

ABSTRACTS COLLECTION

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P271. Negative and Positive Urgency-Related Left Dorsolateral Prefrontal Cortex Activity During Emotion Processing Predicts Manic Symptom Changes One Year Later in Distressed Young Adults

Maya C. Schumer*, Michele A. Bertocci, Haris A. Aslam, Simona Graur, Genna Bebko, Richelle S. Stiffler, Alexander S. Skeba, Tyler J. Brady, E. Kale Edmiston, Henry W. Chase, Sheri L. Johnson, Mary L. Phillips

University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, United States

Background: There is a critical need for identifying robust biomarkers of objective risk factors associated with Bipolar Disorder (BD), particularly those predictive of mania/hypomania and mixed states, as these are pathognomonic features of BD. Moreover, identifying biomarkers of future BD risk informs not only early risk detection and targets for treatment developments, but also aids our understanding of pathophysiological processes underlying BD. Impulsivity is a widely studied characteristic of BD that is elevated during manic and mixed episodes and persistent during euthymic periods. While impulsivity is a multi-faceted trait, emotion-triggered impulsivity, or emotion-based rash action, is perhaps the most important form, as it is associated with a broad range of key outcomes in BD, including and notably suicidality. Negative and positive urgency (NU/PU), defined as the tendencies to act impulsively in response to negative and positive affect respectively, are evident in adults with BD and have been identified as risk factors for future BD, yet neuroimaging studies examining neural correlates of urgency in the context of predicting BD risk are sparse. We previously reported negative relationships between NU and PU-related blood oxygen level dependent (BOLD) activity in the left dorsolateral prefrontal cortex (L DLPFC) during approach emotion processing and lifetime mania risk in a transdiagnostic cohort (excluding young adults with BD diagnosis) of 106 young adults who were seeking treatment for psychological distress. However, it has not yet been tested whether urgency-related L DLPFC activity is a predictor of manic symptoms over time, and if the relationship is specific to mania or if it also extends to depressive symptoms.

Methods: Twenty-one distressed adults ages 18-23 (mean age 20.84 ± 1.49 , 17 female), from the initial aforementioned transdiagnostic cohort that were scanned on a 3T fMRI while performing an implicit facial emotion processing task, completed baseline and 12-month follow-up assessments of hypo/mania and depression measured by the Moods Spectrum Scale (MOODS) Mood Manic and Depressive Domains. Angry and happy face-related activity at baseline scan was examined using an anatomical mask of regions supporting emotion processing and executive function, which included the L DLPFC. Parameter estimates were extracted from separate multiple regression models of NU and PU covarying for age and gender, $p < 0.001$, uncorrected, $k = 20$.

We performed two parallel, separate multiple linear regression models with NU and PU-related L DLPFC BOLD activity, baseline MOODS Mood Manic Domain score, age, and gender as predictors and Mood Manic Domain score at 12-month follow-up as the dependent variable.

To test whether the L DLPFC was specific to predicting mania, we performed two additional multiple regression models (one for NU, one for PU) controlling for baseline depression, with 12-month MOODS Mood Depressive Domain score as the dependent variable.

Results for both the primary analysis with mania and the specificity analysis with depression were each considered significant at $p < 0.025$, Bonferroni-corrected for two models.

Results: The initial models with baseline demographic variables explained 18% of the variance in 12-month MOODS Mood Manic Domain score. The full model including NU-related L DLPFC activity was significant, $F(2,16)=4.88$, $p = 0.009$, with an adjusted R^2 of 0.44, such that the L DLPFC explained 26% of the variance and was significantly associated with mania one year later ($\beta = -8.07$, $t = -2.95$, $p = 0.009$). The full model including PU-related L DLPFC activity was also significant, $F(2,16)=4.2$, $p = 0.016$, with an adjusted R^2 of 0.39, such that the L DLPFC explained 21% of the variance and was significantly associated with mania one year later ($\beta = -7.24$, $t = -2.61$, $p = 0.019$).

In the specificity analysis with 12-month MOODS Mood Depressive Domain score, the full model including NU-related L DLPFC activity was not significant, $F(2,16)=3.56$, $p = 0.029$, with an adjusted R^2 of 0.338. L DLPFC activity was not significantly

to SPG). Linear mixed model was used to analyze the data (fixed factors: group [BDDActive iTBS, BDDSham iTBS, BDDNo iTBS or HCNo iTBS], duration [125 ms, 250 ms, 500 ms or 3000 ms], category [VVS Lower, VVS Higher, DVS Lower or DVS Higher]; random factor: participant).

Results: For positive GC values, there was significant three-way interaction between group, duration and category from tests of fixed effects ($F[27, 135614]=1.89, p=0.004$). For DVSHigher, the active group exhibited stronger DEC than the BDD without iTBS across the four durations, and they achieved similar levels as the controls.

Conclusions: In this proof-of-concept study, we explored the effects of interactions between excitatory neuromodulation and rapid face presentation on dorsal visual stream and ventral visual stream connectivity in BDD. Excitatory neuromodulation induced by iTBS enhanced dynamic connectivity for DVSHigher, achieving similar levels as the healthy controls. These results, showing target engagement and modulation, have implications for designing novel perceptual retraining treatments to remediate perceptual distortions of appearance in those with BDD.

