High Dynamic Range Connectivity: Task-Dependent Functional Connectivity Differences in Euthymic Bipolar Disorder

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Connectivity based on Functional Magnetic Resonance Imaging (fMRI) is providing a fresh perspective on the function of the human brain – especially in neurological illnesses not easily characterized by structural MRI. Functional connectivity is all the more effective because it can be computed without specifying a time-course of task-related activity; thus, even spontaneous abnormalities of brain activity can be identified. This is helpful when the actual time-course of activity is unknown, for instance due to unexpected or not-yet-identified functional differences. Because the scale of neural connectivity far outstrips the scale of normal functional imaging studies, we apply informatics techniques of visualization and pattern identification to make the problem more comprehensible.

One of the most difficult psychiatric disorders to diagnose and treat, that has also proved elusive to parsimonious identification, is Bipolar Disorder (BD). Bipolar disorder is characterized by periods of mania, depression and euthymia (asymptomatic state), and despite well-characterized symptoms its exact physical cause has proved elusive. Recent work has shown that during euthymia a wide variety of brain regions show significant differences from controls. Activation level and size differences have been reported in bilateral striatum [1, 2], Medial Frontal Gyrus (MFG) [3], Inferior Frontal Gyrus (IFG) [1, 3, 2] cingulate [3], thalamus, insula, lingual gyri, left amygdala, intraparietal sulcus, all three temporal gyri, right parahippocamopal gyrus, and intraparietal sulcus [4, 1, 2]. Thus, while euthymic bipolar patients seem to be experiencing normal emotional state, a wide array of regions are in fact acting differently than they would in normal controls.

Our work expands on previous functional connectivity studies by comparing euthymic bipolar subjects and normal controls on the scale of whole-brain connectivity. By utilizing OpenCL we calculate connectivity across the entire brain, then calculate the median connectivity between all pairs of Freesurfer-defined anatomical regions. In so doing, we are able to identify large scale differences in brain connectivity and to localize abnormal activity to particular connection and regions. Further, we apply this method to two different functional tasks: resting state and a task well-known to provoke overactive emotional responses in euthymic bipolar subjects. From these two tasks we are able to determine whether there were areas of overlapping abnormality: both in the connections and in graph metrics. The most dramatic differences between bipolar patients and normal controls was a large-scale connectivity increase during emotion identification, and a large-scale decrease in connectivity during the resting state task.

The large effect size and lack of significant overlap of affected connections indicate a high sensitivity of our methods to small differences in psychological function. Future work could use these data-rich methods as the substrate for machine-learning based feature extraction, and could thus be used to identify potential loci for further analysis. These same informatics-type methods may be used in future research to increase the quality of diagnosis of bipolar disorder, and indeed could be applied to a wider array of psychological disorders.

References


