# Atypically Increased Functional Connectivity in Young Adults with Borderline Personality Disorder

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**Targeted audience:** clinical trainees and researchers in psychiatric disorders. **Introduction**: Borderline personality disorder (BPD) is a prevalent mental illness characterized by pervasive instability in emotion, interpersonal relationships, self-image, and behavior[1]. Our previous functional MRI study reported that compared with healthy control subjects, patients with BPD show no significant Blood Oxygen Level Dependent (BOLD) signal increases in the superior temporal gyrus (STG) and fusiform gyrus (FG), when responding to emotionally congruent and incongruent music-face images[2]. In the present study, we hypothesized that the BOLD characteristics in patients with BPD resulted from altered functional networks that regulate multi-modal sensory inputs. This study utilized topologic network analysis for resting state fMRI (rs-fMRI) in order to investigate which brain networks are mostly affected (or functionally impaired) in young adults with BPD, and thus provide an objective tool to quantitatively access atypically organized neural mechanism related to BPD phenotypes. **Methods:** Subjects included eight healthy women (age: 24.3±3.9 years) and six women with BPD (age: 24.6±3.8 years). Five minute rs-fMRI data were acquired using a 3T GE-Signa scanner at TR = 2000 ms, TE = 35 ms, flip angle = 90°, field of view = 240 mm, matrix size = 64x64, slice thickness = 4 mm, and zero gap covering the whole brain. During the acquisition, each participant was instructed simply to keep eyes closed and to not think of anything in particular. The preprocessing steps using SPM 8 (www.fil.ion.ac.uk/spm) included: first, correction of systematic, slice-dependent time shifts; second, rigid body correction for inter-frame head motion within and across all scans; third, spatial normalization to MNI space for group comparison; fourth, spatial smoothing with an isotropic Gaussian kernel of 8 mm FWHM to increase statistical power. The resulting images were detrended to abandon linear trend, temporally filtered with a Chebyshev band-pass filter (0.01 Hz - 0.08 Hz), and regressed out with the following covariates: rigid body realignment parameters, average white matter signal, average ventricular system signal, and global signal. Filtered-regressed time series were finally parcellated into 116 network node regions by using the Automated Anatomical Labeling (AAL) atlas (www.ansir.wfubme.edu). The average time series of individual node was used to represent spontaneous neural activity in subsequent network analysis. The strength of functional connectivity between each pair of nodes was defined by the magnitude of Pearson correlation coefficent of the average time courses. Multivariate pattern analysis using support vector machine was utilized to identify consensus functional connections providing the highest discriminative power (i.e, pairwise connections whose functional connectivities were significantly changed in BPD patients)[3]. To measure topological efficiency at individual funcional connections, a weighed undirected network matrix was produced by taking a proportional threshold ($P_{th}$) to the cross-correlation coefficient matrix of node time series (i.e., $0 \le P_{th} \le 1$). Two effective network measures were then evaluated at every discrete value of $P_{th}$ : global communication efficiency ($E_G$) and local communication efficiency ($E_L$). $E_G$ measures the degree of functional *integration* to quantify the capacity of parallel information process, where a low value of $E_G$ indicates the presence of disconnected nodes inhibiting parallel processes. In contrast, $E_L$ is a measure of functional *segregation,* where a low value of $E_L$ quantifies the reduction of densely interconnected nodes known as functional clusters or modules[4]. **Results and Discussion**: The diameter of each sphere in Figure 1 represents the corresponding discriminitive power. Several regions exhibited greater power than others, i.e., right pallidum, right cerebellum 6, left olfactory cortex, left anterior cingulate gyrus. Right pallidum (a component of the limbic loop of the basal ganglia involved in the regulation of motivation, behavior, and emotions) exhibited the highest power, and the functional connectivities between this region and the visual areas, the default mode network, limbic system, cerebellum were increased in BPD relative to controls. These altered connectivities showed promise in differentiating BPD from healthy controls (leave-one-out cross-validation, senstivity: 98.75%, specificity: 96.57%, accuracy: 97.86%), which might be used a biomarker for BPD. The subsequent network analysis supplemented our findings by showing that functional integration and segregation of those connections were extremely increased in BPD as well (Fig. 2), suggesting an impaired affective network to integrate emotion perception and regulation in BPD patients.

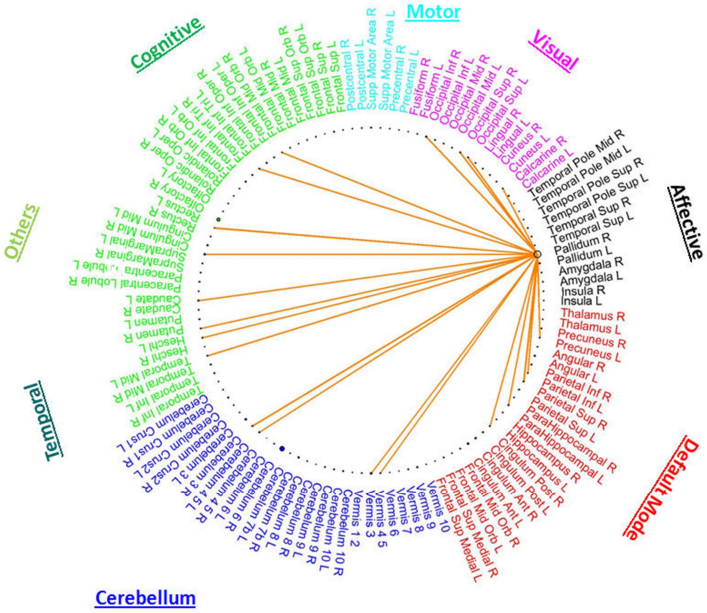


**Figure 1.** Distribution of consensus functional connections showing hyperconnectivity in BPD. Regions are color-coded by category. Each sphere scales regional discriminative power evaluated from multivariate pattern analysis using the leave-one-out cross-validation.

**References:** 1. Gunderson JG. Disturbed relationships as a phenotype for borderline personality disorder. Am J Psychiatry. 2007;164:1637-40. 2. Jeong JW, Kuentzel JG, Diwardkar VA, et al. Atypical auditory-visual integration mechanism in borderline personality disorder: a fMRI analysis using emotional congruence and incongurence in music and face, Proc ISMRM, 2012, p. 3670. 3. Zeng LL, Shen H, Liu L, et al. Identifying major depression using whole-grain functional connectivity: a multivariate pattern analysis, Brain, 2012;doi10.1093/brain/aws059. 4. Rubinov M, Sporns O. Complex network measurs o f brain connectivity: use and interpretations. Neuroimage, 2010;52:1059-69.

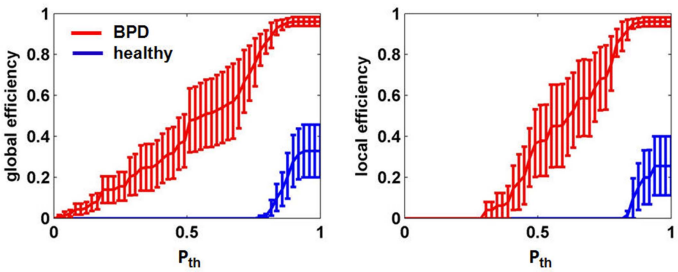


**Figure 2**. Global and local communication efficiency of the network consisting of altered connections in **Fig. 1**. Average and standard error were reported at discrete threshold of $P_{th}$.