Keywords: Body Dysmorphic Disorder, Repetitive Transcranial Magnetic Stimulation (rTMS), Visual Perception, Effective Connectivity, Perceptual Distortion of Appearance

Disclosure: Nothing to disclose.

P424. The Psychosocial and Educational Burden of Obsessive-Compulsive Disorder in Youth

McKenzie Schuyler*, Bowie Duncan, Daniel Geller, Amitai Abramovitch

Massachusetts General Hospital, Boston, Massachusetts, United States

Background: Obsessive-compulsive disorder (OCD) is associated with significant multi-domain impairment. Indeed, OCD is associated with poorer long-term educational attainment, vocational problems, and cognitive dysfunction. Compared to adults, youth with OCD exhibit relatively better cognitive functioning. Nevertheless, they may struggle more in family and peer relationships and may require more assistance in school settings compared to healthy controls. Only a few studies have directly examined these issues. Furthermore, research investigating the impact of comorbidities on psychosocial functioning in pediatric OCD is limited. The goal of the present study was to directly assess psychosocial functioning in a large, well-characterized sample of children and adolescents with OCD.

Methods: A sample of 100 children and adolescents with OCD (Mage = 11.42; 42.0% male) and 138 non-OCD controls (Mage = 11.45; 42.8% male) participated in the study. Participants were administered a battery of measures including the Kiddie Schedule for Affective Disorders and Schizophrenia (KSADS) to assess diagnostic status and comorbidities, the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS) to assess OC symptom severity, the Social Adjustment Inventory for Children and Adolescents (SAICA) to assess psychosocial adjustment, and the Family Environment Scale (FES) to assess family functioning. In addition, information regarding repeated grades, special placement classes and extra help/tutoring was obtained from teachers and parents. We conducted independent samples t-tests to examine group differences in psychosocial, family, and school functioning variables.

Results: Compared to controls, youth with OCD had significantly higher levels of school behavior problems ($p=.001$; Cohen's $d=.43$), problems with spare time activities ($p=.000$; $d=.89$), problems with peer activities ($p=.000$; $d=.71$), and problems with parents ($p=.001$; $d=.49$). Compared to controls,

families of youth with OCD also had significantly elevated current and past family conflict scores ($p=.035, d=.28$ for both), and reduced current and past family cohesion scores ($p=.000, d=.51$; $p=.018, d=.32$). There were no differences in the family expression subscale. Significantly more youth with OCD attended special classes (0.7% vs. 4.3%, $p<.0001$) and received extra help (10.2% vs. 64%, $p<.0001$) compared to controls. There were no differences in rates of repeated grades. OCD severity was significantly correlated with attending special classes and with several SAICA subscales. However, it was not correlated with FES subscales. Finally, comorbidity with attention deficit hyperactivity disorder, conduct disorder, and oppositional defiant disorder resulted in a different pattern of difficulty, primarily in the domain of school behavior problems.

Conclusions: Although pediatric OCD is not associated with substantial cognitive impairments, this population receives more extra help in school, exhibits a higher frequency of enrolling in special classes, and displays significantly more psychosocial and family problems than controls. In addition, there is a differential impact of several comorbid disorders on psychosocial problems in this population. These results highlight the need for careful screening for OCD in this age group, including assessment of comorbid conditions. More research is needed to examine how reassurance-seeking versus measurable academic deficits contribute to help-seeking in this population.

Keywords: Obsessive-Compulsive Disorder (OCD), Pediatric, Family Study

Disclosure: Nothing to disclose.

P425. Tripping Mice and Stoned Fish: Head Twitch Response (HTR) and Behavioral Phenotypic Evidence of Effect Differences Between Synthetic Psilocybin and Psychedelic Mushroom Extract

Leonard Lerer*, Alexander Botvinnik, Katherine Spear, Orr Shahar, Patryk Lipski, Haley Calderon, Karin Blakolmer, Tzuri Lifshytz, Bernard Lerer

Back of the Yards Algae Sciences, Chicago, Illinois, United States

Background: Anecdotal reports suggest that the behavioral and pharmacological effects of psilocybin-containing, "full spectrum" psychedelic mushroom extract (FSME) differ from those of chemical psilocybin (PSIL) in their nature and intensity. A limited number of rodent studies have compared synthetic psilocybin (or psilocin) with crude psychedelic mushroom extract. Furthermore, psychedelic mushrooms contain intermediate products of the psilocybin biosynthetic pathway such as baeocystin, norbaeocystin and aeruginascin that may influence the nature of the effect of psilocybin ("entourage effect") along with other components such as harmines with monoamine oxidase inhibiting properties. In the current study, we compared the effect of PSIL to that of FSME on the mouse head twitch response (HTR), which is correlated with psychedelic effects in humans, on a rodent screening test for antidepressant effect and in a behavioral phenotypic zebrafish model.

Methods: Male C57Bl/6j mice were used in all head twitch experiments. PSIL (98.75% purity) was provided by Usona Institute. FSME, a methanol extract of *Psilocybe cubensis* with a psilocybin content of 1.5%, was provided by BYAS-PEB. Drug doses were calculated so that equal injection volumes of PSIL and FSME contained equal concentrations of psilocybin on a mg per kg basis. Control mice received vehicle (VEH) injections (0.9% NaCl solution). HTR was measured over 20 minutes in a magnetometer-based system using ear clip magnets. The tail suspension test (TST) was conducted using a Noldus Ethovision system by observers blind to treatment status, 48 hours after