Project Details	
Project Code	MRC22NMHBa Bultitude
Title	Using brain stimulation to understand contributions of higher-level motor function to pathological pain.
Research Theme	Neuroscience & Mental Health
Summary	Pain in a given area of the body could be related to how the area is represented in a part of the brain that controls movement (primary motor cortex). However, treatments based on changing this representation have limited success. To work towards better treatment, this project will use cognitive testing and brain stimulation to test the possibility that other brain areas responsible for planning, interpreting, and understanding movement are impaired in chronic pain.
Description	Many chronic pain conditions cannot be explained by pathology in the painful body part and might be driven by changes in the central nervous system, including the motor system. The motor system is thus targeted in treatments for chronic limb pain, but these require intense training, and few patients benefit. Most insights about the motor system in chronic pain concern primary motor cortex (M1). For example, non-invasive brain stimulation has revealed changes in the parts of M1 connecting to affected body parts in people with chronic limb or back pain. However, we suspect there are also changes to 'higher order' motor areas, those used for planning and interpreting movements. For example, people with chronic pain take longer to mentally rotate and identify pictures corresponding to their affected limb, suggesting problems with representing (not just executing) movements. Understanding such changes could help improve treatment. This PhD will use behavioural and non-invasive brain stimulation methods to provide a more in-depth understanding of cortical motor contributions to chronic pain, with a view to discovering potential new targets for treatment. Study 1 will be a large-scale study of action perception and comprehension in people with a variety of chronic pain conditions versus pain-free controls. We will take advantage of recent advances in online neuropsychological testing to administer experiments to participants taking part on their home computer. Online research permits a larger, more heterogeneous, and more representative sample than traditional lab-based research. Impaired performance (e.g. slower, less accurate responses) in participants with chronic pain will indicate problems with perceiving or understanding movements. This study will provide insights into how such changes vary by condition, and by pain location, severity, and duration. Study 2 will compare multiple measures of higher order motor function in people with Complex Regional Pain Syndrome (CRPS) versus pain-free controls in a lab-based study. In CRPS, symptoms are often severe but limited to one limb. This means the equivalent unaffected limb and corresponding brain areas can be used to collect within-subjects control data. Taking advantage of the greater range of tasks that can be applied in lab-based studies, we will use button-press responses, motion tracking, force sensors, and skin conductance responses to measure changes in planning, executing, perceiving, and/or understanding movements. Study 3 will use transcranial magnetic stimulation (TMS) to measure communication between M1 and higher order motor areas in people with upper-limb CRPS versus pain-free

	controls. TMS uses magnetic fields generated on the scalp's surface to stimulate the underlying neurons. The student will choose the precise higher order area (see Q14), however likely candidates are dorsal or ventral premotor cortex and supplementary motor area. In part a, we will use paired-pulse TMS to directly activate the higher order area (conditioning pulse) prior to stimulating the M1 hand area (test pulse). In part b, we will use a behavioural task to activate the higher order area (e.g. viewing videos of hand actions) while applying single-pulse TMS to the M1 hand area (test pulse). Using the two methods of activating the higher order motor area will allow us to understand the impact of pain on both highly specific neurophysiological, and behavioural 'real world', inputs to M1. For pain-free controls, we expect that either way of activating the higher order motor area will lead to descending excitation of M1, thus a larger motor response to the test pulse. However, we predict that this increased responsiveness will be absent in the affected hand of people with CRPS, indicating impaired function of the higher order brain area and/or impaired communication with M1. We will also test for associations between responsiveness and symptom severity and action perception/comprehension.
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