For negative events, no significant difference was observed in the main effect (News: F(1, 58) = 1.838, p= 0.180, η2p=0.031; Group: F(1, 58) = 0.023 p= 0.881, η2p=0.000) and the interaction effect (F(1, 58) = 0.979, p= 0.327, η2p=0.017). Patients with schizophrenia and healthy controls all updated their beliefs to a greater extent in response to good news than bad news.

Discussion: Patients with schizophrenia tended to exhibit negative bias in belief updating only for positive events, but not for negative events. Such a pattern may be crucial for the maintenance of these low pleasure beliefs in these patients. These results highlight the importance of belief updating intervention for patients with schizophrenia.

F16. INFLAMMATORY MARKERS ARE ASSOCIATED WITH PSYCHOMOTOR SLOWING IN PATIENTS WITH SCHIZOPHRENIA COMPARED TO HEALTHY CONTROLS

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Background: Previous data have demonstrated that administration of inflammatory cytokines or their inducers leads to altered basal ganglia function associated with reduced psychomotor speed. Patients with schizophrenia (SCZ) exhibit psychomotor slowing and cognitive impairments. Increased inflammatory markers are seen in some patients with SCZ compared to healthy controls (CON). Previous work has reported relationships between inflammatory markers and cognitive impairment, though most studies have evaluated a small number of inflammatory markers and/or cognitive tasks. We thus measured a broad array of inflammatory markers in addition to a variety of psychomotor tasks. We hypothesized that there would be associations between inflammatory markers and psychomotor speed in SCZ subjects compared to CON.

Methods: 43 patients with SCZ and 29 CON were recruited from the Atlanta Veterans Affairs Medical Center. The following inflammatory markers were measured: tumor necrosis factor (TNF), interleukin (IL)-1beta (IL-1b), IL-6, IL-10, monocyte chemoattractant protein 1 (MCP-1), IL-6 soluble receptor (IL-6sr), IL-1 receptor antagonist (IL-1ra), and TNF receptor II (TNFR2). Principle components analysis (PCA) was used to create factor loadings that were subsequently used in analyses. The following psychomotor tasks were used: Finger Tapping Task (FTT), Reaction Time Task (RTT), Symbol Coding (SC), and Trail Making Test (TMT). T-tests and chi-square tests were performed to test for differences between diagnostic groups. Spearman's rank order correlations were used to test the associations between inflammatory markers and cognitive tasks. Finally, stepwise, backward linear regression models were used to determine the relationship between inflammatory markers and cognition.

Results: There were no differences in age, sex or smoking status between SCZ and CON, but the SCZ group had a higher proportion of black individuals (chi square=4.511, p=0.034). Performance was worse in SCZ than CON on FTT (p=0.002) as well as SC and TMT (both p<0.01). SCZ subjects had higher concentrations of IL-1RA compared to CON (t=-2.004, p=0.049), but no other markers differed significantly between groups.

In SCZ subjects, higher levels of TNF (p=0.034), IL-1b (p=0.047) and IL-10 (p=0.027) correlated with worse FTT performance. Similarly, higher levels of IL-1b (p=0.033) and IL-10 (p=0.027) correlated with worse TMT performance.

The PCA yielded three factors: Factor 1 (TNF, IL-10, MCP-1), Factor 2 (IL-1b, IL-6, IL-1RA), and Factor 3 (IL6sr and TNFR2). In linear regression models, controlling for demographics, smoking, and Toxoplasma gondii IgG serointensity, Factor 1 predicted worse performance on the FTT (p = 0.029) and TMT (p = 0.012). However, factor 3 predicted better performance on the FTT (p = 0.01), RTT(p = 0.000), and SC(p = 0.034).

Fewer and less consistent associations were found between inflammatory markers and cognition in CON subjects in both correlations and linear regressions.

