Thalamic Structure and Function In Youth with and at Familial Risk for Bipolar Disorder

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SUBMISSION DETAILS

What is the Methodological Question Being Addressed? Youth with and at risk for bipolar disorder have early and specific neural network dysfunction while processing rewards. In this presentation, we examined brain circuitry underlying reward processing in youth with and at risk for bipolar disorder relative to youth at risk for depression and low-risk controls without any family history of any psychiatric disorders to examine brain circuitry differences and their association with key symptom dimensions related to aberrant goal pursuit. Brain circuitry underlying reward processing in youth with and at risk for bipolar disorder relative to youth at risk for depression and low-risk controls without any family history of any psychiatric disorders can inform novel targeted early intervention discovery, provide rationales for comparative effectiveness trials by informing participant inclusion, defining mediators and moderators, and inform stratification based on neurobiological risk.

Introduction Youth with and at familial risk for bipolar disorder have aberrant reward function in key prefrontal-striatal networks. However, thalamic structure, function, and connectivity associated with trait and state features of bipolar disorder before and around emergent mania is poorly understood.

Methods Youth with (n=22) versus without (n=23) BD underwent structural neuroimaging during reward processing using the monetary incentive delay (MID) task at baseline and 12 months. Healthy Youth at high and low risk for mood disorders [BD-risk (n=40), MDD-risk (n=41), and HC (n=45) [mean age 13.09 +/- 2.58, 56.3% female] also completed the MID task at baseline and were followed for behavioral and clinical outcomes over 4.37 +/- 2.29 years. Region of interest (ROI) analyses were conducted using an anatomically defined thalamus seed during reward anticipation and feedback. Psychophysiological interaction and whole-brain voxel-wise group differences were also conducted ($Z > 3.1$; FWE-cluster corrected $p < .05$).

Results Relative to healthy controls, adolescents with BD showed greater reductions in thalamic volume from baseline to 12-month follow up (Treatment x time interaction, Left thalamus: $F(45)=8.38$, $p =0.006$; Right thalamus: $F(45)=3.96$, $p =.05$). Among BD youth, reductions in both hemispheres were negatively associated with mania symptom improvement/maintenance ($p<0.05$). Relative to MDD-risk and HC, BD-risk had decreased activation of the thalamus during anticipation of monetary gain $F(2,118) = 4.64$; $p = .01$ (FDR-corrected $p = .04$). BD-risk had less connectivity between the thalamus and left middle frontal gyrus ($Z > 3.1$; $p < .001$) and left superior temporal gyrus ($Z > 3.1$; $p < .05$) compared to MDD-risk. Voxel-wise, BD-risk had decreased activation in the cerebellum during anticipation and outcome of monetary gain relative to MDD-risk and HC ($Z > 3.1$; $p < .001$; $Z > 3.1$; $p < .01$, respectively). Decreased thalamic connectivity was associated with increased impulsivity at baseline and reduced prosocial behavior at follow-up.

Conclusion Compared to typically developing youth, BD youth showed statistically significant volumetric reductions in both the left and right thalamus over the course of 12 months, such that those with worsening scores had greater reductions in volume even after accounting for treatment, suggesting a possible disorder related phenomenon. Reduced thalamic activation and connectivity during reward processing may distinguish familial risk for BD from familial risk for MDD and represent early markers of vulnerability that precede symptom onset and may herald social dysfunction later in development.

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Guidelines I have read and understand the Poster Guidelines

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