Separation of recent-onset psychosis patients from healthy controls based on resting-state functional connectivity pattern classification.

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Background: Multivariate pattern recognition analyses (MVPA) have the potential to identify brain pattern alterations across the entire brain due to their capacity to extract the innate inter-regional dependencies of distributed brain pathologies from high-dimensional training data and generalize the learned discriminative rules to unseen patient cohorts. While MVPA applied on structural data has been confirmed to be a valuable biomarker for patients with psychosis, the MVPA classification based on functional connectivity (FC) alterations might be promising better sensitivity. In this study we investigated whether multivariate pattern classification using whole-brain resting-state FC facilitates the identification of individuals experiencing recent onset psychosis (ROP), as well as how these alterations relate to verbal memory performance.

Methods: We used rsfMRI images from 19 sex and gender matched healthy controls (HC) and 19 ROP patients. Correlation matrices of activity between brain regions were used as features for multivariate analysis. The support vector machine pipeline wrapped into repeated nested cross-validation was used to train a multi-modal diagnostic system and evaluate its generalization capacity in new subjects. The top features were extracted in order to determine the regions of FC that were most discriminative for the classification. Neuropsychological testing of verbal and working memory functions: Rey Auditory Verbal Learning Test, Auditory digit span (forward and backward), and verbal fluency (semantic and phonetic) were correlated with the decisions scores provided by the classification algorithm.

Results: We found an overall classification accuracy, sensitivity, and specificity of 86.8 %, 78.9 %, and 94.7 %, We found an overall alteration of whole-brain FC involving both inter- and intrahemispheric brain connections. Marked long-range alterations driving the classification of ROPs and HCs occurred between the frontal lobe and both the temporal and parietal regions, but also with the right posterior cingulate gyrus, right thalamus, and left pallidum. The decision scores from the SVM classification correlated significantly with the forward digit span scores.

Conclusions: We were able to show that the separation of ROP patients from HCs based on rsFC pattern classification is possible with an accuracy of 86.8%. The working memory performance as measured by Forward Digit Span was associated with the decision scores of the classifier. The most discriminative areas of connectivity are consistent with regions often implicated in studies of the early stages of psychosis.