (AA) we additionally observed an association with PCDH12 (ch5) and NRSN1 (ch6). In participants with predominating Caucasian ancestry (CA) sensorimotor measures were most robustly associated with a SNP in CYBSR3 (ch22, P = 8 × 10^{-10}). Association with sustained pursuit maintenance was identified with a SNP in SH3GL2 (ch9) across all participants (P = 3 × 10^{-8}). In AA participants, we additionally identified associations of pursuit maintenance with a SNP in TMPPRSS5 (ch11) and antisaccade error rate with an SNP in chromosome 7.

**Conclusion:** These association findings may give insights into the behavioral/neurophysiological consequences of genetic variation in systems for eye movement control and their alterations in severe mental illness. Protocadherin 12 (PCDH12) has been suggested for involvement in neurodevelopment and brain morphology in psychotic disorders. By disturbing fast axonal guidance and synaptic specificity, variation in this gene may impact neuronal signaling needed for sensorimotor processing. Variation in Neurensin 1 (NRSN1) may impact processing speed and thus initial eye acceleration by disturbances in transduction of nerve signals and growth. By regulating intracellular signaling and neurotransmitter release, Endophilin-A1 (SH3GL2) may impact sustained pursuit maintenance. Other genes implicated in our association studies represent novel relationships requiring further study.

12. C-REACTION PROTEIN AND SUICIDE ATTEMPTS IN SCHIZOPHRENIA

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**Background:** The risk of suicide and suicide attempts is greatly elevated in schizophrenia. The causes of suicide in this population are not known with certainty. Studies indicate that inflammatory processes may be linked with suicide behaviors. Elevated levels of C-Reactive Protein (CRP), a nonspecific marker of inflammation, have been found in many individuals with schizophrenia but the association with suicide attempts in this population has not been previously studied.

**Methods:** Patients with a diagnosis of schizophrenia or schizoaffective disorder were assessed on the Columbia Suicide Severity Rating Scale and other clinical measures. Participants had a blood sample drawn from which was measured high sensitivity CRP and antibodies to infectious agents and food antigens. The associations between suicide variables and CRP and other immune markers were analyzed in logistic regression models employing age, gender, race, and cigarette smoking as covariates. Odds ratios (ORs) associated with having a CRP level ≥75th and 90th percentiles of a control group were calculated with the same covariates.

**Results:** The 89 participants had a mean age of 38.6 years (SD 13.1) and were 73% male and 43% Caucasian; 24 were hospitalized and 30 had ≥1 assessment. A total of 42 (47%) had made a lifetime suicide attempt including 14 (16%) with ≥2 attempts and 28 (31%) an attempt that required medical attention. A lifetime history of a suicide attempt was significantly correlated with a history of drug/alcohol abuse. There was not a significant association between a suicide attempt history and patient age at time of assessment, gender, race, clinical setting, cognitive score, current cigarette smoking, psychiatric symptom score, or type of medication received. A suicide attempt history was significant associated with elevation in the level of CRP (t = 2.56, P = .01). Having a level of CRP≥75th percentile and ≥90th percentile of the control group was significantly associated with a suicide attempt history (OR 2.6 (95% CI 1.0, 6.8, P = .05) and OR 3.3 (95% CI 1.1, 9.9, P = .04) respectively). We did not find an association between a suicide attempt history and antibodies to food antigens or infectious agents.

**Conclusion:** These results add to the growing body of literature about the role of inflammation in schizophrenia. The identification of blood-based markers may provide for improved methods for the assessment and treatment and, ultimately, prevention of suicide attempts in individuals with schizophrenia.

13. THE EXTENTS OF EXTRACELLULAR AND BRAIN TISSUE RELATED ABNORMALITIES IN SUBJECTS AT CLINICAL HIGH RISK OF PSYCHOSIS

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**Background:** White matter (WM) microstructural alterations are thought to be associated with schizophrenia. It is unclear whether axonal deterioration, demyelination, or neuroinflammation contributes to the onset of psychosis. With advanced diffusion tensor imaging (DTI) analyses, free-water analysis, we explored WM alterations in individuals at clinical high risk (CHR) for psychosis.

**Methods:** Fifty CHR subjects and 30 healthy controls (HCs) participated in this study, which is part of the ShangHai At Risk for Psychosis (SHARP) program. CHR subjects were clinically followed for 1 year after their baseline assessments. Diffusion images were acquired on a 3T Siemens magnet at Shanghai Mental Health Center. Measurements included fractional anisotropy (FA), extracellular free-water maps (FW), and free-water corrected fractional anisotropy (FAT), for each individual. Group comparisons were made using voxel-wise, tract-based spatial statistics.

**Results:** CHR subjects showed widespread FA reductions compared to HCs (P < .05). In contrast, FW analysis showed limited extent of FAT decreases.
FATTY ACIDS IN SCHIZOPHRENIA PATHOLOGY

14. A POTENTIAL ROLE OF PLASMA FREE FATTY ACIDS IN SCHIZOPHRENIA PATHOLOGY

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Background: Schizophrenia (SZ) is a debilitating mental disorder with a global prevalence of 1%. A number of putative mechanisms have been proposed to explain the etiopathogenesis and illness presentation of SZ. Previous findings indicated that SZ patients have increased breakdown of membrane phospholipids due to an increased phospholipase A2 activity. The resulting free fatty acids (FFAs) may serve as a precursor for many important biochemical reactions such as regeneration of membrane phospholipids, production of prostaglandin vasodilators, and so on. Thus, levels of FFAs may have significant implications in the SZ pathology. The present study is thus to test whether levels of plasma FFAs are altered in the SZ patients early in the course of disease development and, if so, whether altered plasma FFAs can be affected by treatment of atypical antipsychotic drugs (AAPD).

