Developmental changes in resting-state functional connectivity in borderline personality disorder: a network analysis approach

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Borderline Personality Disorder (BPD) is a serious mental disorder associated with self-harm, unstable interpersonal relationships, and rapidly changing emotions. Symptoms of BPD often emerge in adolescence and may reflect both neurobiological and socioemotional changes.

Previous research in adults with BPD has identified dysfunctional activity and connectivity of regions involved in emotion processing and social cognition, including the amygdala, medial prefrontal cortex, and middle temporal gyrus. There is, however, a paucity of research on differences in functional connectivity in adolescents with BPD symptoms and no previous work on developmental changes in connectivity in BPD. In this study, we used graph theory analyses of resting-state fMRI data to characterize functional connectivity differences in a sample of adolescents and young adults with BPD symptoms.

Methods: Participants were 88 individuals ages 13-30 with (*n=*45) and without (*n=*43) BPD symptoms (3 or more symptoms on clinical interview) who were matched on age and sex. We collected five minutes of resting-state fMRI data (TR = 1.0s, TE = 30ms, voxel size = 2.3mm isotropic) in a Siemens Tim Trio 3T scanner while subjects lay awake with eyes open. Resting-state network matrices were derived from temporal correlations among whole-brain regions defined by an established parcellation containing 264 regions (Power et al., 2011). Graph analyses were conducted on binary undirected matrices at density thresholds varying from 1-20% (in 1% increments). We focused particularly on group and age comparisons of nodal statistics, including degree, eigenvector, and betweenness centrality. Additional analyses to be presented will include changes in within- and between-network connectivity using community detection methods.

Results: Integrating across density thresholds, the BPD group exhibited higher betweenness in the right anterior cingulate cortex (ACC) and right putamen (all *p*s < .005). BPD patients also had lower degree centrality in the left post-central gyrus and decreased degree and eigenvector centrality in the left superior temporal gyrus. Conversely, the BPD group had higher degree in the right caudate nucleus and right middle frontal gyrus(figure 1), and increased degree and eigenvector centrality in the right middle cingulate cortex. We found positive age x BPD interactions for betweenness centrality in the left ACC, left inferior occipital gyrus, and left inferior parietal lobule. (all *p*s< .01). We also found a positive BPD x age interaction in eigenvector and degree centrality in the left middle cingulate cortex and increased degree in the left ACC as individuals with BPD transition into early adulthood. With development, individuals with BPD symptoms showed less connectivity in the right precentral gyrus (degree, betweenness, and eigenvector centrality, see figure 2) and left postcentral gyrus (degree and betweenness).

Discussion: Across three complementary nodal centrality metrics, we found evidence of regions that differed in BPD during both adolescence and adulthood, as well as regions whose connectivity developed differently in BPD than typically developing controls. In line with a recent meta-analysis of adults with BPD (Visintin et al, 2016), we found increased connectivity in ACC nodes compared to controls, consistent with the notion that enhancement of the default mode network (involved in self- and other-referential thinking) may be implicated in mood-related psychopathology. A novel contribution of our study was the finding that the centrality of the middle and anterior cingulate increases developmentally to a greater extent in BPD than in controls. One hypothesis is that this pattern may be linked with the development of the cingulo-opercular network involved in sustained cognitive control, which has a more protracted developmental course (Velanova, Wheeler, & Luna, 2009). In order to understand the clinical significance of this developmental pattern, we will also present data linking developmental changes in connectivity to clinical and behavioral data.

References

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*Figure 1.*

*Group differences in degree centrality in the left temporal parietal junction, right caudate nucleus, right middle cingulate cortex, right middle frontal gyrus, and right superior temporal gyrus. Networks were thresholded for graphical display at a density of 0.12, which is representative of the connectivity patterns across densities.*



*Figure 2.*

*Interactions between BPD diagnosis and age predicting changes in eigenvector centrality in right precentral gyrus (left panel) and left middle cingulate cortex (right panel).*