Resting State fMRI and EEG Functional Connectivity Before and After a Course of rTMS for Major Depressive Disorder

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BACKGROUND

Depression is hypothesised to be a disorder of functional connectivity within the brain, characterised by abnormal connectivity of RSNs [1]. Successful treatment of depression using antidepressant medications may restore functional connectivity to optimal levels, with the degree of antidepressant response associated with treatment induced changes in RSN connectivity [2,3]. Previous investigations into the effects of rTMS as treatment for MDD on node-based network connectivity using fMRI and EEG are currently limited.

AIMS

The current study used fMRI and EEG to investigate the functional connectivity of the brain in patients with treatment-resistant MDD, before and after a course of daily rTMS therapy administered to the left DLPFC. The aims of the current study were to:

1. **Evaluate if baseline measures of functional connectivity are correlated with subsequent degree of antidepressant response to rTMS treatment.**
2. **Investigate the effect of rTMS on functional connectivity of the brain**
3. **Evaluate if any differences in functional connectivity are correlated with the antidepressant response to rTMS treatment.**

METHODS

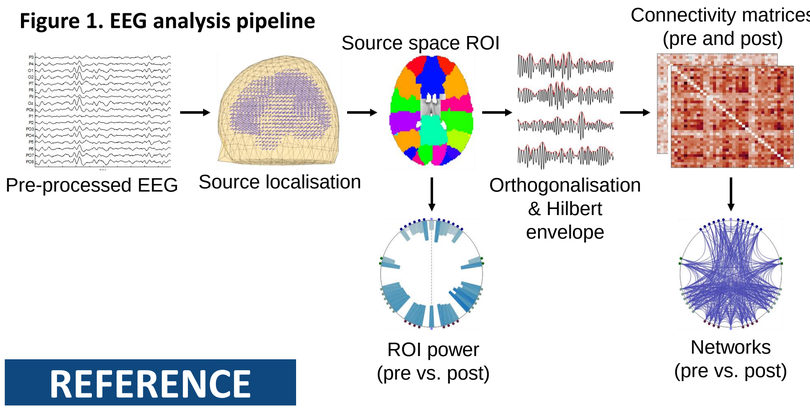
- This study included 26 participants who each completed daily rTMS treatment over four weeks for major depressive disorder (MDD).
- 20 sessions at 120 % of RMT, intermittent 10 Hz bursts, for 4,000 stimuli per day.
- Depressive symptomology assessed by the Montgomery–Åsberg Depression Rating Scale (MADRS) [5].

Δ MADRS = post-TMS MADRS – baseline MADRS / baseline MADRS * 100%

- Neuroimaging was conducted at baseline and following treatment.

To assess fMRI connectivity 264 10 mm spherical functionally-defined nodes were used [4]. The averaged signal from within each node was used in an all-to-all node-wise Pearson's correlation analysis. The EEG analysis pipeline is illustrated in Figure 1. The symmetrically orthogonalised Hilbert envelopes obtained from the 38 ROIs were used in all-to-all Pearson's correlation analysis for pre-TMS and post-TMS. All results were NBS corrected and significance was set at $p < 0.05$ [6].

Figure 1. EEG analysis pipeline



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2. Posner, J., et al., Antidepressants normalize the default mode network in patients with dysthymia. JAMA psychiatry, 2013. 70(4): p. 373-382.
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BASELINE FC CORRELATIONS WITH Δ MADRS

