Abstract:
The heterogeneous human frontal pole has been identified as a node in the dysfunctional network of major depressive disorder. The contribution of the medial (socio-affective) versus lateral (cognitive) frontal pole to major depression pathogenesis is currently unclear. The authors performed morphometric comparison of the microstructurally informed subdivisions of human frontal pole between depressed patients and comparison subjects using both univariate and multivariate statistics. Multisite voxel- and region-based morphometric MRI analysis was conducted in 73 depressed patients and 73 matched comparison subjects without psychiatric history. Frontal pole volume was first compared between depressed patients and comparison subjects by subdivision-wise classical morphometric analysis. In a second approach, frontal pole volume was compared by subdivision-naive multivariate searchlight analysis based on support vector machines. Subdivision-wise morphometric analysis found a significantly smaller medial frontal pole in depressed patients, with a negative correlation of disease severity and duration. Histologically uninformed multivariate voxel-wise statistics provided converging evidence for structural aberrations specific to the
microstructurally defined medial area of the frontal pole in depressed patients. Across disparate methods, subregion specificity in the left medial frontal pole volume in depressed patients was demonstrated. Indeed, the frontal pole was shown to structurally and functionally connect to other key regions in major depression pathology, such as the anterior cingulate cortex and the amygdala via the uncinate fasciculus. Present and previous findings consolidate the left medial portion of the frontal pole as particularly altered in major depression.

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