correlated with AL at trend level (adjusted R = −.251, P = .070). No significant associations were found for negative symptoms (P = .582). AL decreased after treatment with olanzapine, risperidone, or quetiapine was commenced in patients with SCZ and FEP that between the baseline assessment and the 6- and 12-week follow-up.

Conclusion: Our data provide evidence for cumulative physiological dysregulation in patients with SCZ and FEP that is linked to the experience of current positive psychotic symptoms. AL could be a useful model that takes stress, long-term adaptation, and its failures into account to further understand the pathophysiology of schizophrenia.

9. ELEVATED TNF-α LEVELS IN CEREBROSPINAL FLUID OF PATIENTS WITH SCHIZOPHRENIA

Juan Gallego1, Christopher Morell2, Robert McNamara3, Todd Lenz3, and Anil Malhotra4
1Weill Cornell Medical College; 2Zucker Hillside Hospital; 3University Of Cincinnati

Background: Elevated levels of proinflammatory cytokines have provided evidence in support of the inflammatory hypothesis of schizophrenia. Most studies in schizophrenia have reported cytokine levels in peripheral blood, but the number of studies investigating cytokines in CSF in schizophrenia is still very small and those studies typically have small sample sizes. Of the cytokines studied, IL-6 and IL-8 have been most commonly measured and reported while abnormalities in other cytokines, such as TNF-α, have not been reported in CSF of patients with schizophrenia. Therefore, our aim was to study a panel of cytokines in cerebrospinal fluid of a decently large sample of patients with schizophrenia and healthy volunteers. In addition, we examined correlations between these cytokines and psychiatric symptoms.

Methods: Thirty-three patients with schizophrenia-spectrum disorders and 23 healthy volunteers underwent a lumbar puncture. CSF of 15–25 cc was obtained from each subject. CSF cytokine (IL-1β, IL-2, IL-4, IL-6, IL-8, and TNF-α) concentrations were determined in duplicate by enzyme-linked immunosorbent assay (ELISA) and a high-sensitivity MilliplexTM Multiplex kit (HSTCMAG-28SK-06, Millipore, Billerica, MA) per manufacturer’s instructions. In patients, psychiatric symptoms were assessed using the Brief Psychiatric Rating Scale–Anchored version (BPRS-A). Comparisons in cytokine levels between groups were performed using either t-tests for normally distributed variables or Wilcoxon rank-sum tests for nonnormally distributed variables. Correlations were computed using the Pearson’s correlation coefficient.

Results: The mean age of 36.6 years (SD = 11.7) in patients and 38.1 years (SD = 10.1) in controls. Twenty-four (72.3%) of 33 patients and 14 (60.1%) of the 23 healthy volunteers were male. Mean total BPRS score in patients was 28.6 (SD = 9.0). Mean TNF-α values were elevated in patients (6.47 pg/ml [SD = 3.1]) compared to healthy volunteers (3.76 pg/ml [SD = 2.5], P = .001). There were no statistically significant differences in levels between patients and controls in IL-2 (mean = 5.46 pg/ml [SD = 1.9] vs. 4.82 pg/ml [SD = 2.0]), IL-6 (9.31 pg/ml [2.6] vs. 8.9 pg/ml [2.9]) and IL-8 (49.44 pg/ml [11.2] vs. 47.21 pg/ml [12.2]). Levels of IL-1β and IL-4 were not detected in more than 30% of the CSF samples; therefore, these cytokines were not entered in the analysis. Correlational analysis showed that TNF-α was significantly correlated with the conceptual disorganization item on the BPRS-A (r = .39, P = .04). No other correlations were statistically significant.

Conclusion: TNF-α, a pro-inflammatory cytokine and a key participant in the acute phase response of the inflammatory cascade, is elevated in CSF of patients with schizophrenia providing support to the inflammatory hypothesis in schizophrenia. Future studies should focus not only on IL-6 but also on TNF-α to further understand the role of proinflammatory cytokines in schizophrenia.

10. BRAIN STRUCTURE BIOMARKERS AT THE PSYCHOSIS/NONPSYCHOSIS INTERPHASE: FINDINGS FROM THE BIPOLAR–SCHIZOPHRENIA NETWORK FOR INTERMEDIATE PHENOTYPES

Elena Ivleva1, Brett Clementz2, Anthony Dutcher1, Sina Aslan1, Bradley Witte3, Gaurav Poudyal1, Hanzhang Lu4, Shashwath Meda5, Godfrey D. Pearlson6, John Sweeney7, Matcheri Keshavan8, and Carol Tamminga1
1University of Texas Southwestern Medical Center; 2University of Georgia; 3Advance MRI, LLC; UT Southwestern Medical Center; 4Johns Hopkins University, UT Southwestern Medical Center; 5Institute of Living, Hartford Hospital; 6Yale School of Medicine; 7Olin Research Center; 8BIDMC/Harvard Medical School

Background: The study presents whole brain and regional gray matter density (GMD) characteristics contrasted along the psychosis/nonpsychosis interface in (1) schizophrenia—schizoaffective—psychotic bipolar—nonpsychotic bipolar probands, and (2) their first-degree relatives organized by lifetime psychosis expression, from the B–SNIP consortium sample.

Methods: A total of 1652 3Tesla T1-weighted MPRIAGE or IR-SPGR scans were analyzed using Voxel-Based Morphometry (SPM8/VBM8/DARTEL) with subsequent subject-level regional GMD characterization.

Results: Among probands, individuals with schizophrenia (mean d = 0.66) and schizoaffective disorder (mean d = 0.73) showed overlapping and diffusely distributed GMD reductions spanning cortical and subcortical regions, with the largest effects in the frontotemporal, cingulate, and insular cortices, compared to healthy controls. Probands with psychotic bipolar disorder contrasted with controls showed modest GMD reductions (mean d = 0.54), primarily localized to anterior limbic regions. The data for nonpsychotic bipolar probands will be also reported; we predict normal/near-normal GMD characteristics, relative to controls. Among relatives organized by lifetime psychosis manifestations, relatives with DSM-IV Axis I psychotic disorders and Axis II psychosis spectrum personality disorders (schizoid, paranoid, and schizotypal) showed GMD reductions intermediate in magnitude between the psychosis probands and healthy controls, primarily localized to bilateral frontal regions. In contrast, relatives without lifetime Axis I/II psychotic disorders showed GMD not different from healthy controls. No effect of concurrent medications (antipsychotics, mood stabilizers, antidepressants) on GMD outcomes was detected in probands; the majority of relatives were unmedicated.

Conclusion: Our findings indicate divergent GMD characteristics for psychotic versus nonpsychotic phenotypes among probands with severe mental illness and their biological relatives and suggest that GMD alterations may serve as a biomarker unique to psychosis.

11. EXTENDED ASSOCIATION STUDIES OF SMOOTH PURSUIT AND ANTISACCADE EYE MOVEMENTS: FINDINGS FROM THE B-SNIP STUDY

Rebekka Lencer1, Lauren J. Mills2, Ney Alliey-Rodriguez3, James L. Reilly4, Andreas Sprenger5, Jennifer E. McDowell6, Rebecca Shafee7, Steve A. McCarroll7, Matcheri S. Keshavan8, Godfrey D. Pearlson1, Carol A. Tamminga, Brett A. Clementz2, Elliot S. Gershon1, John A. Sweeney1, and Jeffrey R. Bishop7
1University of Muenster; 2University of Minnesota; 3University of Chicago; 4Northwestern University; 5University of Luebeck; 6University of Georgia, Athens; 7Harvard Medical School; 8Yale School of Medicine; 9UT Southwestern