Disrupted functional brain connectivity in the salience network of post stroke depression patients

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Purpose

Poststroke depression (PSD), a common and important neuropsychiatric sequela of stroke, is known to be a multifactorial process.[1] In this study, using resting-state fMRI (rs-fMRI), we investigate possible alteration in functional connectivity (FC) in association with PSD in the salience network (SN), which was most functionally relevant to depression.

Methods

Fifteen PSD patients(64.9 ± 13.4 years) with unilateral left or right MCA infarction and 15 age-matched healthy control (63.13 ± 6.16 years) were recruited. All patients underwent rs-fMRI within one month from onset of stroke (25.6 ± 5.75 days). All subjects signed an informed consent and agreed to participate in the fMRI study. The study protocol was approved by the Institutional Review Board. Rs-fMRI was employed to assess neural activity and resting state BOLD signals during the scan were acquired using a 3.0T GE HD scanner (EPI, TR=2000ms, TE =30ms, flip angle =90, matrix=64x64, FOV=220mm, slice thickness = 4 mm, no gap). Image processing and statistical analyses were carried out using MATLAB v. R2010b and SPM5. For analysis of rs-fMRI data, the Functional Connectivity SPM5 toolbox (http://marsbar.sourceforge.net/) was used for identification of the SN with 15 independent seeds and SN-specific FC. The Pearson correlations were used to evaluate possible correlation between BDI and FC scores.

Results

In PSD patients, SN-specific FC was observed predominantly in intact brain hemisphere, while healthy control subjects showed SN-specific FC bilaterally. (Figure 1, FDR P <0.05) In addition, PSD patients showed a reduction in mean FC scores between ACC and ipsilesional insula, bilateral dorsolateral prefrontal cortex, and bilateral PST, while PSD patients showed increased mean FC scores between ACC and amygdala, hippocampus, and parahippocampus contralesionally. (Figure 2, *p<0.05, **p<0.01) Results of correlation analysis showed strong correlation of FC scores between ACC and parahippocampus in ipsilesional hemispheres with BDI scores in PSD patients (Figure 3, r=0.694, P=0.004).

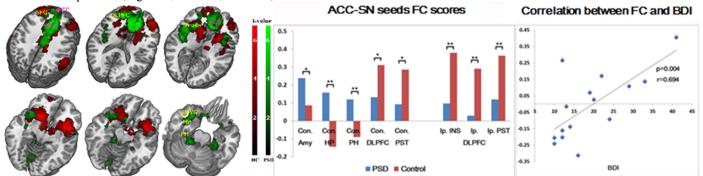
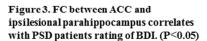


Figure 1. Rs-FC maps of the ACC seed for healthy controls (red) and PSD patients (green) at FDR P<0.05

Figure 2. Significant differences in SN-specific FC in PSD patients as compared to healthy controls. (*p<0.05, **p<0.01)



Discussion

Our findings suggest that increased FC between the ACC and these limbic structures results in alteration of encoding and storage of emotional memory, and PSD patients appear to maintain prolonged negative emotional memories while decreases in FC scores between ACC and other structures may indicate failure to effectively regulate activity in the SN in patients with PSD.[2,3] The strong positive correlation observed between ACC-ipsilesional parahippocampal FC and BDI scores appears to support this interpretation.

Conclusion

The altered FC within multiple SN components observed in PSD patients suggests that increased reactivity to negative emotion in limbic regions and decreased cortical regulation in dorsal frontal regions may be present in PSD.

References

- 1. Whyte EM, Mulsant BH et al. Post stroke depression: Epidemiology, pathophysiology, and biological treatment. Biol Psychiatry. 2002;52:253-264
- 2. Disner SG, Beevers CG et al. Neural mechanisms of the cognitive model of depression. Nat Rev Neurosci. 2011;12:467-477
- 3. Anand A, Li Y et al. Activity and connectivity of brain mood regulating circuit in depression. Biol Psychiatry. 2005;57:1079-1088.