#WeAreAllInThisTogether COVID19 Journal Club

TRAINEE EVENT

DATABLITZ

DAY 1 — ROOM 2
Americas/Europe

August 6, 2020
3 pm EST

Zoom Link:
https://zoom.us/j/2699261041?pwd=TTRnYWFGZm81MGIwYWxIbUtsVUphQT09

Meeting ID: 269 926 1041

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Centre for Multimodal Sensorimotor and Pain Research

UNIVERSITY OF TORONTO

Centre for Multimodal Sensorimotor and Pain Research

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Title: *Widespread Pain is Associated with Poorer Psychological Health in Women with Chronic Pelvic Pain Presumed Secondary to Endometriosis*

Authors: Danielle Perro[1], Miriam Szabo[2], Lydia Coxon[1], Jennifer Brawn[3], Danielle Hewitt[4], Rebecca Dragovic[1], Christian Becker[1], Krina Zondervan[1], Katy Vincent[1]

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Trainee Status: 2nd Year DPhil Student (PhD), University of Oxford - https://www.wrh.ox.ac.uk/team/danielle-perro

Little is known about the burden of extra-pelvic pain (EPP) in women with endometriosis. We aimed to investigate the impact of widespread pain on psychological health, comorbid conditions and reproductive outcomes in those with endometriosis and chronic pelvic pain (CPP). Baseline questionnaires were completed, and included Beck Depression Inventory (BDI), Pain Catastrophizing Scale (PCS) and a body map describing their pain locations. Participants were grouped according to how many regions were affected by EPP: pelvic pain only, isolated (1 additional region), intermediate (2 additional regions), or widespread (3-7 additional regions). 56 women were included in this study. 82% of women reported atleast one EPP region. As predicted, those with more widespread pain had significantly higher PCS ($\chi^2_{(3)}$=10.130, p=0.017) and BDI scores ($\chi^2_{(3)}$=9.465, p=0.024). Although not formally tested, these data suggest that widespread pain is associated with; increasing incidence of comorbidities, reduced incidence of live births and increased prevalence of negative reproductive outcomes. Our data suggests that a majority of women experiencing CPP and endometriosis experience EPP. Use of the body map to determine the widespread nature of women's pain may be an easy screening tool for clinicians to identify patients with EPP who require a multi-modal approach to pain management.

Local ethical approval was obtained prior to the recruitment of any participants. Relevant REC Reference Numbers: 12/SC/0371, 15/SC/0372.

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Whole CNS imaging of pain modulation: from brain to spinal cord

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Abstract:

Distraction from pain is a robust strategy to decrease pain perception. Previous studies have shown this process to involve cortical regions, brainstem nuclei and the spinal cord. However, no study has simultaneously imaged the whole CNS to study the interactions that mediate attentional analgesia.

We applied an optimized whole CNS imaging technique during an attentional analgesia paradigm. In 39 healthy human subjects, thermal stimuli were applied to the left forearm (C5-C6 dermatome) at two temperatures (noxious/innocuous), whilst they simultaneously performed a rapid serial visual presentation task with two levels of difficulty (easy/hard).

Analysis of pain ratings revealed a decrease in pain scores in the hard task|high temperature condition indicating an attentional analgesia effect ($P = 0.002$).

ROI-based permutation testing revealed a significant spinal cord response to noxious stimulation, with parameter estimates mirroring pain scores (e.g. reduced activity with lower reported pain intensity). The RVM showed a significant task*temperature interaction, reflecting its role in analgesia. In addition, psycho-physiological interaction analyses identified a cortical-brainstem pathway whereby ACC recruits PAG and RVM to modulate spinal cord activity. All imaging results are presented for $P < 0.05$, TFCE corrected.

This is the first study to demonstrate cognitive pain modulation via simultaneous whole CNS imaging.

