Personalised, connectome-guided transcranial magnetic stimulation selectively modulates functional network connectivity in post-concussive syndrome

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Background

Post-concussive syndrome (PCS) encompasses a wide spectrum of clinical presentations and is linked to dysfunctions involving default mode, central executive, and salience networks, collectively referred to as the triple network model. Current treatment strategies lack specificity. Connectome-guided transcranial magnetic stimulation (cgTMS) provides a personalised neuromodulation approach, but its mechanistic effects in PCS are not well defined. In this study, we aimed to investigate the impact of cgTMS on network connectivity and clinical symptoms in patients with PCS.

Materials and methods

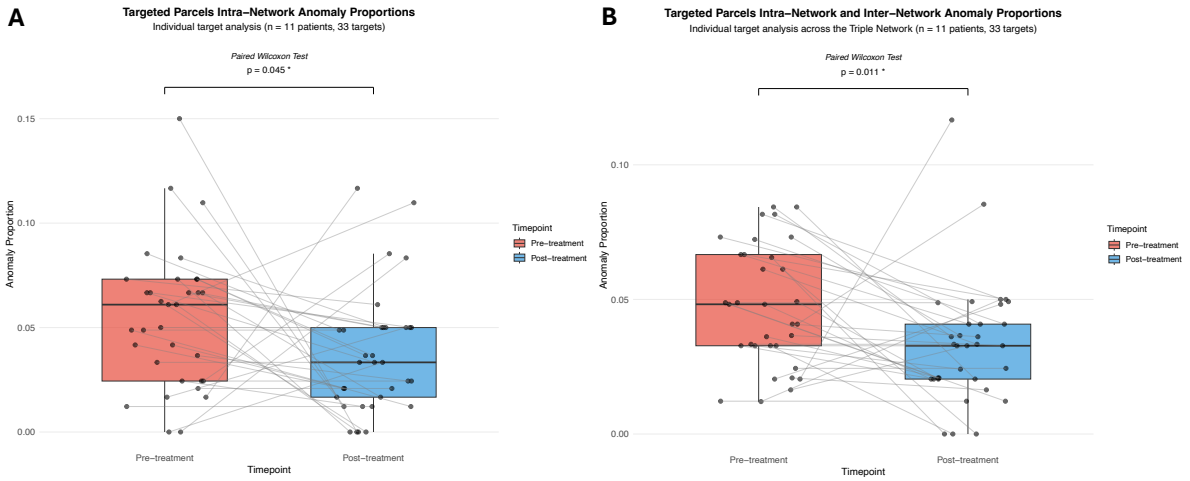
Fourteen PCS patients completed a five-day theta burst protocol targeting abnormally connected parcels within the triple network model. Resting-state fMRIs before and six weeks after treatment were analysed for parcel-level and network-level changes relative to normative data. The non-targeted sensorimotor net work (SMN) served as an internal control. Clinical outcomes were assessed using minimal clinically important difference (MCID) for the Rivermead Post-Concussion Symptoms Questionnaire (RPQ-13) and EuroQol-5 Dimension (EQ-5D).

Results

cgTMS reduced abnormal connectivity in targeted parcels within their networks (p = 0.045, Figure 1A) and across the triple network model (p = 0.011, Figure 1B). At the network level, stimulation increased intra-network anomalies (p = 0.026, Figure 2A), while no significant changes were observed in the control SMN (p = 0.906, Figure 2B) or at broader brain scales (Figure 3). Clinically, 60% of patients achieved at least MCID on the RPQ-13 and 50% on the EQ-5D.

Conclusion

These findings indicate that cgTMS promotes adaptive reorganisation within the triple network rather than strict normalisation, consistent with persistent TBI-related structural alterations. This supports the hypot hesis that targeted, connectome-guided interventions can selectively modulate dysfunctional networks and may represent a promising patient-tailored therapeutic strategy for PCS.



<u>Figure 1. cgTMS decreased connectivity anomaly proportion in the targeted parcels.</u> Box-plots showing the proportion of abnormal connections pre-treatment (red) and post-treatment (blue) (**A** and **B**). Abnormal connectivity of the targeted parcels within its own network (intra-network connectivity) (**A**). Abnormal connectivity of the target parcels towards the triple network model (intra- and inter-network connectivity) (**B**).

