Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

nociceptive withdrawal thresholds (n=10/group) using von Frey filaments by a blinded observer. 2-way ANOVA analyzed data. The results demonstrate after 8 weeks of H6D, there is a decrease in mechanical nociceptive thresholds seen in the orofacial region. These findings support the conclusion that a H6D triggers mechanical allodynia in both the DRG and TG systems. Therefore, dietary intervention may represent novel therapeutic approaches for treating chronic pain conditions. NIDCR T-32 DE14318 and R01 NS110948.

Clinical Trials

Integrating pragmatism and rigor - impact of the pandemic on a randomized controlled trial of a complex intervention

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The objectives here were to present a model of transparent reporting and pragmatic RCT design adaptation, and to promote discussion regarding best practices for overcoming the challenge of detecting intervention-specific changes in pain within the context of variable psychosocial factors due to the pandemic. Methods included an ongoing randomized, double-blind, placebo-controlled trial is examining the effect of pain education combined with exercise on pain in patients with chronic Achilles tendinopathy. We hypothesized that a biopsychosocial approach to patient education would reduce movement-evoked pain more than standard care (biomedical education and exercise). Since March 2020, challenges have included a temporary halt of in-person human subjects research, adapting virtual screening procedures to maintain confidentiality and safety, need to obtain telehealth license in multiple states, inability to use specialized laboratory equipment to evaluate secondary outcomes, and gradual resumption of in-person visits with PPE. As COVID-19 prevented the trial from proceeding as planned, we adapted our design to both exploit new opportunities and maintain high standards of transparency and rigor. We maintained study enrollment by modifying screening, evaluation, and treatment to accommodate virtual participation with consistent content. We adjusted our aims to include an a priori hypothesis that differential effects of a biopsychosocial versus biomedical approach on pain may be magnified during a pandemic. Additionally, strategies developed to adapt to an altered research-environment may be useful tools for future RCTs to facilitate participant recruitment and retention. We logged changes in a time-stamped manner on Open Science Framework; full disclosure will be ensured in final reports at Clinicaltrials.gov and publications. Adaptive designs are at risk of low confidence unless full transparency is integrated into research processes. Our own efforts to integrate changes to research design and conduct, with contemporary standards of transparency and rigor, provide opportunities for future research practice during and post-COVID. Funding for this study was provided by the National Institute of Arthritis Musculoskeletal and Skin Disease (NIAMS) research grant R00 AR071517 and by the Collaborative Research Grant from the International Association for the Study of Pain (IASP). Research reported in this publication was supported by the National Center for Advancing Translational Sciences of the National Institutes of Health under Award Number UL1TR002537. These funding sources had no role in study design, collection, analysis/interpretation of data, or decision on submission for publication. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Conceptual Design and Protocol for the Acute to Chronic Pain Signatures Program (A2CPS)

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The United States faces a crisis due to the high prevalence of chronic pain and associated opioid use disorder and overdose deaths. While the majority of acute pain resolves within weeks, 20-50% of people with acute pain persists well beyond the initial insult. The mechanisms driving the transition from acute to chronic pain states are poorly understood. Through a National Institutes of Health (NIH)-funded initiative, the A2CPS Program was formed to identify putative biomarkers (individual or biosignature combinations) that predict susceptibility or resilience for the transition from acute to chronic pain after surgery (total knee replacement and thoracotomy). The A2CPS consortium includes two multisite clinical centers (MCCs), one Clinical Coordinating Center (CCC), one Data Integrations and Research Center (DIRC), and 3 OMICS centers along with representation from the NIH Pain Consortium, Common Fund, and National Institute of Drug Abuse. During an initial planning year, the A2CPS developed study aims, biomarker selection, and a study protocol. Candidate biomarkers were selected across multiple domains (clinical, biospecimen, psychosocial, and brain structure/function). Data will be collected from two MCCs (n=3600 individuals) before, during and after surgery to determine factors that predict the transition from acute to chronic pain 6 months later. Subjects will be comprehensively phenotyped across measures of pain, behavioral and psychological, quantitative sensory testing, brain imaging, proteomics, genomics, metabolomics, and lipidomics. Determining biomarkers prior to and in the acute phase after surgery could provide the basis for interventions to prevent the onset of chronic pain and contribute to our understanding of the dynamic processes underlying the transition from acute to chronic pain. Furthermore, if any of the predictive biomarkers play a mechanistic role in development of chronic pain, then the molecules, pathways, constructs, and/or brain circuits identified could serve as new potential therapeutic targets for reversing chronic pain or increasing patients' resilience. National Institutes of Health Grants: NS112873, NS118922, DA049110, NS112874, DA049115, DA049116, DA049113.

Impact of COVID-19 on a Pragmatic, Cluster Randomized Clinical Trial for Fibromyalgia

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Our objective was to present our experience on adapting to the challenges of COVID-19 pandemic on a pragmatic clinical trial. Transcutaneous Electrical Nerve Stimulation (TENS) in Physical Therapy (PT) Study (FM-TIPS) is a pragmatic, cluster-randomized clinical trial examining if the addition of TENS to routine PT improves movement-evoked pain in fibromyalgia (FM). FM patients (n=600) were enrolled from 24 PT clinics (12 PT only, 12 PT with TENS) across five healthcare systems. COVID-19 has significantly impacted PT practice and in-person interactions. In response, all PT clinics saw reduced volumes of patients, some clinics furloughed PTs, and some clinics were permanently closed. This led us to put contracts, reliance agreements, and training of clinics on hold and to seek additional clinics that could fill the gap for those who could no longer participate. It also led to a delay in onboarding healthcare systems and inpatient enrollment. In order to protect the integrity of the study and minimize missing data due to potential restrictions of in-person visits we developed alternative strategies. This includes procedures for home instruction of TENS via telehealth, a plan for bringing on backup clinics, and a plan for training virtually and in-person using personal protective equipment and social distancing. Assessment of primary outcome and questionnaire data were transitioned for the patient to perform at home through a patient-portal with embedded patient-specific videos. We have also set up a phone line for patients to call with additional questions or concerns. The impact of COVID-19 on statistical design and analysis was discussed including a plan for uneven enrollment across clinics and a sub-analysis of data for patients enrolled during or after the pandemic. In conclusion, COVID-19 altered the original study design of this large-pragmatic trial to account for greater flexibility for providers and patients to facilitate continued enrollment. NIH.

Identifying Treatment Effect Moderators in the TARGET Trial: A Secondary Analysis

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The purpose of this secondary analysis was to identify treatment effect moderators from a large, pragmatic, cluster randomized trial for prevention of chronic low back pain (LBP). The TARGET trial was conducted at 76 primary care clinics in 4 health systems across the United States between May 2016 and June 2018. Practices were randomly assigned (1:1) to stratified care (intervention) or usual care (control). The intervention included identifying high risk