Methods: Twenty-five first-episode, antipsychotic-naive patients (FEAN) with SZ were recruited to compare with 29 age- and gender-matched healthy controls (HC) subjects. Blood samples were collected at baseline and 4-weeks after initial treatment with AAPD. Plasma FFAs were quantitatively determined by capillary gas chromatography.

Results: (1) Levels of plasma total FFAs in the FEAN-SZ patients were significantly lower (P < 0.02) than those in HC subjects, with specific reductions in 16:0, 18:0, 16:1(n-7)c, 18:1(n-9)c, and 18:2(n-6) c FFA levels. (2) Following 1-month (1-m) treatment with AAPD, the altered plasma FFAs in FEAN-SZ were no longer significantly different from the HC subjects. (3) Significant baseline correlations within several fatty acid families [16:0 vs. 18:0, 16:0 vs. 18:1(n-7)t, 18:0 vs. 18:1(n-9)c, and 18:1(n-9)t vs. 18:1(n-9)c] were shown in all groups, whereas other correlations [14:0 vs. 22:0, 15:0 vs. 21:0, 16:0 vs. 22:0, 16:0 vs. 16:1(n-7)c, 16:1(n-7)c vs. 16:1(n-7)t, 18:2(n-6) vs. 20:4(n-6) were only found in the HC subjects. (4) Following 1-m AAPD treatment, the insignificant correlations between 15:0 and 16:0, 16:0 and 16:1(n-7)t, 18:0 and 18:1(n-9)t as well as 21:0 and 22:0 in baseline FEAN-SZ patients became significant like HC subjects.

Conclusion: These findings imply that there is an imbalanced free fatty acid biosynthesis in early course unmedicated SZ patients and that reduced levels of plasma FFAs may reflect a depleted pool of FFAs during the early (patho)etiologic course of SZ. Insignificant pretreatment correlations between 15:0 and 16:0, 16:0 and 16:1(n-7)t, 18:0 and 18:1(n-9)t as well as 21:0 and 22:0 in FEAN-SZ patients may represent biochemical domains of therapeutic impact. Moreover, reductions of 18:2n6 may reflect a decreased pool of 20:4n6 fatty acids for subsequent production of prostaglandin vasodilators. These may have important implications for understanding of the blunted niacin-induced flushing response in schizophrenia.

15. NEURONAL AUTOANTIBODIES AND BLOOD-BRAIN BARRIER DISRUPTION IN SUBJECTS AT ULTRA-HIGH RISK FOR PSYCHOSIS

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Background: Neuronal surface autoantibodies (NSAbs) have been identified in patients with psychotic disorders, with meta-analytical evidence indicating a higher prevalence in first-episode psychosis (FEP), probably dependent on the assay used. The causal significance of these NSAbs is unclear, with a suggestion that that blood–brain barrier disruption (BBBD) may be an important additional factor. We aimed to establish whether, prior to illness onset, NSAbs and BBBD are present in subjects at ultra-high risk (UHR) for psychosis.

Methods: Sera from 260 UHR subjects in the EUGIEI study and 110 healthy controls were tested with a fixed cell-based assay (CBA) using HEK293 cells that had been transfected to express one of 30+ NSAbs; IgG, IgA and IgM binding was assessed using indirect immunofluorescence. Levels of S100B, a putative marker of BBBD, were assessed using a chemoluminescence assay in this cohort and an FEP cohort (n = 226).

Results: NSAbs were present in 8.8% of UHR subjects and 7.3% HCs (ns) with NMDAR the most frequent antigen. Serostatus did not predict transition to psychosis, and 2 of 3 seropositive patients who transitioned to psychosis had antibodies of diverse Ig isotype. Patients with brief limited intermittent psychotic symptoms (BLIPS) were twice as likely to be seropositive at baseline compared to patients who transitioned to psychosis. Interestingly, subjects who were positive on fixed CBA for any NSAb or for only NMDAR antibodies showed trends towards higher negative syndrome scores across multiple scales. These subjects had impaired verbal memory scores as measured by the Rey auditory verbal learning test (RAVLT) (P = .0019), a finding that mirrors patients with NMDAR encephalitis and may be reflective of hippocampal dysfunction.

Samples were also tested for NMDAR IgG antibodies using a live CBA; this detected a higher prevalence of NMDAR IgG antibodies in the total cohort than did fixed CBA (19 subjects (5.1%) vs 2 (0.5%); P = .0025). Mean S100B levels were higher in FEP subjects than in UHR subjects (P < .001) and controls (P < .0001). UHR subjects with high S100B levels surprisingly showed lower total psychopathology scores (BPRS; P = .032, less negative symptoms (SANS; P = .039), and disability (GAF; P = .009), whereas in FEP S100B levels were associated with worse positive psychotic symptoms.

Conclusion: A minority of subjects at risk of psychosis have NSAbs detectable in serum; these individuals may have worse negative symptoms and demonstrate impaired neurocognition. Further work is required to clarify the immunological and neuroanatomical substrates of these changes. BBBD may be progressive with the development of psychosis. The paradoxical finding of improved symptoms and function in subjects with evidence of greater BBBD differentiates UHR subjects from later stage psychosis and represents an exciting avenue for further investigation.

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16. INVESTIGATION OF THE AUDITORY STEADY STATE RESPONSE IN SCHIZOPHRENIA, SCHIZOAFFECTIVE, PSYCHOTIC AND NONPSYCHOTIC BIPOLAR DISORDERS

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