pain-specific Stroop performance. Future research examining pain and aging interactions in relation to cognitive inhibitory processes may improve our understanding of the impact of pain-related information on executive function in aging.

Ethical, Legal, Financial, & Education

(341) Quantifying Chronic Pain: A Mixed-Methods Analysis of Chronic Pain Sufferers' Public and Private Discourse

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Persons with chronic pain experience negative health outcomes associated with experiences of stigmatization and delegitimization. Because stigma and doubts of legitimacy stem from how cultures create, value, and communicate knowledge, this research considers how persons with chronic pain navigate cultural perceptions of pain when they make rhetorical decisions about what and how they communicate. This project is particularly concerned with how persons with chronic pain do or do not take advantage of a preference for quantification in U.S. medical contexts. For example, persons with chronic pain might quantify their pain on a numerical scale, in terms of time required to complete an everyday task, or in terms of medicinal dosage or expenses. To that end, this poster reports on the results of a two-part mixed-methods study: 1) a statistical analysis of 2,105 tweets about daily chronic pain experiences, and 2) a discourse analysis of 15 interviews with persons with chronic pain. By drawing data from two different sources—social media posts and research interviews—this study allows for comparison of public and private discourses by persons with chronic pain, finding that both groups use rhetorics of quantification but for different purposes and audiences. In addition to expanding scholarship on the communication trends and challenges among persons with chronic pain, this study contributes to this area of scholarship a rare examination of communication outside an explicitly medical context. That is, in addition to discourses with medical professionals, this study provides insight into how persons with chronic pain communicate about pain with family, friends, coworkers, and even strangers. The findings of this study are relevant to both medical professionals and laypersons who communicate with persons with chronic pain and wish to mitigate the risk of incidental stigmatization or delegitimization in their writing or speech.

Molecular and Cellular Biology

(342) Molecular Transcriptomic Effects of General Anesthesia on Gene Expression in Frontal Lobe, Hippocampus, and Amygdala after Administration of Ketamine and Isoflurane

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General anesthesia and monitored sedation are vital to nearly all procedural aspects of modern medicine. Inhaled agents such as halogenated gases have long been an integral aspect of anesthesia. In recent years, the noncompetitive NMDA antagonist and dissociative anesthetic ketamine has seen increasing utilization in general anesthesia, as well as in the treatment of chronic pain and depression. The use of ketamine for such chronic conditions has raised questions into its addictive potential, and its potential role in the treatment of existing addictions. New investigations using high density electrical recordings and other multidimensional techniques have led to a clearer understanding of how these agents work, and how they can be utilized to fill clinical needs. To further study their effects at the molecular level, we used deep RNA sequencing to examine the time course (1hr, 10hr, or 10hr + 24hr recovery) of gene changes induced in the frontal cortex, hippocampus, and amygdala during ketamine or isoflurane administration. When compared to isoflurane, the transcriptional signature of ketamine showed similarities and differences that suggested region-specific gene regulation patterns that highlight the molecular underpinnings of the broad clinical uses of ketamine. The evaluation of brain regions subserving the diverse functions of learning and memory, executive function, and emotional-affective dimensions yielded insight into the neural localization of anesthetic actions and potential vulnerabilities associated with general anesthesia. Our investigation demonstrates unique region-specific and time-dependent transcriptional signatures that bridge molecular and systems level findings to expand current understanding of the shifts in neuronal activity associated with general anesthetics and their downstream effects.

(343) Localized Sympathectomy Drives Macrophage Polarization to Reduce Chemotherapy-Induced Neuropathic Pain

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Chemotherapy-induced neuropathic pain (CINP) is a disabling condition affecting up to 80% of patients during treatment with antineoplastic drugs, including the frontline chemotherapeutic agent paclitaxel. There are no FDA-approved drugs to treat CIPN and many drugs that are used for the treatment of other neuropathic pain states have shown poor or no analgesic effect on CINP, which suggests unique mechanisms underlie CINP. Paclitaxel is a common drug for various solid cancers. However, it is often associated with neuropathic pain, which is generally localized in the distal extremities of the body and can persist for months or years after the end of the treatment. Although the exact mechanisms underlying paclitaxel CINP remain incompletely known, there are several line of evidence indicating that immune cells in dorsal root ganglia (DRGs) play critical roles in the development and progression of CINP. Interestingly, our recent study has shown that sympathetic innervation not only drives immune responses in organs such as the thymus, spleen and lymph nodes, but also orchestrates localized immune responses in DRGs maintaining inflammatory pain. Here, we report that localized "microsympathectomy" (mSYMPX) significantly reverses mechanical allodynia in male and female mice after paclitaxel. Mechanistically, the mSYMPX analgesic effect is driven by an anti-inflammatory polarization of macrophages and TGF-β1 signaling in DRGs. Thus, localized sympathetic blockade may offer a novel therapeutic approach for the clinical relief of CIPN.

(344) A Photoswitchable GPCR-Based Opsin for Synaptic Inhibition

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The development of diverse molecular tools to manipulate the activity of defined cell types has greatly accelerated our understanding of the neural circuits underlying complex behaviors. The most commonly used opsins are light-gated ion channels or pumps to control activity on millisecond timescales. While optogenetic activation can be precisely tuned across a range of firing frequencies, neuronal inhibition has proven to be more problematic. The most commonly used inhibitory opsins are chloride or proton pumps requiring constant illumination, and biophysical constraints due to different subcellular ion gradients can trigger unwanted excitation. The development of opto-GPCR chimeras grants spatial and temporal control of distinct G-protein coupled intracellular signaling cascades, and in contrast to binary on/off manipulations, modulating endogenous activity patterns may more accurately reflect circuit dynamics. However, these rhodopsin-based approaches possess several limitations, including high photosensitivity and irreversible activation. Here we have identified a novel photoswitchable GPCR-based opsin that engages endogenous inhibitory signaling cascades to silence synaptic transmission. This UV/blue light-sensitive opsin couples to G-proteins to reversibly inhibit neuronal voltage-gated calcium channel function, with similar efficacy to endogenous $GABA_BRs$. Long-term optical inhibition can be achieved with pulsed light, does not desensitize, and most importantly, inhibition is rapidly reversed by illumination with amber light. This opsin can also be stimulated by 2-photon excitation, permitting subcellular activation of G-protein subunits, which may allow for precise patterns of inhibition deep within tissues. Lastly, we found that optical stimulation in vivo inhibits dopamine neurons to reduce motivated behaviors. We are now adapting this GPCR-based opsin to serve as a novel scaffold for next-generation opto-XR chimeras with photoswitchable control of GPCR signaling cascades to better understand the roles of these important therapeutic targets in different pain circuits.