Discussion: Psychomotor speed and processing speed were significantly worse in SCZ than CON subjects. Inflammatory markers were more predictive of psychomotor slowing in SCZ subjects than in CON. This finding is consistent with prior studies demonstrating that inflammatory stimuli alter basal ganglia function associated with reduced psychomotor speed as well as a recent study demonstrating similar findings in patients with major depressive disorder. As such, this study provides further support that peripheral inflammatory markers in patients with SCZ may contribute to psychomotor slowing. Psychomotor speed may serve as a relevant outcome variable for future studies targeting inflammatory mediators to treat patients with neuropsychiatric disorders such as SCZ.

F17. EXAMINATION OF THE FINDINGS SUGGESTING NIEMANN–PICK DISEASE TYPE C IN PATIENTS WITH SCHIZOPHRENIA

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Background: Once dystonia or dysmetria occurs in patients with schizophrenia, we usually know that antipsychotics might have induced these involuntary movements. However, some of these patients have severe neurological symptoms to be considered as adverse effects. In fact, we were able to identify probable Niemann–Pick disease type C (NPC) in such patients. NPC is a rare, progressive genetic disorder characterized by the inability of the body to transport cholesterol and other fatty substances (lipids) inside the cells. The symptoms are varied, such as jaundice, splenomegaly, hepatomegaly, vertical supranuclear gaze palsy, cerebellar ataxia, dystonia, dysphagia, resistant psychotic symptoms, and slow-progressive impairment of intellectual ability. NPC is difficult to diagnose, particularly adult-onset NPC. Diagnosis of NPC is confirmed by staining skin cells (fibroblasts) or by bone marrow smears of the affected individual for determining the level of cholesterol accumulation (filipin staining) and identifying known mutations in the NPC1 or NPC2 gene (gene sequencing). Recently, some studies have reported on the probable biomarkers for NPC.

In the present study, we measured some biological markers of NPC in plasma and urine. Furthermore, the mRNA expression levels of NPC1 and NPC2, which are pathological genes of NPC, were compared between patients with schizophrenia and normal controls.

Methods: Blood and clinical data were obtained with the approval of the institutional review boards of Dokkyo Medical University School of Medicine. The study design followed the ethical norms of the Ministry of Health, Labor, and Welfare of Japan. We obtained written informed consents from all patients in this study. Five patients with neurological symptoms were evaluated using the NPC Suspicion Index. Furthermore, several biological markers were measured. In addition, mRNA expression levels of NPC1 and NPC2 were measured and analyzed in patients with schizophrenia and healthy controls.

We measured bile acid content in urine with LC/MS/MS and serum oxysterol with Q-TOF LC/MS in five patients with neurological symptoms. In addition, whole-genome sequences were analyzed in one patient by a particular company. The mRNA expression levels of NPC1 and NPC2 were measured using the TaqMan method and we performed their semi-quantitative assessment with beta-actin. The Mann–Whitney U test was performed to compare mRNA expression levels between patients with schizophrenia and normal controls by using SPSS Statistics.
Results: One patient had significantly high biological marker levels for NPC. No patients without this patient have significantly high biological markers as the disease. The mRNA expression levels of NPC1 and NPC2 in patients with schizophrenia were significantly higher than that in normal controls.
Discussion: The mRNA expression levels of both NPC1 and NPC2 in patients with schizophrenia were higher than those in healthy controls. Further investigation is required, including resequencing of NPC1 and NPC2, to understand the implications of the results.

F18. PSYCHOPATHOLOGY AND SELF-CONCEPT IN A LONGITUDINAL COHORT OF CHILDREN WITH FAMILIAL HIGH RISK OF SCHIZOPHRENIA OR BIPOLAR DISORDER

