home setting could facilitate future research and clinical care. The objective of this study was to develop a home QST (HQST) tool-kit that is safe, easy to use, and detects changes in sensory and pain processing. The HQST tool-kit was developed using inexpensive, portable, and widely available tools that have been tested in adult populations or best mimic LQST equipment. Thirty-two young healthy adults underwent sensory testing on their forearm using standard in-person LQST, followed by "simulated HQST" via video guidance in a separate room from the investigator before and after application of either a lidocaine or capsaicin cream. We observed good agreement between HQST and LQST scores, with significant correlations observed between the pinprick, pressure, cold and heat measures (|rho| range = 0.36-0.54). The participants rated the HQST protocol as highly acceptable and safe. Qualitative analyses of participants' comments revealed that the current HQST protocol appears useful, but requires improvement before future implementations. HQST was able to detect hypoesthesia to vibration after lidocaine cream application ($p = 0.024$), and could detect hypo- and hyperalgesia to pressure and heat pain sensitivity tests after application of lidocaine and capsaicin creams, respectively (p-value range = < 0.001-0.036). Despite limitations, HQST tool-kits may become a cost-effective, convenient, and scalable approach for improving sensory profiling in clinical care and clinical research.

Differential Deoxyribonucleic Acid Methylation in Painful Versus Non-Painful Degenerating Intervertebral Discs: A Human Case Study

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Chronic back pain poses a significant health concern. Though back pain is often attributed to disc degeneration (DD), intervertebral disc (IVD) degeneration is frequently experienced without pain. Why does DD lead to discogenic LBP in some cases and remain asymptomatic in others? A growing body of evidence suggests epigenetic modifications, such as DNA methylation, contribute to pathological DD. Understanding DNA methylation in discogenic LBP is crucial due to its reversibility, offering a promising therapeutic target. The goal of this study was to identify DNA methylation patterns associated with painful vs. pain-free DD. In a case involving a subject with LBP and DD at multiple IVD levels, a lumbar discogram was performed before surgery to pinpoint the discs causing pain. Despite severe degeneration, one spinal level (L5/S1) scored 0/10 on the discogram while L3/L4 and L4/L5 produced pain reports of 10/10 and 8/10, respectively. Next, DNA was isolated from the nucleus pulposus of discs collected during surgery. Methylation analysis was conducted using Illumina Infinium MethylationEPIC v2.0 BeadChip. SeSAMe pipeline in R determined methylation levels (beta values). After filtering for greater than 20% effect size, 315 gene-associated promoter sites were identified. Pathway enrichment analysis revealed terms related to nerve growth (e.g., TRK receptor binding, substrate adhesion-dependent cell spreading, netrin-1 signaling), as well as immune processes (e.g., neutrophil extravasation, T-cell polarity, CD28 co-stimulation). These findings suggest a potential epigenetic mechanism behind the disconnect between DD and pain; thus, raising the possibility of diagnostic or therapeutic strategies for discerning or treating painful disc degeneration.

Evaluation Of Socioeconomic Status and Spine Health in Chronic Low Back Pain Using Deep Learning Based Image Analysis

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Chronic low back pain (cLBP) is a complex disease with biological, psychological, and social components. The interaction of these components is poorly understood. Socioeconomic status (SES) and disc degeneration are strong indicators of cLBP, yet the explicit relationship between SES and disc degeneration has not been investigated. The purpose of this research is to investigate the relationship between SES and disc degeneration in cLBP. The UK Biobank includes a collection of 50,000 participants with lumbar spine dual x-ray absorptiometry records and SES data. A preliminary 590 participants are presented here. We utilized deep learning to automate the analysis of an existing spine imaging dataset to enable a large-scale assessment of disc degeneration, specifically the measure of disc height index (DHI). A deep convolutional neural network was developed that receives a DEXA scan as input and outputs a quadrilateral that correspond to the boundaries of five lumbar vertebral bodies. Our deep learning model accurately predicts the quadrilaterals in unseen test data is preliminary evidence that we can produce robust segmentations from DEXA scans (Intersection Over Union = 0.933). We used a linear regression model to evaluate how income, education, and employment impact DHI, while adjusting for age. Currently, we found that there was no statistically significant difference between any of the variables ($p > 0.05$) other than age ($p < 0.05$). Our findings indicate that there may be other drivers of pain that outweigh the impact of anatomical features, such as psychosocial factors. Funded by the National Institute of Health (R00AR077685 and T32AR073157).

Exploring the Relationship Between Temporal Summation and Conditioned Pain Modulation in Patients After Surgery – A Preliminary Investigation

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Temporal summation of pain (TSP) and conditioned pain modulation (CPM) are commonly used psychophysical paradigms to investigate pro- and antinociceptive aspects of endogenous pain modulation, and are putative phenotypic contributors to the risk for the development of chronic pain. Studies comparing the relationship between the two paradigms have largely been conducted in healthy controls; however, research is warranted in chronic pain populations. The current study measured TSP and CPM in 38 individuals who underwent surgery within the previous 24 months (89% female, ages 14-59 years) and 45 healthy pain-free controls (71% female, ages 15-62 years), and assessed the correlations between these two paradigms. In line with published protocols, TSP was performed using Von Frey filaments. For the CPM paradigm, pressure pain threshold of the non-dominant trapezius was used as the test stimulus and the dominant hand in an ice bath was used as the conditioning stimulus. Results of Wilcoxon Signed Rank Tests showed significant increased pain rating for TSP during repetitive stimuli ($p < .001$), and between baseline and conditioning for CPM ($p=.002$). Results of a Spearman's correlation revealed approaching significance association between TSP and CPM in the patient group, but not in controls. Preliminary findings may suggest distinct aspects of central pain processing of this cohort and contribute to our understanding regarding the methodology and interpretation of these paradigms in clinical pain populations. Data collection is ongoing, further investigations with larger sample size will be conducted to verify the current findings. Funded by National Institutes of Health (R35GM142676–01).

Exploring the Single-Cell Transcriptome Landscape of the Human Dorsal Root Ganglion in Diabetic Peripheral Neuropathy

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Diabetic Peripheral Neuropathy (DPN) stands out as a very common and clinically consequential complication of diabetes. DPN is characterized by nerve conduction impairment, dieback of nerve endings from the skin, spontaneous pain, and numbness in extremities. In this study, we conducted single-nucleus RNA sequencing on human dorsal root ganglion (DRG) tissues recovered from organ donors with a documented history of diabetes and neuropathic pain. Employing 10x Genomics technology, we performed single-nucleus RNA sequencing on eight human DRG samples each from individuals with DPN or healthy donors. Our primary objectives encompassed elucidating distinct populations of neurons and comprehending their transcriptomic variations between healthy and DPN DRGs. Additionally, we sought to characterize the diversity of transcriptomic changes in non-neuronal cells and explore their neuro-immune interactions in DPN. Our analysis revealed significant alterations in non-neuronal cell populations, including T cells, macrophages, and adipocytes within human DRG of DPN donors. Our work presents a comprehensive single-cell transcriptomic landscape of human DRGs in DPN donors, providing insights into molecular profile changes associated with DPN. The interactions between neuronal and non-neuronal cells could offer valuable insights into the underlying mechanisms of this condition, assisting in the development of novel therapeutics to alleviate DPN. Funded by National Institute of Health (U19 NS130608).