

From heterogeneity to precision: Mapping the future of rTMS for musculoskeletal pain

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Chronic musculoskeletal (MSK) pain remains one of the most pervasive causes of disability worldwide, affecting millions of individuals and imposing a substantial burden on patients, healthcare systems, and society.¹ As conventional pharmacological and physical therapies provide only partial pain relief, non-invasive brain stimulation has emerged as a compelling frontier.² In this issue of the *British Journal of Pain*, Liang et al. present a timely and comprehensive systematic review and meta-analysis on the therapeutic effects of repetitive transcranial magnetic stimulation (rTMS) for MSK pain, and on the stimulation parameters that may modulate efficacy. Their work adds an important piece to the growing puzzle of how non-invasive brain stimulation might contribute to pain alleviation.

The review synthesizes data from 22 studies (23 trial comparisons), comprising over 1150 patients, and provides evidence of a significant reduction in pain intensity following active rTMS compared to sham, alongside improvements in mood and quality of life. These findings are clinically meaningful. They reinforce the idea that rTMS, originally developed as a research tool to probe cortical excitability,³ may offer tangible benefit for chronic pain patients—particularly those for whom existing treatments provide incomplete relief.⁴ The analysis also points to concrete factors that can inform clinical and research design. The finding that higher frequencies, intensities, and session numbers are associated with larger effects supports a dose-response relationship in neuromodulation—already observed for other disorders⁵—offering practical guidance for balancing induction and maintenance phases of treatment. The methodological approach is comprehensive, combining a broad database search with standardized mean differences and sensitivity analyses to ensure the stability of the findings. No review to date has integrated this breadth of evidence across MSK conditions, making this synthesis an invaluable reference point for both clinicians and researchers.

As with any meta-analysis pooling broad and varied literature, interpretation requires nuance. The reported heterogeneity is substantial, reflecting wide variability in both patient populations and stimulation protocols. The included studies span fibromyalgia, chronic low back pain, shoulder pain, and myofascial pain. While all “musculoskeletal,” these conditions differ markedly in pathophysiology and central representation. Similarly, cortical targets ranged from the primary motor cortex (M1) to the dorsolateral prefrontal cortex (DLPFC) and anterior cingulate cortex (ACC), with stimulation frequencies from 1 to 20 Hz and session numbers from 1 to 20. This diversity reflects a field still exploring where and how rTMS exerts its effects, but it also means that the pooled estimate should not be interpreted as a one-size-fits-all measure of efficacy.

Methodological quality is another source of variability. Nine of 22 studies failed to adequately describe random sequence generation, and only 10 employed allocation concealment—fundamental safeguards against selection bias that should be standard in randomized trials. This represents a high risk of bias in nearly half of the included evidence base. Without proper randomization and allocation concealment, systematic differences between groups at baseline may be mistaken for treatment effects, and no analytical approach can fully compensate for flawed trial design. Additionally, blinding integrity remains a challenge in rTMS pain research, where expectancy effects are non-trivial and sham procedures vary considerably in their credibility. These factors may contribute to inflated estimates of effect and deserve careful attention in future trials. It should be noted that the authors also performed multiple subgroup analyses examining frequency, intensity, and session number independently. These parameters are often interdependent (for instance, higher frequencies are frequently paired with higher intensities), complicating causal interpretation.

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Future work should employ factorial designs or meta-regression approaches that explicitly model such interactions.

Liang et al. rightly attribute inconsistent findings across trials to differences in protocols and pain subtypes. Another underappreciated source of variability may lie within individuals themselves.⁶ Intraindividual fluctuations in cortical excitability, attention, or pain state can profoundly shape responses to rTMS.^{7–9} Recognizing and quantifying this within-person variability could pave the way for personalized brain-state-dependent¹⁰ and closed-loop^{11,12} stimulation paradigms—approaches that adjust parameters in real time according to neural feedback. The discussion also provides a thoughtful overview of possible mechanisms of action of rTMS, including long-term potentiation^{13,14} and modulation of cortical excitability.^{15,16} Rather than firm conclusions, these are valuable hypotheses guiding future experimental studies. Integrating neuroimaging or electrophysiological markers could help bridge the gap between clinical efficacy and mechanistic understanding.

Although the review supports the potential of rTMS as a non-pharmacological pain intervention, several pragmatic questions remain. The real-world implementation of rTMS depends not only on its efficacy but also on factors such as cost-effectiveness, accessibility, and feasibility in routine care. Most studies focus on short-term pain relief, leaving open questions about long-term durability and maintenance. These considerations fall beyond the scope of this review, yet issues of accessibility, cost, and patient burden remain central to the clinical adoption of rTMS, which typically involves 10–20 sessions over 2–4 weeks. Moreover, while adverse events are rare, systematic reporting of side effects¹⁷—including headache frequency or the very low but non-zero risk of seizures^{18,19}—would enhance safety transparency.

A further consideration concerns depth and focality. Some protocols target medial or deeper regions such as the ACC^{20,21} or posterior insula,^{20,22} yet the ability of conventional rTMS to reach these structures selectively is limited. Advances in coil design, computational modeling, and novel techniques such as temporal interference magnetic stimulation²³ may eventually extend stimulation depth while preserving focality, but this remains an open frontier.

Despite these caveats, the work by Liang et al. represents an important milestone. It not only consolidates the existing evidence but also highlights the gaps that future research must fill. The field of pain neuromodulation stands at a crossroads between promise and caution. The findings are encouraging, but their reliability depends on improved methodological

consistency. Moving forward, several directions appear promising. Standardization of core outcome measures and sham procedures will improve comparability across trials. Dose-finding studies can clarify optimal combinations of frequency, intensity, and duration. Incorporating neurophysiological markers such as cortical oscillations or connectivity patterns could enable more mechanistically grounded and individualized protocols. Finally, studies assessing cost-effectiveness and feasibility in community settings will determine whether rTMS can move from specialized research centers to routine pain management.

In summary, the meta-analysis by Liang et al. underscores both the potential and the complexity of using rTMS to treat MSK pain. The findings invite cautious optimism: rTMS appears capable of alleviating pain and improving well-being, yet its effects are shaped by multiple layers of variability—from study design to individual neurobiology. As research advances toward more standardized, personalized, and mechanistically informed approaches, the hope is that rTMS will transition from experimental promise to practical relief for patients living with chronic MSK pain.

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