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Background: For both schizophrenia and bipolar disorder, the single largest risk factor for developing the disorder is having a positive family history of the disorder. Therefore, children of parents with schizophrenia or bipolar disorder constitute relevant study populations for studying etiological pathways and early antecedents of these severe mental disorders. The aim of this study was to explore potential differences in trajectories of psychopathology and self-concept from age seven to age nine in children with familial high risk of schizophrenia or bipolar disorder and controls.
Methods: A cohort of 522 children were recruited using the Danish nationwide registers. 202 children had at least one parent with a schizophrenia spectrum disorder, 120 had at least one parent with bipolar disorder and 200 were controls. Children in the control group were matched to children of parents with schizophrenia spectrum disorders on age, gender and municipality. Children in the control group could not have parents with schizophrenia spectrum disorders or bipolar disorder but were not excluded for any other reasons. At baseline, when the children were seven years old, they went through a comprehensive assessment including e.g. cognitive skills, motor functioning, psychopathology and self-concept. Psychopathology was examined with a variety of assessment tools including Child Behavior Checklist (CBCL). Self-concept was assessed with the 'I Think I Am' questionnaire, which measures five domains of self-concept. At the first wave of follow-up, at age nine the children's psychopathology and self-concept were once again assessed with the CBCL and the 'I Think I Am'.
Results: The differences in psychopathological profiles and self-concept as well as differences in trajectories from age seven to age nine between the groups will be presented at the meeting.
Discussion: The differences in trajectories of psychopathology and self-concept will be discussed in the context of possibilities for developing early intervention strategies towards children with familial risk of schizophrenia or bipolar disorder.

F19. TREATMENT RESPONSE OVER THREE RANDOMIZATIONS IN THE TREATMENT OF EARLY-ONSET SCHIZOPHRENIA SPECTRUM DISORDERS STUDY (TEOSS)

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Background: We sought to characterize the trajectory of symptom change in the Treatment of Early-Onset Schizophrenia Spectrum Disorders Study (TEOSS), the largest randomized control trial in early-onset schizophrenia.
Methods: TEOSS randomized 119 youths ages 8–19 years old to 8 weeks of treatment with molindone, risperidone, or olanzapine (First Randomization). TEOSS defined treatment response as: completion of 8 weeks of treatment with the randomized antipsychotic, a Clinical Global Impression-Improvement (CGI-I) Scale score of 1("very much improved") or 2 ("much improved"), and a 20% reduction in symptoms on the Positive and Negative Syndrome Scale (PANSS). If participants did not respond to the initial randomized antipsychotic, participants were re-randomized to one of the two remaining antipsychotics (Second Randomization, n=50). If participants did not respond to the second antipsychotic, participants received the remaining antipsychotic (Third Randomization, n=23). Prior work found there was no statistically significant difference in response rates in the First Randomization when comparing molindone (50%), risperidone (46%), and olanzapine (34%) [Sikich et al. 2008]. Our study extends prior work by reporting the response rates for the Second and Third Randomizations, and also by reporting how long it took for youths to improve clinically with each antipsychotic.
Results: When combining all three Randomizations, response rates were: molindone 36.8% (25/68), risperidone 48.4% (31/64), and olanzapine 33.3% (20/60) (p=0.19). Response rates for the Second and Third Randomizations were: molindone 14.8% (4/27), risperidone 40.9% (9/22), and olanzapine 33.3% (8/24) (p=0.28). For youths who responded in the First Randomization (n=55), those randomized to molindone took 5.4 weeks (SD=2.4), risperidone 4.4 weeks (SD=2.3), and olanzapine 4.1 weeks (SD=2.4) to achieve and sustain a CGI-I of 1 ("very much improved") or 2 ("much improved") (p=0.24). When we combined the Second and Third Randomizations, it took youths randomized to molindone (n=4) 5.3 weeks (SD=2.8), risperidone (n=13) 4.8 weeks (SD=2.4), and olanzapine (n=4) 6.0 weeks (SD=2.2) to achieve and sustain a CGI-I of 1 or 2 (p=0.71). When we combined all three Randomizations, it took youths randomized to molindone (n=25) 5.4 weeks (SD=2.4), risperidone (n=33) 4.6 weeks (SD=2.3), and olanzapine (n=18) 4.6 weeks (SD=2.4) to achieve and sustain a CGI-I of 1 or 2 (p=0.39).
Discussion: This is the largest study in early-onset schizophrenia to look at response rates after failing randomized antipsychotic treatment. Furthermore, our study reports the average time it takes to achieve clinically-significant improvement in early-onset schizophrenia. ClinicalTrials.Gov Identifier: NCT00053703.

F20. THINK APP: A MOBILE APP–BASED INTERVENTION FOR ADOLESCENTS WITH FIRST-EPISODE PSYCHOSIS

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