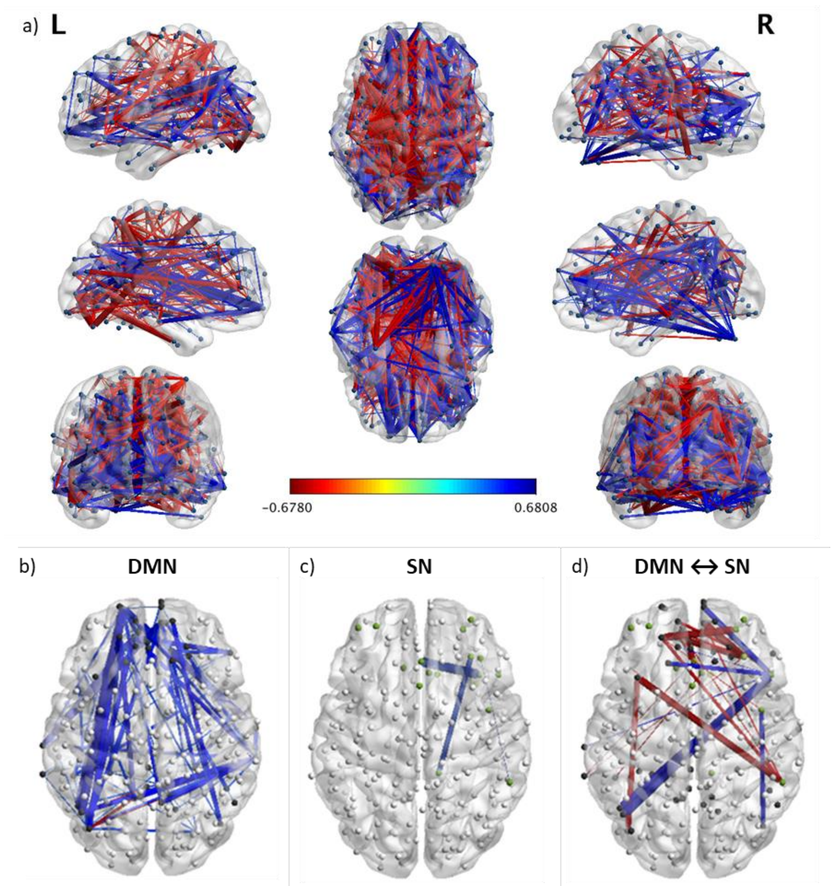

Figure 2. Significant correlations of baseline fMRI all-to-all connectivity between 264 functional nodes with Δ MADRS across the whole brain (a), default mode network (DMN) (b), salience network (c), and between nodes of the DMN and SN (d). Cool colours represent positive correlations, i.e. lower baseline connectivity correlated with larger antidepressant response.

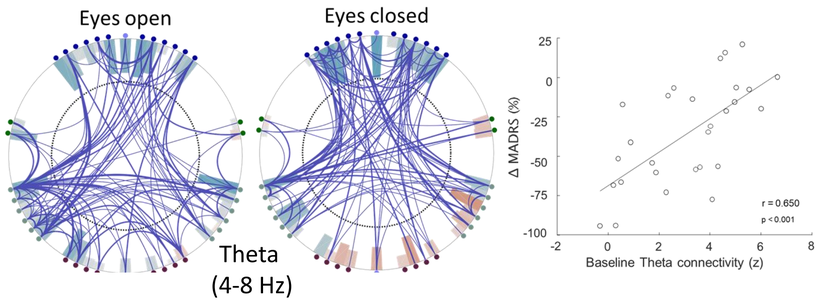

Figure 3. Correlations of baseline source-level EEG resting state theta power and connectivity with the antidepressant response, eyes open and eyes closed. Scatter plot of baseline theta connectivity and Δ MADRS. Cool colours represent positive correlations, i.e. lower baseline connectivity correlated with larger antidepressant response.

At baseline both negative and positive correlations between fMRI connectivity and Δ MADRS (Figure 2a). When masked by networks, positive correlations were found between several nodes spread across the DMN and Δ MADRS (Figure 2b). That is, those participants who responded to rTMS and showed the largest reduction in MADRS scores showed the lowest baseline connectivity within the DMN nodes. Baseline theta connectivity measured using EEG was also negatively correlated with Δ MADRS (Figure 3). Such that lower baseline theta was associated with greater antidepressant response.

