educational preparation, hands-on observation of value of ACP in surgical patients and influences from attending and residents. DISCUSSION/SIGNIFICANCE: While current ACP research in surgery focuses on physician-led patient engagement in ACP discussions, there is a paucity of research focusing on how to develop a team-based approach to ACP discussions in surgery. This study will provide information necessary for the development of interventions that increase team-based ACP for surgical patients.

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Potential Drug Therapy for Fragile X Tremor/Ataxia Syndrome*,†

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OBJECTIVES/GOALS: Fragile X-associated tremor/ataxia syndrome (FXTAS) is a devastating rare neurological disorder that negatively impacts movement and cognition. To date, there are no effective pharmacological treatments for FXTAS. Our goal was to develop a cell culture model of FXTAS to investigate promising therapeutics. METHODS/STUDY POPULATION: To establish mitochondrial dysfunction, normal human cell lines and human-induced pluripotent cells were treated with multiple concentrations of glucose/ glucose oxidase (GluOx) at 2,12, and 24 hour time points to induce varying intensities of oxidative stress. The degrees of oxidative stress were measured by apoptosis and mitochondrial reactive oxygen species (ROS) production. Curcumin and MSKE compounds effective against oxidative damage in mitochondria were used to rescue glucose oxidase-induced oxidative damage in both cell lines. To test the ability of these drugs to restore mitochondrial health, cell viability and cellular superoxide production were assessed by propidium iodide and the MitoSox fluorescence assay, respectively. RESULTS/ANTICIPATED RESULTS: We anticipated that GluOx at varying concentrations and time points would proportionally increase levels of apoptosis and mitochondrial ROS, reflective of mitochondrial damage, with the most severe dysfunction occurring at a dose of 25 nM and the longest duration of 24-hr exposure. Administration of MSKE in concentrations ranging from 10-8 to 10-5 M in half log increments, did not reverse the oxidative defects induced in the cell lines. However, curcumin concentrations increased cell viability at the 2, 12, and 24 hour time period. Results indicate that the research design should be modified by increasing the concentration of both glucose and MSKE to provide a reliable test of the hypothesis. DISCUSSION/SIGNIFICANCE: These studies illustrate the usefulness of this in vitro model to test novel therapeutics in neuronal FXTAS models and expand the discovery of mitochondrial markers for the syndrome.

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Eliminating System xc- Signaling Between Astrocytes and Neurons Selectively Impairs Complex Cognition

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OBJECTIVES/GOALS: We aim to determine whether non-neuronal, non-synaptic glutamate signaling mechanisms can be targeted to produce highly specific, narrow changes in brain function that would benefit CNS disorders. To do this, we investigated cognitive changes produced through manipulating the activity of the astrocytic glutamate release mechanism system xc-. METHODS/STUDY POPULATION: System xc- (Sxc) activity was eliminated by mutating the gene Slc7a11 through pronuclear injection of zinc-finger nucleases into Sprague Dawley rat embryos to create a line of rats lacking Sxc (MSxc rats). To confirm a lack of Sxc activity, we verified that tissue from MSxc rats had a complete lack of xCT, which is the regulatory subunit of Sxc that is encoded by Slc7a11. We also verified that astrocyte cultures generated from MSxc tissue lacked cystine-evoked glutamate release. Next, we measured development (body weight), CNS regulation of metabolism, and other indicators of generalized, non-specific brain function as well as behaviors that are reliant on executive function, such as cognitive flexibility, impulse control, decision-making, and response inhibition. RESULTS/ANTICIPATED RESULTS: Eliminating Sxc was not lethal and did not impair development or produce widespread changes in brain function as is commonly observed when deleting other glutamate mechanisms. MSxc rats did not differ from wildtype in growth rate, central regulation of metabolism as reflected by absolute or diurnal changes in core body temperature, locomotor activity in a familiar or novel environment, or simple forms of cognition such as novel object recognition, or operant responding (food and cocaine-reinforced). In contrast, behaviors that rely on executive function were impaired. MSxc rats displayed deficits in cocaine reinstatement and attentional set-shifting. We anticipate MSxc rats to also show impairments in decision-making in the rat gambling task and response inhibition in the stop-signal reaction time task. DISCUSSION/SIGNIFICANCE: Eliminating Sxc activity in rats produced deficits in behaviors reliant on executive function without impacting development or simple brain function. These results highlight the potential of targeting Sxc to enhance cognition without generating therapeutically limiting adverse effects resulting from non-specific changes in brain function.

