2023 Multidisciplinary Research Program in Medicine Project: Turning pain off - Neurophysiological markers of pain 'onsets' and 'offsets' in response to contact heat and cold stimuli.

Hypothesis or Research Question(s): Research question: Can painful temperature based "offsets" be quantified using evoked potentials? Hypothesis: Temperature based onsets and offsets will depend on the direction of temperature change, as opposed to the amount of temperature change.

PROJECT BACKGROUND & SUMMARY

Pain assessments in humans are often predicated on the visual analog scale (VAS) or numerical rating scale (NRS), where participants rate their pain from 0 being no pain to 10 being the worst tolerable pain. Of course, comparability across individuals presents as a challenge with VAS/NRS assessments, as 5/10 for one individual may not mean the same for another. While the "objective assessment of pain" remains elusive, recent advances in neuroimaging techniques, specifically the use of nociceptive evoked potentials, provide insight into some of the mechanisms and pathways involved in pain perception.

Briefly, noxious stimuli applied in the periphery results in activation in nociceptors and the recruitment of small and thinly myelinated afferents, which synapse in the dorsal horn of the spinal cord before ascending via the spinothalamic tract to supraspinal structures. The response of supraspinal structures to peripheral noxious stimuli can be quantified by way of evoked potentials via surface electroencephalography (EEG). With outcomes assessed in both the time and time-frequency domains, pain-related evoked potentials function to provide assessments of spinothalamic tract function, and are reliably related to pain perception. Overall, pain-related evoked potentials continue to present a promising avenue to quantify mechanisms of pain perception in humans.

Recently, the notion of evoked potential "offsets" was addressed at length by Somervail et al. 2022. Briefly, when providing auditory stimuli to the somatosensory system in ascending and descending tones, the resultant evoked potentials presented distinct "onset" and "offset" responses. This is of particular importance, as it suggests the somatosensory system may differentially encode when stimuli "turn on" and "turn off", and that this can further be quantified using evoked potentials. Translating these ideas to the use of pain related evoked potentials, the rapid increased and decrease of temperatures may provide an avenue to similarly explore evoked potential "offsets". The overarching goal of our proposed study is to explore pain related evoked potential offsets, in response to contact heat and cold stimuli. Pragmatically, such an exploration may provide insight into how the pain both turns on, and perhaps more important to clinical applications, how pain turns off.

BENEFIT TO THE STUDENTS

Students will be invited to be involved in all steps of the research process. The current state of the project is preliminary pilot testing of equipment and ethics application. This timeline will work perfectly for summer students to pickup and carry out all aspects of the project, from data collection and analysis, to statistical analysis and results preparation. One main aspect of the project where students will have freedom, under close supervision, is in the development and validation of a heat and cold stimulation protocols to deliver "onset" and "offset" stimuli. Dr. XXX’s lab is already equipped with a TCS II stimulator (QST Lab, Strasbourg, France), and have multiple approved human research ethics using this equipment for the delivery of contact heat and cold stimuli.

Under the supervision of Dr. XXX, the postdoctoral mentor for the proposed project, the students will design and implement a Matlab (Natick, Massachusetts: The MathWorks Inc) user interface that can be reliably used to deliver and monitor contact heat and cold stimuli delivery protocols. From there,
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Students will then be equipped to carry out the proposed study, by recruiting a small cohort of young healthy participants, to explore onset and offset evoked potentials in response to contact heat and cold stimuli. Through collection and subsequent analysis, students will then have the opportunity to learn advanced electroencephalography (EEG) data analysis techniques. Dr. XXX is well suited to take the lead here, evidenced by his recent publications on time-frequency analysis of contact heat stimuli. Here, students will develop technical expertise as well as problem solving and troubleshooting skills.

For the processing of EEG data, students will have the opportunity to complete some of their work remotely. This will ensure the successful completion of their project, regardless of changes in COVID-19 restrictions. Further, in the event project data collection must be halted due to COVID-19 restrictions, students will have the opportunity to translate their data processing skills to other ongoing projects within the labs. Multiple deliverables are expected to arise from this project. It is expected to produce one publication, and multiple conference abstracts. Further, we will support the open sharing of the student's developed Matlab user interface. This will enable other research groups that use the same temperature stimulator the opportunity to make use of tonic heat and tonic cold pain assessments. There will be the opportunity for the students to earn co-authorship, as well as present at local or international conferences.