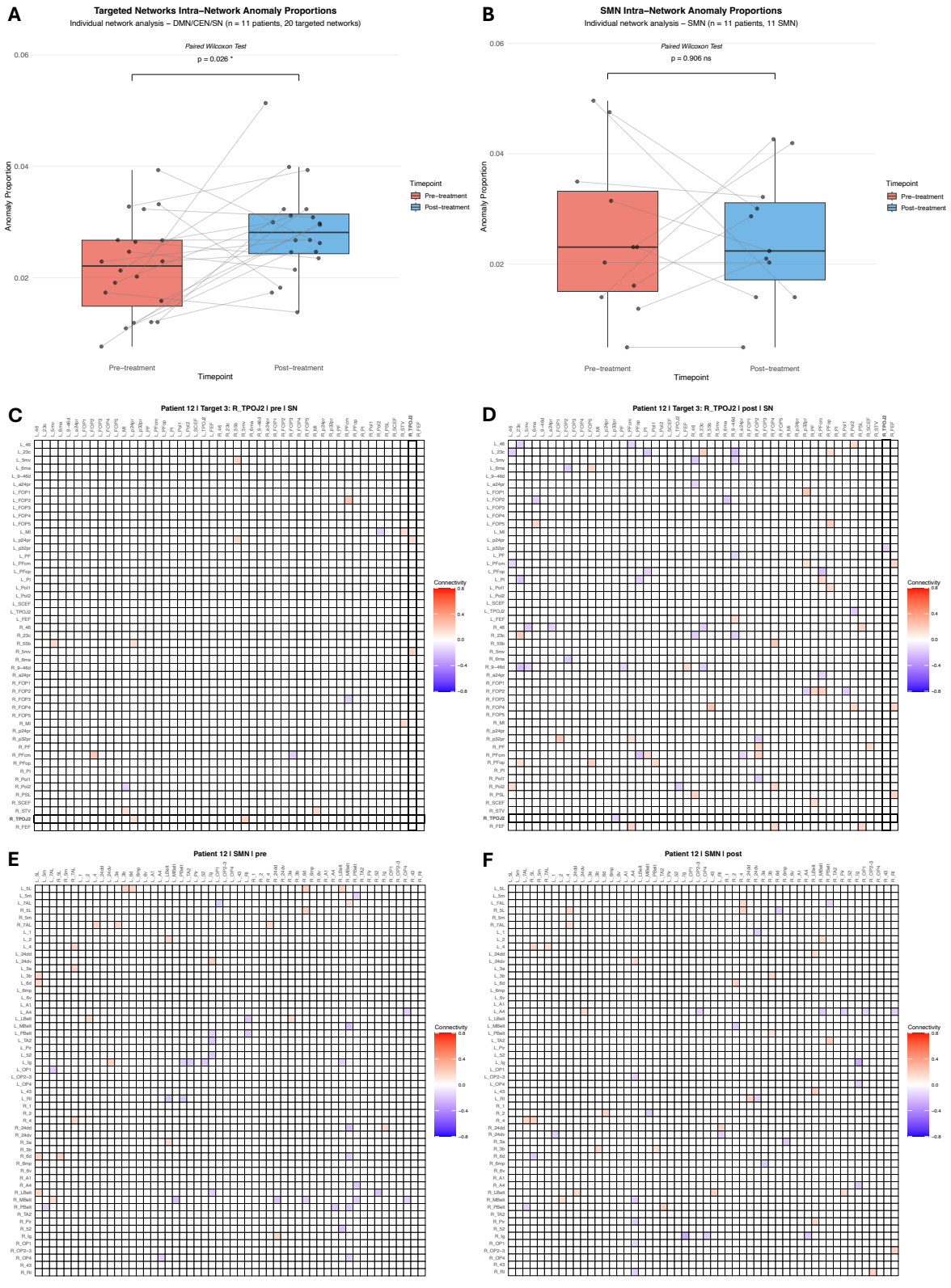


Figure 2. cgTMS increased connectivity anomaly proportion in the targeted networks. Box-plots showing the proportion of abnormal connections pre-treatment (red) and post-treatment (blue) (**A** and **B**). Abnormal connectivity of the targeted network (intra-network connectivity) (**A**). Abnormal connectivity of the SMN (intra-network connectivity) (**B**). Illustrative case heatmaps representing the abnormal connections between parcels of a network, hyper-connectivity (red), hypo-connectivity (blue) and normal connectivity (white), targeted parcels (black outline) (**C** and **D**). Connectivity in a targeted network pre-treatment (**C**) and post-treatment (**D**). Connectivity in the SMN pre-treatment (**E**) and post-treatment (**F**).

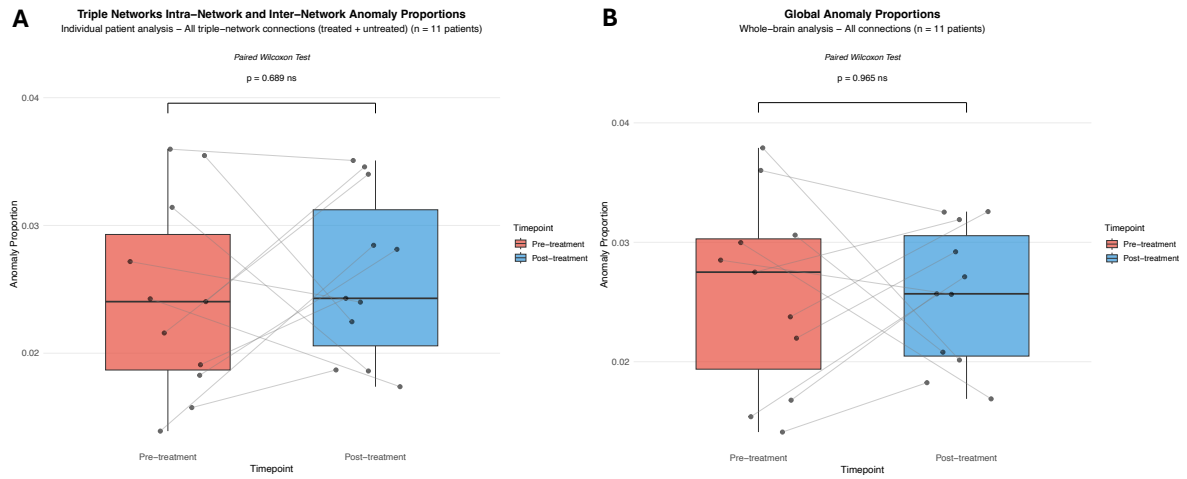


Figure 3. cgTMS didn't change connectivity anomalies across the triple network. Box-plots showing the proportion of abnormal connections pre-treatment (red) and post-treatment (blue) (**A** and **B**). Abnormal connections across the triple network, both intra-network and inter-network connectivity (**A**) and across all brain connections (**B**).