Project Details	
Project Code	MRCNMH26Ba Khatibi
Title	Neural Mechanisms of Pain Relief: Comparing Cognitive Training and Neurostimulation Interventions
Research Theme	NMH
Project Type	Wet and dry lab
Summary	Neuropathic pain (like diabetic-related peripheral neuropathy) is a persistent condition where the source of the pain isn't tissue injury. Instead, it comes from damage or dysfunction in the nervous system. It is often resistant to conventional pain treatments; yet new cognitive training and neurostimulation methods show promise. This PhD will compare these two interventions by determining the effectiveness and neural mechanisms of each on thermally induced pain in neurotypical participants. The student will gain experience in cognitive psychology, psychophysics, neurostimulation, and cutting-edge neuroimaging methods that will reveal brain and spinal cord function during these pain interventions.
Description	**Background** Pain arises from a dialogue between incoming nociceptive signals and higher-order cognitive processing. People who habitually interpret ambiguous bodily sensations as threatening report more intense and disabling pain. Experimental work has shown that these interpretation biases can be shifted with short computer-based cognitive bias modification for interpretation (CBM-I); in turn, altered bias predicts reduced pain during cold-pressor and contact-heat tasks. A second, mechanistically distinct route to analgesia is non-invasive neurostimulation. Transcranial electrical stimulation (tES) applied to the primary motor cortex (M1) consistently elevates thermal pain thresholds in healthy volunteers. Although transcranial electrical stimulation (tES) targeted to the primary motor cortex (M1) reliably elevates cold-pain thresholds in healthy adults (frontiersin.org), and cognitive-bias modification for interpretation (CBM-I) reduces pain interference and intensity in chronic-pain populations, the two interventions have never been tested head-to-head, nor has anyone mapped whether they recruit shared or distinct nodes within the cortical-brainstem-spinal pain-control network. This blind spot constrains evidence-based optimisation—without mechanistic insight, we cannot decide which therapy to deploy, combine, or tailor to a given patient. Simultaneous brain-cervical-spinal fMRI now overcomes that barrier by capturing task-dependent coupling between periaqueductal grey, brainstem nuclei and dorsal-horn neurons in real time. Filling the gap is clinically pressing: despite modern analgesic protocols, 10–50 % of surgical patients still transition to persistent post-surgical pain, highlighting the need for scalable, non-drug preventives whose mechanisms—and relative efficacy—are clearly understood. **Key Research Question** Which intervention—interpretation-bias modification or focal neurostimulation—yields greater analgesia, through what brain–brainstem–spinal mechanisms?

	Work-package 1 (Months 0 – 18): Experimental comparison. The project begins with a triple-arm, double-blind randomised controlled trial in 60 healthy volunteers who will receive either pain-benign CBM-I (four 20-minute sessions), focal transcranial electrical stimulation of M1 (15 minutes), or a sham procedure. Heat pain will be induced with a contact thermode. At the same time, we measure peak VAS pain, thermal detection and tolerance thresholds, attentional bias via a dot-probe task, and memory bias through an unexpected free-recall test of pain-related versus neutral words. Early data will identify short-term analgesic "responders" who qualify for the imaging phase. During this work package, the student will help refine the trial design, develop and pilot the CBM-I materials and the neurostimulation montage, coordinate data collection, draft the preregistration, and take the lead on a first-author methods paper. Work-package 2 (Months 19 – 36): Mechanistic imaging. Simultaneous brain–spinal fMRI will be collected before and after the more effective WP1 intervention in 30 responder participants. Analyses will focus on changes in functional and effective connectivity along the descending pain-control pathway (anterior cingulate cortex → periaqueductal grey → rostral ventromedial medulla → dorsal horn). The student will optimise shimming and physiological-noise correction, build custom Python/MATLAB pipelines that integrate the Spinal Cord Toolbox with CONN, and present interim findings at major conferences such as OHBM or SfN. Work-package 3 (Months 37 – 48): Integration and dissemination. In the final phase, behavioural and imaging datasets will be combined. Mediation modelling—implemented in either Bayesian or frequentist frameworks, at the student's discretion—will test whether intervention-driven shifts in cognitive bias or neural connectivity explain observed analgesia. The student will write the thesis, prepare at least three first-author manuscripts, release all code in an open repository alongside an interactive visualisation dashboard, and draft follow-on fellowship or grant applications to extend the programme of research. **Ownership & Flexibility** • Technique choice: Early pilot data will let the student decide which neurostimulation technique provides a cleaner contrast with CBM-I for the full RCT. • Bias focus: If WP1 reveals stronger links between pain relief and either attentional or memory bias, the student may add secondary tasks to other WPs and refine analyses accordingly. • Imaging innovation: The student is encouraged to develop novel denoising or connectivity-estimation methods for combined brain–spinal data, with potential for standalone publications. **Expected Impact** The project will (i) provide the first head-to-head test of interpretation-bias training versus focal neurostimulation for experimental pain; (ii) reveal how such methods modulate nociceptive signalling along the whole neuraxis; and (iii) offer a pragmatic, drug-free strategy to manage pain and reduce its interference with an individual's functioning. The

	student will emerge with advanced skills in psychophysics, neurostimulation, simultaneous brain–spinal imaging, and statistics, well-positioned for a career at the interface of cognitive neuroscience and pain medicine.
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