Subtyping Schizophrenia Subjects Using Working Memory and Approach Motivation Neuroimaging Markers

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Introduction

- Negative symptomatology is central to psychotic disorders, particularly common in individuals with schizophrenia.
- Working memory (WM) and approach motivation (AM) behaviors, constructs in the Research Domain Criteria (RDoC) project, have shown relationships with various components of negative symptoms (1).
- Brain systems involved with AM (2) and WM (3) constructs may be involved with these disorders.
- Functions of multiple brain regions have been linked with various components of negative symptoms (1). Thalamus (Th) is central to WM functions (5). NAc and Th have been observed to show altered morphology in individuals with negative symptoms (6, 7).
- In this study, we compiled measures across two levels of analysis (imaging and behavior) for two constructs (WM and AM) from two dimensions (positive valence and negative cognitive systems).

Methods

- Participants: MPRAE scans from 220 subjects (100 schizophrenia, 120 controls). Surfaces of Th, Cd, NAc computed using high-dimensional brain mapping methods (9) and Principal Components Analysis (PCA) to generate PC scores for each individual representing shape (8).
- Standardized cognitive performance and psychopathology (positive symptom, negative symptom, and disorganized thoughts) measures.

Cluster Analysis

- Hierarchical clustering, followed by k-means clustering were performed on the first ten PC scores from Th, Cd, NAc of all subjects. A similar process was run on just the schizophrenia subjects.

Statistical Analysis

- Cognitive performance and psychopathology measures of the schizophrenia clusters were compared to each other as well as with controls using MANOVA.

Shape Difference

- Scatter plots show the first 3 principal components (PC) of Th and Cd (left panel), and Th and NAc (right panel). The PCs were used as examples of visualizing the distribution of clusters. They were also the most important in determining cluster membership.
- Plot of Th and Cd shows a clear separation of cluster 0 and cluster 1.
- Plot of Th and NAc does not show a separation between cluster 0 and cluster 1.
- This suggests that the NAc shape scores were not significant determinants of cluster membership. This corroborates the finding that shape scores were not significantly different between clusters 0, 1, and controls.

Results

A. Schizophrenic Clusters 0 and 1

B. PC 1 of Th & Cd

C. PC 1 of Th & NAc

D1. Cognitive Performance

Figure shows cognitive performance of schizophrenia subjects in cluster 0 vs. cluster 1.

IQ = Crystallized IQ; WM = Working Memory; EM = Episodic Memory; RA = Executive Function.

Table shows cognitive and psychopathology measures for which cluster 0 and cluster 1 significantly differed.

* Indicates unequal variances were assumed.

D2. Psychopathology

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Conclusions

- Clustering using neuropsychometric measures yielded significant differences among negative symptom pathology and WM constructs. The subgroup with more severe surface deformities exhibits (1) increased deficits in cognitive functioning, (2) increased severity in negative symptoms, and (3) increased severity in positive symptoms.
- These findings are consistent with the previous work identifying neuropsychological impaired and near-normal subgroups of schizophrenia using neuropsychological measures with the impaired subgroup showing more severe cortical thinning (8).
- This study demonstrates a proof of concept of a convergent, multiamodal approach to studying neurobiological dimensions.

References