Reduced Functional Connectivity in Major Depression: A Whole Brain Study of Multiple Resting-State Networks

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Introduction

Major depressive disorder (MDD) is a common psychiatric disease, characterized by a pervasive low mood and failure to suppress negative thought. fMRI studies have shown abnormal amygdala, subcortical and prefrontal cortex activations in MDD when performing emotional and cognitive tasks (Ebmeier, Rose, & Steele 2006). However, the persistent nature of the symptoms also indicates altered brain function in absence of goal directed behavior (i.e., task-free). This can be studied by measuring functional connectivity in the brain using resting-state (RS)-fMRI. Few studies have applied this method in depression. Decreased connectivity of the dorsal anterior cingulate cortex with the medial thalamus and the left pallidostriatum was found in MDD during rest (Anand et al. 2005). Also, depressives showed increased connectivity of the subgenual anterior cingulate and thalamus in a study of the default mode network (Greicius et al. 2007). Here we study MDD related changes in whole-brain functional connectivity, unbiased by selection of specific regions of interest or networks.

Methods

3.0T RS-fMRI data from 19 first episode, medication-free MDD patients (diagnosed within six months prior to this study) without psychiatric comorbidity were selected from the NESDA neuroimaging study (Penninx et al. 2008) and subsequently age- and gender-matched to 19 healthy controls (HC). Symptom severity was assessed by a clinician-administered rating scale (Montgomery & Asberg 1979). Independent component analysis as implemented in FSL (Beckmann & Smith 2004) was employed on the concatenated datasets of all subjects to estimate 20 spatially independent signal sources (i.e., components). Next, subject-specific spatial maps of the 20 components were calculated adopting a two-step multiple linear regression (dual regression) method. Firstly, the group component maps were regressed to the preprocessed individual datasets to derive component-specific time courses. Secondly, these time courses were regressed to the same datasets to identify individual spatial maps. Thirteen components were identified as functionally relevant resting-state networks (RSNs) and selected for between groups voxel-wise random-effects analysis on the set of subject-specific component maps.

Results

MDD patients showed decreased connectivity in three RSNs. The first RSN includes areas involved in processing of emotional stimuli (figure 1-1). In this network, involvement of the bilateral amygdala is absent in MDD together with reduced left insula connectivity (figure 2-1). Part of the visual system is depicted in the second RSN (figure 1-2). Bilateral decrease of lingual gyrus connectivity is found in MDD (figure 2-2). The third RSN includes regions that are commonly found activated during attention and working memory paradigms (figure 1-3). In this network, reduced connectivity is found in the left orbitofrontal cortex in MDD patients (figure 2-3). No correlations are found between symptom severity scores and the decreased connectivity in the three RSNs.

Conclusion

The present study in an unmedicated patient sample without comorbidity and age/gender-matched controls did not find the MDD-related changes in functional connectivity identified in previous studies. However, we do demonstrate loss of functional connectivity in MDD in several regions known to be involved in processing of emotional information. The results further suggest that these abnormalities may persist after amelioration of depressive symptoms.

References

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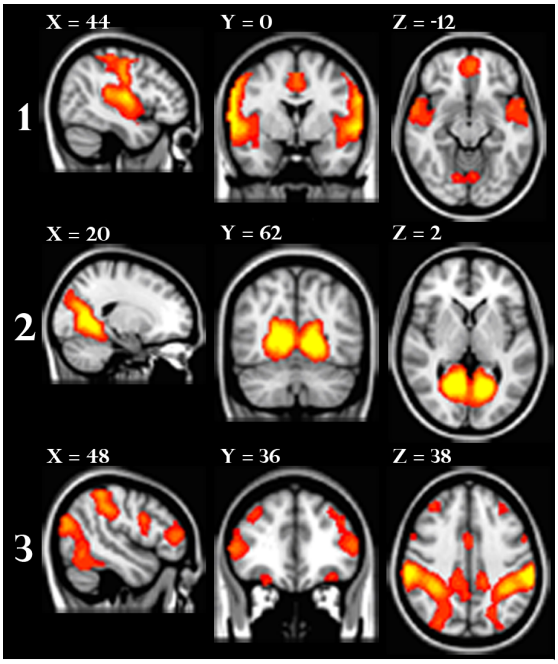

Figure 1 Group ICA results for the three RSNs. The left hemisphere corresponds to the right in these images.

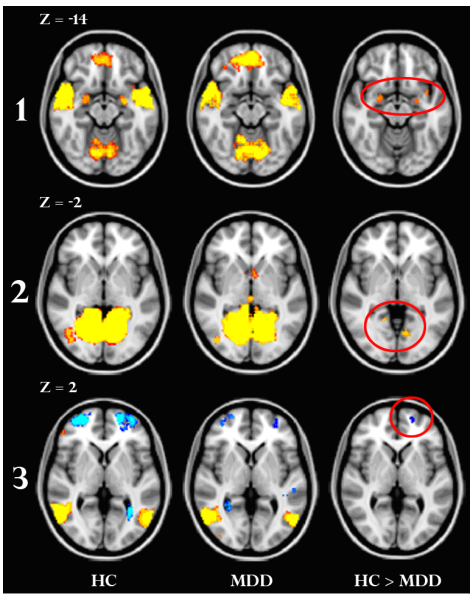

Figure 2 *Z*-maps for the group main and between group effects in the three RSNs. Red-to-yellow indicates a positive relation with the RSN-associated time course, blue-to-light-blue a negative. Group main effects are FWE-corrected at $P<.05$. Between group effects are FDR-corrected at a rate of 1%. The left hemisphere corresponds to the right in these images.