A BP ANNs Study on the Dynamics of Resting-state fMRI Functional Connectivity for the Depression

Chuangjian Cai[1], Xue Xiao[1], Yan Zhu[2], and Kui Ying[3]

[1]*Department of Biomedical Engineering, Tsinghua University, Beijing, Beijing, China,* [2]*Yuquan Hospital, Tsinghua University, Beijing, China,* [3]*Department of Engineering Physics, Tsinghua University, Beijing, China*

Target audience: Psychologists, behaviorists, pattern identification investigators, fMRI investigators, neuroimaging scientists, and clinicians.

Purpose: It has been growing attention to use machine learning techniques or pattern recognition methods for functional MR imaging (fMRI), which help to identify the features of some brain disease, such as depression [1]. The previous work was based on static analysis. Some dynamic functional connectivity (fc) for resting-state fMRI (rs-fMRI) may be at least as important as the static fc (Catie Chang et al., 2009). In our study, we utilized dynamic functional connectivity analysis of rs-fMRI with BP ANNs (Back Propagation, Artificial Neural Networks) to investigate the dynamic differences between the depression and the control group for better understanding the neuropsychological basis of the depression.

Methods: Subjects included 10 depression patients and 12 healthy controls (males, right-handed, aged 20~25years). Rs-fMRI data was acquired using a 3T scanner (SIEMENS MAGNETOM Trio, T2-weighted axial structural images) with TR/TE=2000/30ms, slice thickness=4mm, FOV=210mm, and GRE-EPI. Each subject underwent a seven-min eyes-closed resting-state scan. Pre-processing using DPARSF (http://www.restfmri.net/forum/DPARSF) consisted of slice timing, realignment, normalization and spatial smoothing (FWHM=4mm). Images were also detrended and temporally filtered (0.01~0.08Hz). The nuisance covariates, including six motion parameters, global mean signal, white matter and cerebrospinal fluid signal, were regressed out. Covariates removed images were finally parceled into 116 regions (AAL atlas, www.ansir.wfubme.edu). The extracted time series of all the voxels in one region were averaged to represent the neural activity of that region. To measure the strength of functional connectivity, Pearson correlation coefficient [2] between each pair of regions was employed, and the dynamic connectivity of the two nodes was calculated using sliding window (width=80 seconds). We calculated the correlation coefficients distribution and then utilized the standard deviation as the dynamic feature in BP ANNs-based analysis. Kendall tau rank correlation coefficient [1] was used to measure the classification power. Features were then ranked according to this parameter to select those with coefficients greater than the presupposed threshold as the feature for final differentiation. Features selected were used to train BP ANNS (first layer=300, second layer=1) to classify, and the resulting network of BP was used to get the predicted value of the test sample (repetition times=35, fitted to normal distribution to obtain the mean value, which is the final value predicted, and standard deviation); The leave-one-out cross validation was performed. The performance of BP ANNs as a classifier was quantified based on accuracy of successful prediction and generalization rate calculated from the results of cross-validation. Then permutation tests were performed to evaluate the reliability of the BP ANNs classifier. To further test our method, we also applied BP to static functional connectivity analysis and employed another classifier, SVM (Support Vector Machine), to compare with BP ANNs.

Fig. 1.

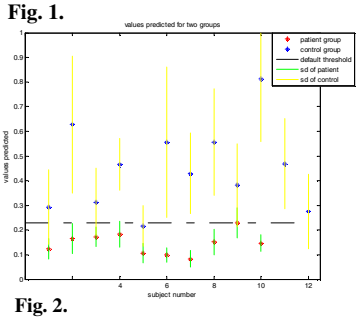
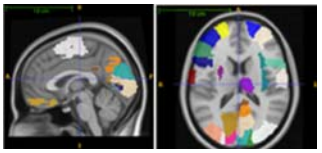


Fig. 2.



Results: A general rate of 95.45% was achieved while the accuracy was 100% for patients and 91.67% for controls. With the default threshold set to be 0.23, only one of the controls was predicted wrongly (Fig. 1). 45 pairs of brain regions and 38 brain regions (Fig. 2) picked out more frequently were finally extracted (number of occurrence greater than 10) (Fig. 3). The visual, default mode and cognitive networks were more related. For the distribution of permutation test (repetition times=781), p was zero, indicating a small probability of being wrong. BP ANNs performed better than SVM (Fig.4).

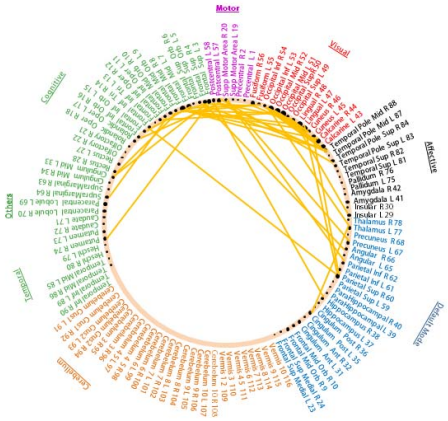


Fig.3 Distribution of functional connections. Regions in different category are color-coded. Each sphere scales the number of occurrence for regions picked out.

Discussion: The brain regions extracted out belonged to several major networks, including the default mode network, affective network, visual cortex areas, and cognitive network. Those pairs of brain regions with high discriminative power could consist of two regions from the same or different network, which reflected brain's complex internal relations. (1)Default mode network: The default mode network, is known to be involved in self-referential activity (Raichle, 2001; Greicius et al., 2003). Dynamic functional connectivity in several regions, including bilateral hippocampus gyrus, thalamus, posterior cingulate cortex, precuneus and angular gyrus, exhibited large weights. Abnormal change of the default mode network in depression has been reported in several previous studies (Greicius et al., 2007; Bluhm et al., 2009; Sheline et al.,2010; Zhou et al., 2010b); (2) Affective network, temporal network and others: In the affective network, regions such as insula, superior temporal gyrus and middle temporal gyrus, had discriminative relations with motor network. According to a previous research on the affective network, insula was found to show decreased regional homogeneity and the volumes of superior temporal gyrus turned to be abnormal with anxiety disorder (Z Liu et al., 2010; Michael et al., 2002). The altered connectivity between those nodes suggested the regularity of dynamic characteristics convincingly. The combination of BP ANNs and dynamic features works better than traditional method in discriminating depression patients from healthy controls. ANNs has the ability to determine the underlying relations regardless of the problem's dimensionality and system nonlinearity [3]. The SVM classifier, by contrast, is not optimal due to its simple projection. ANNs may be favorable under the condition where the model might be highly nonlinear.

Feature type/Pattern Recognition	General Rate	Patients	Controls
Dynamic/BP	95.45%	100%	91.67%
Static/BP	72.73%	80%	66.67%
Dynamic/SVM	54.55%	0	100%
Static/SVM	72.73%	60.00%	83.33%

Fig. 4. Comparison between BP and SVM.

References:

1. Zeng et al. Brain, 2012, 135(5): 1498-1507. 2 **2.** J.W Jeong et al. Proc. Intl. Soc. Mag. Reson. Med. 21 (2013) 3581 **3.** Basheer I A et al. Journal of microbiological methods, 2000, 43(1): 3-31