Examining emotional pain among individuals with chronic physical pain: Nomothetic and idiographic approaches

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Non-physical stimuli may have the capacity to evoke pain affect that is similar to that associated with acute physical pain, a phenomenon referred to as emotional, psychological, or social pain. Given high co-occurrence of pain and depression, as well as neurobiological overlaps in painful and emotional experiences, emotional pain may be an important component of chronic pain syndromes. I will present data examining self-reported emotional pain among chronic pain patients using both nomothetic (i.e., group-level) and idiographic (i.e., individual-level) approaches. At the group level (*N* = 65), emotional pain severity was significantly positively correlated with physical pain severity, psychosocial illness impact, and pain catastrophizing. Three individuals from the group provided intensive longitudinal data that was used to assess these relationships within individuals. Idiographic analyses suggested that one individual did not display a significant correlation between physical and emotional pain, and two individuals displayed correlations larger than expected based on the group-level data. These results suggest that self-reported emotional pain is associated with the physical and psychological impacts of chronic pain. However, idiographic models revealed heterogeneity that may have implications for treatment. For example, perhaps psychological treatment is indicated when emotional and physical pain are highly correlated for a given individual.

Note. Funding for this study was received from the Washington University Department of Psychological & Brain Sciences. There are no conflicts of interest to report. All procedures were approved by the Washington University in St. Louis Institutional Review Board.

Prior Therapeutic Experiences, Not Expectation Ratings, Predict Placebo Effects: An Experimental Study in Chronic Pain and Healthy Participants

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Abstract

Introduction. Many clinical trials fail because of robust placebo responses. Prior therapeutic experiences and patients' expectations may affect the capacity to respond to placebos in chronic disorders.

Objective. This study including 763 chronic orofacial pain and healthy participants was to compare the magnitude and occurrence of placebo effects and determine the putative role of prior therapeutic experiences versus expectations.

Methods. We tested placebo responsiveness in a laboratory setting by using two distinct levels of individually tailored painful stimulations (high pain and low pain) to reinforce expectations and provide a hypoalgesic experience. Afterwards, both levels of pain were set at a moderate pain level to test for placebo effects. Pain and expectation ratings were assessed using visual analogue scales.

Results. In both chronic pain and healthy participants, placebo effects were similar in magnitude, with more responders in the healthy participants. Although chronic pain participants reported larger pain-relief expectations, expectations did not account for the occurrence of placebo effects. Rather, prior experience via conditioning strength was associated with placebo effects in both pain and healthy participants.

Conclusions. These findings confirm the importance of assessing therapeutic history while raising questions about the utility of expectation ratings.

Disclosure Statement. The authors have no conflicts of interest to declare.

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Title: Pain Reprocessing Therapy for chronic back pain: A randomized controlled trial

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Abstract:
We conducted a randomized controlled trial (N = 100) for chronic back pain testing a novel psychotherapy, Pain Reprocessing Therapy (PRT), which rests on two scientific premises: a) for many patients, persistent pain is a "false alarm" of tissue damage that need not be feared; and b) psychosocial threats, including threatening emotions, can amplify pain. Compared to a no-treatment control group, PRT yielded large effects on the primary outcome, a 0-10 pain intensity scale. At post-treatment, M_{PRT} pain = 1.18 (SD = 1.24) and M_{NoTx} = 3.13 (1.45), with Hedge's g = -1.42 [-1.87 -0.95]. Effects were largely maintained at 12-month follow up, M_{PRT} pain = 1.51 (1.59), M_{NoTx} = 3.00 (1.77), g = -0.88 [-1.33 -0.41], $p < .001$. Pain intensity reductions were mediated by pre-to-post treatment reductions in pain-related fear and avoidance, $\beta_{path\text{-}ab}$ = 0.24, $p < .001$, with mixed evidence for mediation by reductions in depression, $\beta_{path\text{-}ab}$ = 0.03, p = .08, anger, $\beta_{path\text{-}ab}$ = 0.05, p = .05, or anxiety, $\beta_{path\text{-}ab}$ = 0.01, p = .21. PRT effect sizes on pain intensity were roughly double those reported by other common treatments, suggesting promise for treatments effectively reducing pain-related fear and avoidance.

