Diagnositic prediction for social anxiety disorder via multivariate pattern analysis of the regional homogeneity

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Target audience: Psychiatrists, neurologists and radiologists will benefit in having another approach in diagnosing social anxiety disorder.

Purpose: Despite decades of efforts have been spent studying the pathogenesis of social anxiety disorder (SAD), there are still no objective biological markers that can be reliably used to identify individuals with SAD. Multivariate pattern analysis (MVPA) with neuroimaging data has been successfully employed in predicting diagnosis of psychiatric disorders. Support vector machine (SVM), [1] the most commonly used MVPA analysis for pattern recognition in neuroimaging literature, has showed potential clinical value in separating patients with SAD from healthy controls individually using functional connectivity or grey matter volume. [2, 3] However, regional homogeneity (ReHo), which could reveal important information about local connectivity and reflects the temporal synchrony of the regional fMRI BOLD signals, [4] has never been studied with MVPA. We therefore examine the diagnostic potential of regional homogeneity (ReHo) underlying neural correlates of SAD using SVM.

Methods: The study was approved by the local research ethics committee, and written informed consent was obtained from all participants. Forty Structured Interview for the DSM-IV (SCID) Patient-Edition confirmed SAD patients and an equal number of healthy controls were recruited and scanned resting-state functional MRI. Psychological ratings and clinical symptoms associated with SAD were evaluated with the Liebowitz Social Anxiety Scale (LSAS). Patients with SAD and control subjects were pair-wise matched in age, gender and handedness. The MRI examinations were performed on a whole-body 3.0 T MR scanner (Siemens Trio, Erlangen, Germany) with a 12-channel head coil. The resting-state fMRI sensitized to changes in BOLD signal levels were obtained with a gradient-echo planar imaging sequence (TR/TE=2000/30 ms; flip angle=90°, slice thickness=5mm with no gap). Each functional run contained 205 volumes of which the first 5 were discarded to ensure steady-state longitudinal magnetization and subjects' adaptation to the environment. The ReHo maps were calculated using DPARSF Version2.1 (http://www.restfmri.net) for each subject. Subsequently, SVM implemented in the PROBID software package (http://www.brainmap.co.uk/probid.htm) was used to investigate the diagnostic accuracy of whole brain local connectivity in predicting individuals with SAD. Statistical significance of classification accuracy was set at $p < 0.001$ after permutation testing (1000 times).

Results: SVM allowed the classification of the two groups with diagnostic accuracy of ReHo was 77.5% (sensitivity=72.5%, specificity=82.5%, $p \leq 0.001$). The set of regions showed different value between the diagnostic groups mainly located in frontal, temporal and occipital regions, with default mode network (DMN), dorsal attention network, self-referential network and sensory networks mainly involved, while the left medial prefrontal cortex (mPFC) was identified with the highest weight. Across all of the patients, the test margin (the shortest distance from the optimal hyperplane) was found not correlated to total LSAS scores, and subscales ($p>0.05$).

Discussion: To our best knowledge, the current study is the first to examine the capability of SVM with ReHo in distinguishing patients with SAD from healthy subjects, and involves the largest sample of SAD patients in employing MVPA approach. By identifying the inter-group differences in whole brain ReHo pattern with an overall classification accuracy of 77.5%, the present study suggests local connectivity and synchronization extracted from fMRI bold signal could be a potential biomarker to identify SAD patients. Additionally, that no significant association was found between the test margin and clinical symptoms as assessed by LSAS scores suggested the distance away from the hyperplane might not be driven or affected by the symptoms, indicating the discriminating pattern of ReHo obtained was relatively stable.

Conclusion: By presenting widespread differential map of coherence abnormalities which could be used to identify patients with SAD at the individual level, this study provides evidence that the ReHo of brain has the diagnostic potential and can possibly act as a supplementary approach to identify SAD, especially regions with high weight. Future studies with the integration of ReHo with other different imaging modality measurements may give a better insight into the imaging biomarkers of the condition.

Figure 1. The discrimination maps for ReHo. These regions were identified by set the threshold to ≥30% of the weight vector scores. Warm color (positive value) indicated higher discriminated values in SAD than in healthy controls; while cool color (negative weights) indicates higher values in healthy controls than in SAD.

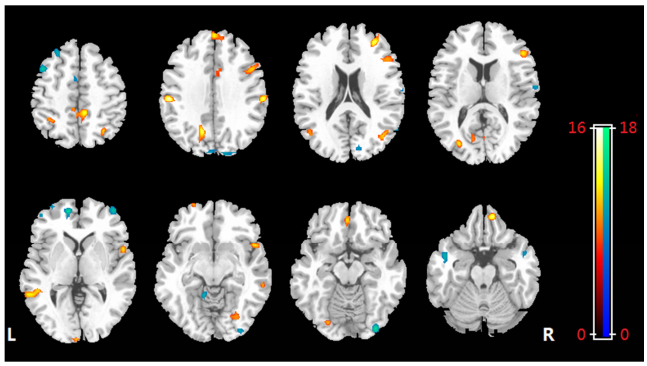
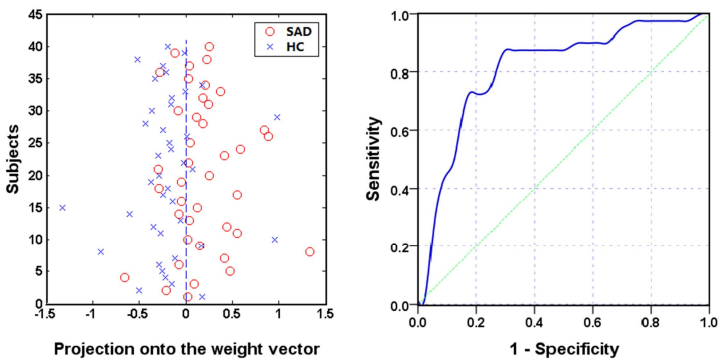


Figure 2. Classification plot (left) and receiver operating characteristic (ROC) curve (right) for the discrimination between SAD patients and healthy controls using ReHo maps, yielding an accuracy of 77.5% (sensitivity=72.5%, specificity=82.5%, P≤0.001).



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