T22. PITUITARY GLAND VOLUME DIFFERENCES IN INDIVIDUALS WITH PSYCHOSIS: RESULTS FROM THE BIPOLAR-SCHIZOPHRENIA NETWORK ON INTERMEDIATE PHENOTYPES (B-SNIP) STUDY

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Results: Thirty patients were diagnosed with schizophrenia, delusional disorder, schizoaffective disorder, bipolar disorder or a long-term unspecified nonorganic psychosis during follow-up, while 23 patients achieved complete remission. Eight patient samples showed autoreactivity to the N-terminal fragment of the PAGE protein family (PAGE2B/PAGE2/PAGES3), whereas no such autoreactivity was seen among the controls. PAGE autoreactivity was associated with a significantly increased risk of being diagnosed with schizophrenia during follow-up (odds ratio 6.7). An antiserum raised against the N-terminal fragment stained an unknown extracellular target in human cortical brain tissue (Zandian et al., Transl Psychiatry 7: e1177; doi:10.1038/tp.2017.160). We are currently investigating the identity of this target. In addition, two other putative new autoantibodies found primarily among the patients, and rarely in the controls, will be discussed at the meeting.

Discussion: Our findings suggest that autoreactivity to the N-terminal portion of the PAGE protein family is associated with schizophrenia in a subset of patients with first-episode psychosis. In addition, we propose that searching for novel autoantibodies in an unbiased way may be feasible using state-of-the-art proteomic methods, and can yield useful biological markers for immune involvement in subgroups of individuals diagnosed with psychiatric disorders.

T21. ALTERATIONS OF CRY2 AND PER3 GENE EXPRESSION ARE ASSOCIATED WITH GRAY MATTER ABNORMALITIES OF THALAMIC-LIMBIC NETWORK IN UNIPOLAR DEPRESSION AND BIPOLAR DEPRESSION

Chengcheng Zhang*,1, Peiyan Ni1, Tao Li¹
1West China Hospital, Sichuan University

Background: The current study aimed to identify shared and distinct brain structure abnormalities and their relationships with circadian gene expression in patients with bipolar depression and unipolar major depression.

Methods: A total of 103 subjects participated in this study, including 32 patients with bipolar depression (BDP), 26 patients with unipolar depression (UDP) and age, sex-matched 35 healthy controls (HC). Magnetic resonance imaging scans and then used optimized voxel-based morphometry to explore group differences in regional gray matter volume (GMV). Circadian gene mRNA expressions in peripheral blood were measured on a microarray platform. The circadian-related gene mRNA expressions have significantly decreased in the patients with BDP, and the increased GMV focused on the thalamus. The circadian-related gene mRNA expressions have significantly decreased in the patients with BDP.

Results: The GMV of the thalamus-limbic pathways had significantly increased in BDP cases relative to comparison subjects, while in UDP the increased GMV focused on the thalamus. The circadian-related gene mRNA expressions have significantly decreased in the patients with BDP, however with higher expression levels in the UDP cases. In addition, the GMV of right thalamus in the UDP was positively associated mRNA level of CRY2 gene, while the GMV of right hippocampus in the UDP was negatively associated mRNA level of PER3 gene.

Discussion: Our study identified the relationship between abnormalities of thalamic-limbic network and alterations of circadian gene pathway in BDP and UDP. The shared GMV abnormality was the right thalamus. PER3 might be critical to hippocampus dysfunction in UDP, and CRY2 might be critical to thalamus dysfunction at a right-hemisphere function in BDP.

T22. PITUITARY GLAND VOLUME DIFFERENCES IN INDIVIDUALS WITH PSYCHOSIS: RESULTS FROM THE BIPOLAR-SCHIZOPHRENIA NETWORK ON INTERMEDIATE PHENOTYPES (B-SNIP) STUDY

Synthia Guimond*,1, Samantha Tingue2, Gabriel A. Devenyi3, Yun-Xiang Tang4, Luke Mike4, M. Mallar Chakravarty4, John A. Sweeney4, Godfrey D. Pearlson4, Brett A. Clementz4, Carol A. Tamminga4, Matcheri S. Keshavan1
1Harvard Medical School, Beth Israel Deaconess Medical Center; 2Emmanuel College, Beth Israel Deaconess Center; 3McGill University; 4Second Military Medical University; 5Beth Israel Deaconess Center; 6University of Texas Southwestern; 7Yale University; 8University of Georgia; 9University of Texas Southwestern Medical Center

Background: When exposed to stress, the hypothalamic-pituitary-adenal axis is hyperactivated, which can cause the enlargement of the pituitary gland. Hence, pituitary gland volume could be a biomarker of stress present in psychosis. However, it remains unclear if individuals with psychosis have larger pituitary gland than healthy people. Previous studies investigating this question used small samples and reported inconsistent results. In the current study, we used an automated multi-atlas segmentation method to investigate the differences between pituitary gland volumes in a large sample of individuals on the psychosis spectrum.

Methods: Data collection was completed across six sites in the Bipolar-Schizophrenia Network on Intermediate Phenotypes (B-SNIP) consortium with a total of 755 participants included in the study - 174 individuals with schizophrenia (SZ), 115 with schizoaffective disorder (SZA), 167 with psychotic bipolar disorder (PBD), and 299 healthy controls (HC). Structural magnetic resonance images were acquired and pituitary gland volumes were obtained using the automated MAGeT-Brain algorithm. General linear model and post-hoc independent t-tests were used to analyze the differences between subgroups of patients using clinical diagnosis and agnostic Biotype classification (Biotype 1 being the most cognitively impaired). We also explored potential effect of antipsychotic intake, symptoms severity and duration of illness. In all analyses, we used Bonferroni correction for multiple comparisons and entered confounds as covariates (age, sex, race, intracranial volume, and site).

Results: Overall, the pituitary gland volumes were not significantly different between patients and HC. No significant main effect of diagnosis was observed, but SZ patients had trending larger pituitary volume compared to HC (p=.033, uncorrected). We observed a significant main effect of Biotype (p=.003), with Biotype 1 having significantly larger pituitary gland than HC and Biotype 2 (p=.004 and p=.013). In the patients group, no significant relationship between the pituitary gland and the amount of antipsychotic intake was observed (r=.02, p=.68). Significant correlations with the pituitary gland volume were observed with symptoms severity (r=.22, p=.000), and with the duration of illness (r=-.18, p=.002). Importantly, Biotypes did not significantly differ in terms of symptoms severity nor duration of illness.

Discussion: As a group, individuals with psychosis do not have abnormal pituitary gland volume, but larger pituitary gland is related to shorter duration of illness and greater symptoms severity. Therefore, larger pituitary gland volume could be a state-related biomarker of psychosis. Moreover, while we did not observe any significant subgroup differences using clinical diagnosis, our results suggest an increase in pituitary volume in biotype 1 patients compared to HC. These findings clarify previous inconsistent reports, and encourage further investigation of stress biomarkers in individuals with psychosis with lower cognitive abilities. In the future, this could lead to the development of more targeted treatments for this specific subgroup of patients.

T23. DYNAMICS OF NEURONAL METABOLISM AFTER THE ACUTE ONSET OF PSYCHOSIS – A TWO YEARS FOLLOW-UP 1H/31P-MR-SPECTROSCOPY STUDY IN NEUROLEPTIC NAIVE UHR TRANSITION PATIENTS

Stefan Smesny*,1, Diana Berberich1, Alexander Gussow1, Kerstin Langbein1, Mario Walther1, Juergen Reichenbach1
1University Hospital Jena; 2University of Applied Sciences Jena

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