The University of Colorado Institutional Review Board approved all procedures, including informed consent.

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Ethics statement: All authors agree to the content included in the abstract. The authors declare no competing financial interests. The study was approved by the Dana-Farber Cancer Institute Institutional Review Board, and met the scientific and ethical guidelines for human pain research of the Helsinki Accord (http://ohsr.od.nih.gov/guidelines/helsinki.html) and the International Association for the Study of Pain.

Title: *Long-term impact of cerebellar mass resection on pain processing, and cognitive and emotional sequelae: mixed methodology*

Abstract:

The cerebellum has been associated with cognition and affect, but long-term consequences of cerebellar insult on pain, executive functioning, fear of pain, and anxiety are unknown. This study utilized MRI lesion mapping, quantitative sensory testing, fMRI, psychological questionnaires, and clinical interviews (CI) on 12 patients (with matched healthy controls) treated with surgery only for non-malignant astrocytomas. Lesions were restricted to the cerebellum, with 5 patients having tumors in Crus I within the posterior cerebellar hemispheres, previously related to cognitive and affective processing. Crus Patients (CPs) had significantly lower pain tolerance to cold pressor tests than controls. No significant differences were detected between subject groups for heat/cold detection thresholds and heat/cold pain thresholds. CPs also showed significantly decreased fMRI responses to painful heat in anterior insula. No significant differences were found on psychological or cognitive measures. CIs showed patients were within normal bounds. Results suggest surgical resection of this region in children may increase the risk of developing pain disorders. Survivors also showed positive long-term outcomes in aspects of executive functioning, anxiety, and fear of pain possibly explained by recooperative neuroplasticity, a lack of sensitivity in the testing, or a lack of effect of the surgery itself on these functions.

Limits of Decoding Pain in the Brain

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ABSTRACT
High-profile studies claim the ability to assess mental states across individuals by decoding brain activity using multi-voxel patterns derived with "machine learning" tools. The fine-grained patterns present in these decoders are purportedly necessary for discriminating between mental states (e.g., painful versus nonpainful state), capturing perception properties (e.g., intensity of pain), and accurately identifying a given mental state (e.g., whether someone is in pain). Here, we present compelling evidence that pain decoding efficacy is grossly overstated. By perturbing pain decoders with spatial smoothing and randomly sampling their weights, we demonstrate that the fine-grained patterns used in the multi-voxel decoders are not necessary for discrimination performance. Discrimination, pain intensity mapping, and identification perform similarly across decoders, with and without perturbations. Importantly, pain identification performs poorly across all decoders. We go on to show that simple decoders, built from averaged and thresholded brain activity maps, perform similarly to more sophisticated decoders. Our results challenge the superiority fine-grained patterns in decoder pain, and as such, have important legal, medical, and ethical implications.

Presenter: Andrew Vigotsky (PhD Candidate)
Length: 168 words
Ethics statement: This work is based on deidentified data from previously published work and thus was exempt from IRB review.

Title: Patterned change in EMG activity in response to phasic pain during gait.

Authors: Jeffrey-Gauthier R[1,2], Bertrand-Charette M[1,2], Roy JS[1,2], Mercier C[1,2], Bouyer L[1,2]

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INTRODUCTION: Pain changes the way we move, which brings short-term relief but could contribute to long-term pain chronicization. This is poorly understood, which limits our ability to guide adaptation towards recovery. Using repeated exposure to electrical, phasic pain evoked at heel strike during gait, the objectives of this study were to: 1) reveal central components of adaptation with catch trials (pain expected but absent); 2) verify whether movement-related pain relief is essential for this adaptation to occur by comparing phasic pain relieved by heel off (controllable) versus a 300-ms fixed duration (uncontrollable).

METHODS: EMG activity was recorded from both flexor and extensor muscles contributing to gait in 15 healthy participants during five conditions of treadmill walking: Baseline, Pain 1, Washout 1, Pain 2 and Washout 2. Pain conditions, controllable and uncontrollable, were randomized. Catch trials occurred every 30 steps during pain conditions.

