Project Details	
Project Code	MRCNMH24Br Dunham
Title	Is faulty fibre function to blame for fibromyalgia? – tracking down chronic pain to its source.
Research Theme	Neuroscience & Mental Health
Summary	Fibromyalgia (FMS) is a common chronic pain condition. FMS pain is classically thought to originate in the brain, due to sensitization of central pain processing. Recent research challenges this, suggesting that sensitisation of peripheral nerves drive the pain. This project will directly record from pain nerves in FMS patients, whilst quantifying their pain sensitivity. It will clarify our mechanistic understanding and will improve treatment of FMS pain.
Description	Chronic pain is growing epidemic associated with an "opioid crisis" caused by the harms of current pain killers. There is an urgent need to better understand pain mechanisms in patients, to inform personalised treatments. Fibromyalgia (FMS) is a common chronic pain condition with an unclear cause and no effective treatment. Traditionally, it has been though that fibromyalgia pain originates in the brain due to abnormal processing of sensory input. However, recent research challenges that view with data suggesting that abnormal activity in peripheral nerves may drive the pain. To determine the role of peripheral nerves in FMS, we will record their activity directly using microneurography. This specialized technique is the only way to record from individual pain nerves in people. We have developed a unique set of open-source tools to make these rare and valuable recordings efficient, and more informative. An additional method to assess both peripheral and central pain mechanisms in people is to use quantitative sensory testing (QST). Here, controlled stimuli, e.g., temperature or pressure, are applied to a participant and their response, i.e., painful, or not, is recorded. It has been proposed, but never proven, that a rigorously defined QST protocol (German Network for Neuropathic pain, DFNS) can reveal underlying pain mechanisms. This project will combine microneurography and QST, the two gold standard techniques, to determine pain generating mechanisms in patients with FMS. QST has been used to generate data suggesting that FMS pain is centrally driven. Two such measures include Offset Analgesia (OA) and Mechanical Hyperalgesia (MH). In OA, pain evoked by heating is disproportionally reduced with a subsequent small reduction in stimulation temperature. MH is present when pressure stimuli that are painful in healthy volunteers are found to be more painful in patients. People with FMS have more pain with both OA and MH. These observations have been interpreted in the context of sensitised central mechanisms. However, they could be more simply explained by peripheral hyperexcitability. The project will quantify OA and MH in FMS patients, whilst making direct neuronal recordings via microneurography, to better understand the role of peripheral sensitization in FMS pain. Key Research Question: What are the peripheral mechanisms driving pain in fibromyalgia? Objectives 1. Use microneurography to quantify hyperexcitability in A- & C- fibre nociceptors in FMS patients. 2. Compare pain mechanisms defined with comprehensive QST protocols (DFNS) to microneurography determined nociceptor function. Do QST profiles predict the presence of

	peripheral pain generators in FMS? 3. Re-evaluate tests of "central sensitisation" in FMS patients during microneurography – What is the role of peripheral sensitisation in Offset Analgesia and Mechanical Hyperalgesia? Ownership The student will receive training and support from the highly experienced supervisory team drawn from across the GW4, with opportunities to discuss project direction with patient partners. They will be empowered to drive their own research. First, by conducting a literature review to 'get up to speed' and to enable hypotheses development. They will be trained in the gold standard techniques of microneurography and quantitative sensory testing, including training in the DFNS protocol in Germany. They will attend classroom-based teaching on project design, statistical analysis, data presentation etc., provided by the GW4 Universities. Depending on their results and interests, the student will then be in a strong position to direct their project. Importantly, they will be embedded within an inclusive, supportive, and inquisitive research environment where multiple related projects are running including, sensory testing device-development, human multi-contact microneurography, and design / implementation of novel interventional studies.
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