DIFFERENCE IN FC FROM PRE TO POST-TMS

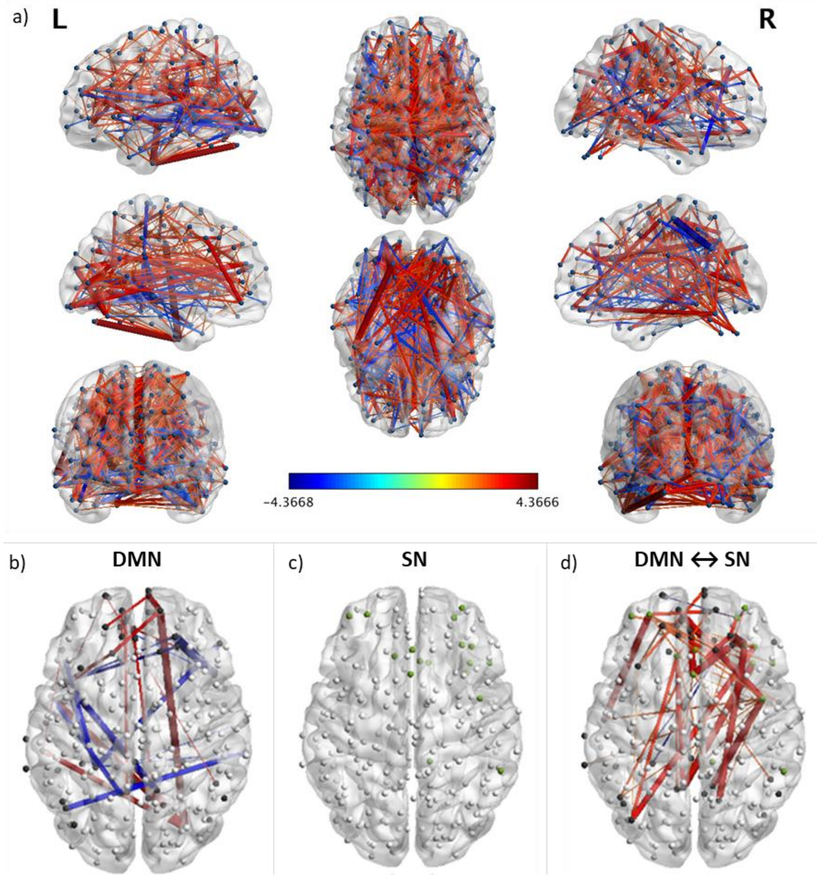

Figure 4. Effect of rTMS on 264 functional nodes all-to-all connectivity comparing baseline and post-TMS connectivity across the whole brain (a), default mode network (DMN) (b), salience network (c), and between nodes of the DMN and SN (d). Warm colours represent increases in connectivity.

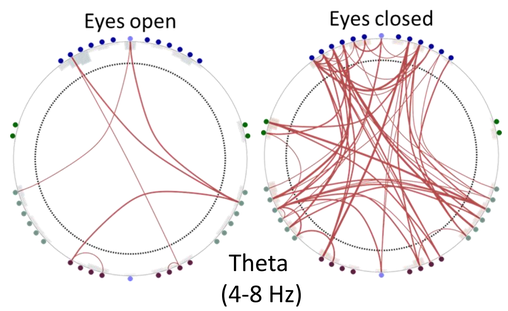

Figure 5. The effects of rTMS on source-level EEG resting state theta power and connectivity in depressed individuals. Eyes open and eyes closed. Warm colours represent increases in connectivity

The majority of significant differences following rTMS was increases in node based fMRI connectivity following treatment (75% positive, $p < 0.001$) (Figure 4a). Increased connectivity was found between the DMN and SN nodes (Figure 4d). Theta connectivity measured using EEG was found to increase following rTMS (Figure 5). Results were not found to correlate with Δ MADRS

CONCLUSIONS

- Responders to rTMS have low baseline fMRI connectivity within the DMN at baseline.
- Low baseline EEG theta connectivity was associated with greater antidepressant response.
- rTMS increased fMRI connectivity between the DMN and SN
- rTMS increased EEG theta connectivity
- Differences in both EEG and fMRI connectivity were not associated with antidepressant response, indicating changes did not underly treatment effects of rTMS. This may be due to lack of power due to low sample size.