RESULTS: The ipsilateral tibialis anterior swing-to-stance burst was reduced during both pain conditions ($p < 0.001$) and persisted during catch trials regardless of stimulus controllability ($p = 0.48$).

CONCLUSIONS: This model of phasic pain reveals central contributors to movement adaptation to pain and stimulus characteristics that allow it, showing potential to elucidate mechanisms of movement adaptation to pain.

ETHICS STATEMENT: All procedures were approved by the Sectoral Research Ethics Board in Rehabilitation and Social Integration and comply with guidelines from the Committee for Research and Ethical Issues of the International Association for the Study of Pain.

Confidence in subjective pain

Troy C. Dildine, Elizabeth A. Necka, & Lauren Y. Atlas

Word count: 200

Pain is a personal experience that is communicated via self-report. While verbal reports facilitate treatment, it is unknown whether people vary in confidence about their pain or introspect on pain judgments. However, a rich literature on the neuroscience of metacognition in other cognitive and perceptual domains suggests that people do introspect on decisions, indicating this may be important in evaluating pain. To address this gap, we measured confidence in pain and tested whether confidence related to reaction time (RT) or number of eye fixations during pain rating. Eighty healthy volunteers experienced acute thermal stimulation and rated pain and confidence on continuous visual analogue scales. Confidence varied across trials ($M_{uncertainty\ 0\text{-}100} = 9.48$, $SD_{uncertainty\ 0\text{-}100} = 15.63$), indicating that individuals can report metacognitive aspects of pain and vary in confidence over time. In addition, slower RTs were associated with decreased likelihood of confidence ($\beta_{1Logistic} = -0.55$, $p = 0.002$) and linearly associated with uncertainty ($\beta_{1Linear} = 0.40$, $p < 0.001$). Taken together, this work demonstrates that individuals can provide pain metacognitive judgments and suggests that RT might serve as an implicit marker of pain rating confidence. Future studies can leverage these findings to evaluate the role of confidence in pain modulation.

Ethics Statement and Conflict of Interest Disclosures: All participants provided informed consent in accordance with the Declaration of Helsinki and all study procedures were approved by the National Institutes of Health (NIH) Combined Neuroscience IRB (Protocol 15-AT-0132). The authors report no conflicts of interest.

The Influence of Neuropathic Pain-Like Symptomatology on Placebo Analgesia in Temporomandibular Joint Disorder

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Abstract

Temporomandibular Joint Disorder **(**TMD) is a chronic orofacial pain condition affecting an estimated 5 – 15 % of the adult population. TMD is primarily considered a musculoskeletal pain disorder, though patients may present with concurrent neuropathic pain-like symptoms either in the orofacial region or in other parts of the body. Though studies show reductions in opioid receptor availability and alterations in pain modulation in neuropathic pain, the specific effect of neuropathic pain symptomatology on Placebo Analgesia (PA) is yet to be understood. We hypothesized that the presence of a neuropathic pain-like symptom profile would decrease PA magnitude and responsiveness. In a cohort of 114 participants, we compared TMD participants with neuropathic pain-like symptoms with TMD participants with have no neuropathic pain-like symptoms as well as with pain-free healthy controls. Neuropathic pain assessment was carried out using two validated tools, the Douleur Neuropathique 4 (DN4) and the PainDETECT Questionnaire (PDQ). Our results showed that the presence of a co-occurring neuropathic pain-like symptom profile in TMD participants increased PA in comparison to TMD participants without any neuropathic pain symptoms and to those matched healthy controls. We also show that this effect is mediated by reinforced expectation.

Ethics Statement: This study was approved by the University of Maryland Baltimore, Institutional Review Board (#HP00068315) and all participants provided both verbal and written informed consent before participation. All experimental procedures were conducted in conformance with the Declaration of Helsinki (World Medical Association, 1964). Due to the involvement of deception during Placebo Analgesia procedures, all participants were debriefed at their conclusion of the study.