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Quantifying Heavy Metals in Interstitial Fluid for Remote Monitoring of Chronic Exposures

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OBJECTIVES/GOALS: Our hypothesis is that microneedle array (MA) extraction of interstitial fluid (ISF) will enable minimally invasive quantitation of heavy metal (HM) exposure. We aim to establish analytical parameters for ICP-MS analysis of HMs, quantify baseline HM content in ISF vs other fluids, and characterize a mixed HM exposure model. METHODS/STUDY POPULATION: Ten healthy human volunteers were recruited into the study, approved by the UNM Human Research and Resource Committee Each subject had blood and urine collected. ISF was also collected using 3D-printed MAs inserted into the forearm. Additionally, twelve Sprague Dawley rats were unexposed (n=6) or exposed (n=6) to ad libitum water containing a mixture of uranium (U), cadmium (Cd), vanadium (V), and arsenic (As), each at 5X the maximum contaminant level (MCL) for drinking water under a protocol approved by the UNM animal care and use program. Human and animal fluids were analyzed, using ICP-MS, to quantify the levels of U, Cd, V, and As. RESULTS/ANTICIPATED RESULTS: Recent advances in ISF extraction and analysis suggest a minimally invasive method that can be adapted to monitor HM exposure and biological loads

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longitudinally in both localized and dispersed communities. ISF can be collected with MAs and is a rich source of disease and exposure biomarkers. However, determining biological loads remains challenging due to the need to collect blood or urine from a dispersed rural population over time. Our preliminary results suggest similar HM concentrations in ISF, compared with blood in small unexposed human and animal populations. All four metals can be successfully quantified in tandem using ICP-MS. DISCUSSION/SIGNIFICANCE: Chronic exposure to heavy metals (HM) is associated with detrimental health effects. Exposure to multiple HMs is suspected to have additive or synergistic harmful effects. We envision a wearable microneedle patch that could be mailed to individuals or distributed through community centers, worn for a few hours, and returned to a central laboratory.

Other

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Can supervision support implementation of evidence-based practices in substance use disorder treatment programs? A qualitative analysis of organizational and environmental contexts in Arkansas

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OBJECTIVES/GOALS: Supervision is a promising strategy for supporting high-fidelity implementation of evidence-based practices (EBPs) in substance use disorder (SUD) settings. In this study, we explore current supervision practices in community SUD programs and identify organizational and environmental factors that shape them. METHODS/STUDY POPULATION: We interviewed 25 leaders and counselors at 8 community SUD programs in Arkansas, and 16 leaders at external stakeholder organizations (e.g., regulators, payers, licensing boards). Interview guides were based on the i-PARIHS framework. Interviews were conducted on Zoom or phone, lasted ~1 hour, and were recorded and transcribed. Below we outline findings based on preliminary analyses; full thematic analyses will be completed before presentation. RESULTS/ANTICIPATED RESULTS: Participants generally recognized the importance of utilizing EBPs and supporting their use through supervision. Counselors professional backgrounds and training vary substantially, necessitating continuing education and supervision. However, different professional, licensing and regulatory standards create a complex web of requirements and practices. Supervisors typically require clinical experience, but are rarely trained in supervision. They are internal or external to the organization, and provide individual or group supervision. Supervisors most often rely on case summaries and chart reviews, sometimes on direct observations and role-playing, and rarely (one program) on session recordings. Supervision goals are broad, and while EBP use is encouraged, it is rarely the focus of supervision. DISCUSSION/SIGNIFICANCE: To enhance supervision in community SUD settings and improve implementation of EBPs, new supervision strategies need to fit the various norms, expectations, and standards (e.g., professional, regulatory) that characterize community SUD programs, their workforce, and their environments.

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Gaps in Physical Therapists' and Physical Therapist Assistants Knowledge and Use of the CDC's STEADI for Falls Risk Screening of Older Adults in the United States

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OBJECTIVES/GOALS: Studies using Medicare data indicate that physical therapists (PTs) and physical therapist assistants (PTAs) are not providing falls prevention to at-risk older adults in rehabilitation. We aimed to identify PTs and PTAs knowledge and use of the Centers for Disease Control and Prevention's STEADI fall prevention toolkit. METHODS/STUDY POPULATION: We conducted a cross-sectional survey distributed to a convenience sample of PTs and PTAs in the United States through email blasts and social media. Descriptive statistics were used to summarize the demographic characteristics of the respondents. Some categorical variables were combined to provide more meaningful classifications or due to small frequencies. We used independent samples t-tests for continuous data, and chi-square and Fisher's Exact tests for categorical data to compare characteristics between respondents that do and do not conduct falls risk screenings.Frequency counts and percentages were used to summarize survey responses related to falls risk screening and knowledge/use of STEADI. SASÂ® version 9.4 was used for all statistical analyses. RESULTS/ANTICIPATED RESULTS: PTs and PTAs (N = 425) who responded to the survey and worked in clinical settings with older adults were included. Eighty-nine percent of respondents reported conducting clinical falls risk screening, yet only 51% were 'familiar' to 'very familiar' with STEADI. Twenty-two percent of respondents were not familiar at all with STEADI. Of the respondents who were 'very familiar with the STEADI (n = 132, 31.1%), 84.1% (n = 111) reported using STEADI in clinical practice. Seventy-six percent of respondents who use the STEADI implemented it by choice even though the majority (52.1%, n = 63) did not have it embedded in their workflow or documentation. DISCUSSION/SIGNIFICANCE: PTs and PTAs in the United States have some familiarity with and use STEADI in clinical falls prevention, and those who are very familiar with it use it by choice. Further research is needed to address the knowledge gap of STEADI and support PTs and PTAs providing falls prevention to older adults attending rehabilitation.

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