Latent Volumetric Structure of Gray Matter in Adolescent Bipolar Disorder Using Factor Analysis and Structural Equation Modeling

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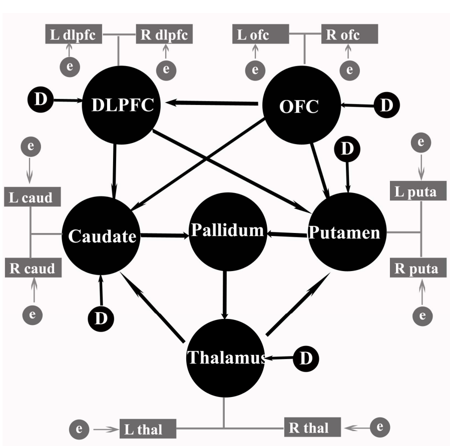
Background: Abnormalities of the cortico-striatal-thalamic-cortical (CSTC) circuit and limbic-cortico-striatal-thalamic-cortical (LCSTC) circuit have been hypothesized in mood disorders; however, the spatial relationships between these regional structures have not been examined. We used structural equation modeling (SEM) to assess the *a priori* statistical relationships among the latent variables, which may influence the volumes of other regions or structures, within the CSTC and LCSTC circuits.
Methods: Participants included 59 healthy controls (HC) (M/F=32/27, age 17.71 ± 2.74 y) and 59 subjects with bipolar disorder (BD) (M/F=31/28, age 17.69 ± 2.81 y). Structural 3D-SPGR MRI brain scans were acquired at 1.5 T (TR/TE=24/5ms, 1x1x1mm^3, FOV= 256 mm). Segmentation and labeling of cortical and subcortical brain volumes were generated with the Freesurfer software package. Pearson's partial correlation of the regional brain volumes, including prefrontal cortex (PFC, including superior, middle and inferior frontal gyri), orbitofrontal cortex (OFC), anterior and posterior cingulate gyri, thalamus, caudate, putamen, pallidum, hippocampus, and amygdala, for individuals were conducted after controlling for age, gender and intracranial volume covariates. Principle component analysis (PCA) decomposed the correlation matrices into six principal components in each group. SEM examined the plausibility of different relationships between neural circuit volumes within the CSTC (Fig. 1) and LCSTC (Fig. 2) pathways.
Results: Six factors were extracted, including basal ganglia system (caudate, putamen and pallidum), limbic system (cingulate gyrus, PFC and OFC), amygdalo-hippocampal (A-H) complex system, para-limbic system (anterior cingulate gyrus and hippocampus), pre-limbic (OFC, thalamus, putamen, pallidum),and infra-limbic system (A-H, and posterior cingulate gyrus). For the CSTC circuit, the significant latent variable equations were the path from pallidum to thalamus, the path from putamen to pallidum, and the path from OFC to PFC in both HC and BD. In addition, the path from OFC to putamen, and the path from thalamus to OFC were significant in HC ($t > 1.96$, $p<0.05$). For the LCSTC circuit, the significant latent volumetric structure included the path from hippocampi to amygdale, the path from OFC to anterior cingulate gyrus, and the path from OFC to PFC for both HC and BD. In addition, the path from anterior cingulate gyrus to posterior cingulate gyrus, and the path from amygdale to OFC were significant in BD. BD differed from HC on the estimated parameters in the path from OFC to amygdale (HC-BD, t=-2.21, $p<0.05$) in the LCSCT circuit and a trend in the path from OFC to putamen (HC-BD, $t = -1.93$, $p<0.05$).
Conclusion: Our results suggest different patterns between adolescent HC and BD for the spatial relationships, mainly from the projection of orbitofrontal cortex to subcortical structures within the CSTC and LCSTC circuits. These differences may point to abnormalities that underlie these mood disorders.



Fi.g. 1

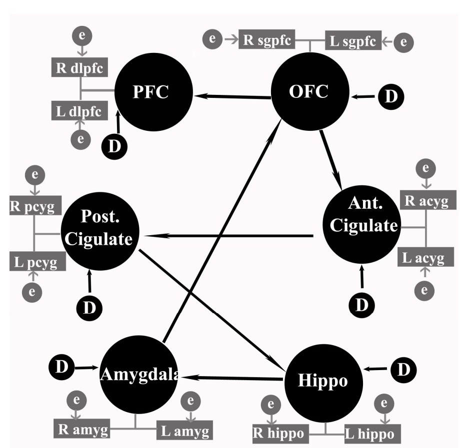


Fig. 2