Dual-site dual-device neuromodulation for anxiety

Lucy Webster, Jemima Shickle, Richard Morriss, Paul M Briley

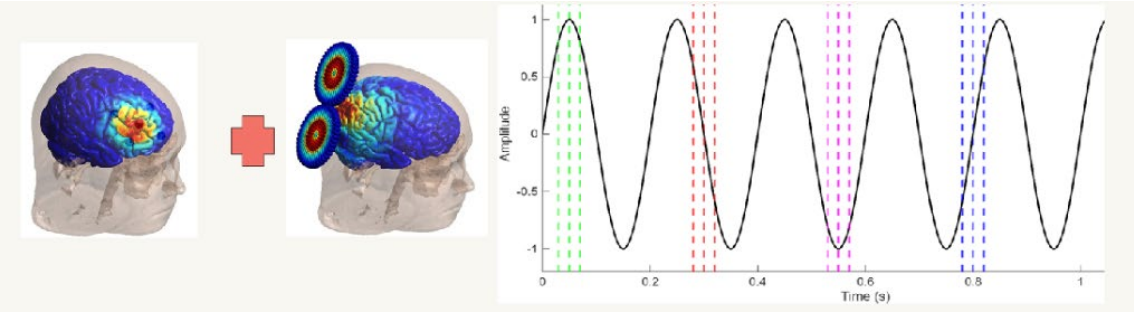
Background & brief methodology

Anxiety disorders affect an estimated 301 million people worldwide, and relapse or resistance to psychotherapy and pharmacological treatments is common. Transcranial magnetic stimulation (TMS) is an approved neuromodulation treatment for mental health conditions, yet clinical response remains variable. Augmenting TMS with complementary neuromodulation approaches, such as transcranial alternating current stimulation (tACS), may enhance its therapeutic efficacy.

This project examined the effects of right-hemisphere dual-site, dual-stimulation neuromodulation in healthy volunteers, assessing outcomes related to anxiolytic effects across mood, autonomic function, and EEG measured neural activity.

High definition tACS was applied to the right dorsolateral prefrontal cortex (DLPFC) at 5 Hz and 1 mA for 3 minutes. Continuous theta-burst stimulation (cTBS) was delivered to the right posterior parietal cortex (PPC) during the final 40 seconds of tACS (600 pulses at 70% of resting motor threshold). Four stimulation conditions were implemented, with cTBS triplets delivered in phase alignment with the tACS waveform at the peak, trough, ascending, or descending phase.

Funding provided by Neuromod+ enabled the purchase of high-definition tACS electrodes, WASP electrodes for the Neutral, Predictable, Unpredictable (NPU) threat task, a gold-standard paradigm for assessing anxious arousal, participant vouchers and behavioural outcome measures.



Outputs/Impact

To our knowledge, this is the first study to develop a protocol combining tACS and TMS applied to separate brain regions to target anxiety related processes, representing a novel integrative neuromodulation approach. Delivering tACS to the right DLPFC and TMS to the right PPC, we found that phase alignment was important: two of four conditions produced anxiolytic effects, including increased calmness and reduced tension (visual analogue scales), enhanced parasympathetic activity (↑ RMSSD), reduced sympathetic arousal (↓ heart rate), and modulation of frontal and parietal alpha and beta activity at rest and during tasks.

These results provide an initial idea of how dual-site, phase-aligned stimulation may influence anxiety, while demonstrating a novel technique that aligns with Neuromod+ priorities of advancing innovative neuromodulation approaches and exploring their potential mechanisms. The next study will test whether the dual, phase-aligned approach produces greater anxiolytic effects than TMS or tACS alone. We are also in early discussions with industry (Ergomed) regarding a potential collaboration to explore this dual-device, dual-site approach in a multi-site feasibility/acceptability study in patients with anxiety.

This project was presented as an oral presentation at the Non-Invasive Neuromodulation Workshop, University of Nottingham, December 2025, and as a poster presentation at the UK Symposium on Neuromodulation and Neurotechnology, Newcastle, November 2025, providing opportunity to disseminate findings to leading neuromodulation researchers and practitioners.