Neuromod+ Flexible Funding Award

Developing a dual neuromodulation approach for major depressive disorder

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Background

Transcranial magnetic stimulation (TMS) is a NICE-recommended neuromodulation treatment for major depressive disorder (MDD), but clinical response is variable (Briley et al., 2024a, doi.org/10.1038/s44184-024-00077-8). We are developing an approach that combines TMS with a second form of neuromodulation – transcranial electrical stimulation (tES) – to improve rate, extent, and reliability of response by optimising the brain state during stimulation (Briley et al., 2024b, doi.org/10.1162/imag_a_00073). This award supported an MRes project piloting our approach in people with moderate-severity MDD to prepare for a full-scale mechanistic study. It also supported a survey of prospective acceptability of TMS, tES, and dual neuromodulation, which was co-produced with people with lived experience of MDD, and featured short videos illustrating neuromodulation approaches.

Findings

We delivered five sessions of dual neuromodulation (intermittent theta burst stimulation TMS – iTBS – with concurrent synchronised transcranial alternating current stimulation tES – tACS) or single neuromodulation (iTBS alone) to twelve people with moderate-severity MDD. Dual neuromodulation led to a more positive shift in emotional bias (a marker of potential antidepressant efficacy; Harmer & Cowen, 2013, doi.org/10.1098/rstb.2012.0407) than single neuromodulation. A marker of target engagement (task-related fronto-central theta power, Hsieh & Ranganath, 2014, doi.org/10.1016/j.neuroimage.2013.08.003; Li et al., 2016, doi.org/10.1093/cercor/bhu191) was also increased. The two approaches were similar in adverse effects. Experience and feedback from qualitative interviews were used to refine the study design to maximise acceptability and feasibility.

Nearly five hundred people with lived experience of mental health conditions completed our co-produced survey. Qualitative responses were mapped to components of the Theoretical Framework of Acceptability (Sekhon et al., 2017, doi.org/10.1186/s12913-017-2031-8). Findings highlighted low initial awareness of neuromodulation, but interest and hope in these approaches when small amounts of information were provided. Responses also identified several potential barriers to uptake of interventions, as well as suggestions for reducing these barriers. Prior awareness strongly impacted likely uptake, but age, gender, ethnicity, carer experience and level of disability also played important roles.

Collaborations, impact, and further funding

- Supported a successful MRes student (YP). YP is now in a full-time research position and due to be PI on a HRA ethics study of mechanisms of dual neuromodulation in MDD
- Led to a Nottingham NIHR BRC funded PhD studentship on optimising and understanding mechanisms of dual neuromodulation (PB and RM are supervisors)
- Led to a new collaboration with Mersey Care NHS Foundation Trust / University of Liverpool around approaches to boost response to TMS for depression
- Led to establishment of a local Neuromodulation Experts-by-experience Advisory Team (NEAT). Six people with lived experience of depression and neuromodulation treatments (in a clinical or research context), with diversity in age, gender, ethnicity and neurodiversity. Met monthly for past 18 month, co-produced survey on prospective acceptability of neuromodulation

- Contributed to a successful NIHR Capital Investment application (£441k) for equipment for neuromodulation clinical research in Nottingham
- Led to a Nottingham BRC Innovation Fund award (£15k) to explore other tES approaches for augmentation of TMS for MDD
- Underpinned an NIHR Postdoctoral Award application for PB on developing TMS augmentation approaches for depression (interviewed, outcome awaited)
- Findings of this work are contributing to a new policy development project on Implementing TMS for Treatment Resistant Depression in the NHS. This work is led by Nottingham BRC with funding from University of Nottingham

Outputs

- MRes thesis. Peng Y (2026). Improving transcranial magnetic stimulation (TMS) treatment for depression. University of Nottingham, UK
- Paper under review. Tan SF, Shickle J, Webster L, Katshu MZUH, Lankappa S, Atkinson-Clement C, Kaiser M, Morriss R, Briley PM (submitted). Prospective acceptability and perceived barriers of non-invasive brain stimulation for mental health treatment: a nationwide survey of people with lived experience of mental health conditions
- Conference talk. Briley PM, Webster L, Peng Y, Tan SF, Shickle J, Morriss R (2025). Boosting the effects of transcranial magnetic stimulation (TMS) using synchronised transcranial alternating current stimulation (tACS). Brainbox Initiative 2025 Conference, London, UK
- Conference poster and published abstract. Tan SF, Briley PM (2025). Co-producing a survey of prospective acceptability of neuromodulation for mental health conditions with lived experience experts. International Congress of the Royal College of Psychiatrists. Abstract in BJPsych Open, 11(S1), S73. DOI: 10.1192/bjo.2025.10239
- Three short videos illustrating neuromodulation approaches (TMS, tES, and dual neuromodulation), co-produced with our Neuromodulation Experts-by-experience (NEAT) PPI group (e.g., https://www.youtube.com/watch?v=5XXQN3EAQWU)

Alignment to Network Aims

- Techniques – Development of a next-generation combination neuromodulation approach (iTBS with concurrent, synchronised, theta tACS)
- Translation – Pilot study in people with MDD, leading to a HRA ethics submission for an upcoming full-scale multi-session study
- Mechanisms – Improving understanding of mechanisms of neuromodulation (on neural oscillatory activity and emotion processing)
- Involvement – Establishment of a PPI group and co-production of neuromodulation survey