MARCKS levels would be increased in BAL cell lysates from horses with EAS, and that inhibition of MARCKS in zymosan-stimulated BAL cells (*ex vivo*) would diminish respiratory burst. METHODS/STUDY POPULATION: Lysates were prepared from BAL cells isolated from horses with no, mild/moderate and severe EAS. Relative MARCKS protein levels were determined using equine specific MARCKS ELISA (MyBioSource). Cultured BAL cells were pretreated with a MARCKS inhibitor peptide (MANS), control peptide (RNS) or vehicle control and stimulated with zymosan for 5 hours. Reactive oxygen species levels were determined by luminescence to evaluate respiratory burst. Data were analyzed by One-way ANOVA ($p<0.05$). RESULTS/ANTICIPATED RESULTS: We determined that normalized MARCKS protein expression is significantly increased in BAL cell lysates from horses with mild/moderate or severe EAS, compared to horses with normal BAL cytology. Preliminary findings also suggest that MANS treatment of zymosan-stimulated equine BAL cells *ex vivo* attenuates levels respiratory burst. DISCUSSION/SIGNIFICANCE OF IMPACT: These findings point to a possible role for MARCKS protein in the pathophysiology of EAS and support MARCKS inhibition as a potential therapeutic strategy.

4377

Missed Opportunities to Prevent Homicide: An Analysis of the National Violent Death Reporting System

Justin Cirone[1], Jennifer Cone[1], Brian Williams[1], David Hampton[1], Priya Prakash[1], and Tanya Zakrison[1]
[1]University of Chicago

OBJECTIVES/GOALS: The goal of this study is to better understand the homicide victim population who were institutionalized within 30 days prior to their death. Improved knowledge of this population can potentially prevent these future homicides. METHODS/STUDY POPULATION: A retrospective analysis of the 36 states included in the 2003-2017 National Violent Death Reporting System was performed. Demographics of recently institutionalized homicide victims (RIHV) in the last 30 days were compared to homicide victims who were not recently institutionalized. Circumstances of the homicide, such as suspected gang involvement, were also compared. Parametric and non-parametric statistical analyses were performed. Significance was set at $p<0.05$. RESULTS/ANTICIPATED RESULTS: There were 81,229 homicides with 992 (1.2%) RIHV. The majority of RIHV were Black (49.6%) and older than victims who were not recently institutionalized (37.2 vs. 34.8, $p<0.001$). RIHV had a high school degree or higher in 54.8% of cases and the primary homicide weapon was a firearm in 67% of the deaths. They were more likely to be homeless (3.1% vs. 1.5%), have a mental health diagnosis (9.2% vs. 2.3%), abuse alcohol (6.1% vs. 2.2%), or abuse other substances (15.2% vs. 5.8%) [all $p<0.001$]. These victims were most commonly institutionalized in a correctional facility or a hospital compared to other facilities such as nursing homes. Homicide circumstances for RIHV were more likely to involve abuse/neglect (4.3% vs. 2.2%, $p<0.001$), gang violence (7.6% vs. 5.6%, $p=0.002$), or a hate crime (1.0% vs. 0.1%. $p<0.001$). DISCUSSION/SIGNIFICANCE OF IMPACT: Contact with an institution such as a hospital or prison provides high-risk patients the opportunity to potentially participate in violence intervention programs. These institutions should seek to identify and intervene on this population to reduce the risk of violent homicides.

4141

Molecular Signatures of Cocaine Toxicity in Postmortem Human Brain and Neurons

Emily Frances Mendez[1], Laura Stertz[1], Gabriel Fries[1], Ruifeng Hu[1], Thomas Meyer[1], Zhongming Zhao[1], and Consuelo Walss-Bass[1]
[1]The University of Texas Health Science Center at Houston

OBJECTIVES/GOALS: The goal of this project is to identify new therapeutic targets and biomarkers to treat or prevent cocaine toxicity by investigating proteomic, transcriptomic and epigenetic signatures of cocaine exposure in human subjects. METHODS/STUDY POPULATION: Cocaine is a highly addictive neurotoxic substance, and it is estimated that 1.9 million Americans are current users of cocaine. To study the molecular effects of cocaine, we generated preliminary proteomics and next-generation RNA sequencing (RNAseq) data from human postmortem dorsolateral prefrontal cortex (Broadmann area 9 or BA9) of 12 cocaine-exposed subjects and 17 controls. Future directions for this project include RNAseq and DNA methylation analysis of neuronal nuclei sorted from human postmortem BA9 and a human induced pluripotent stem cell-derived neuron (hiPSN) model of cocaine exposure from the same postmortem subjects from whom we have brain samples. RESULTS/ANTICIPATED RESULTS: We found alterations in neuronal synaptic protein levels and gene expression, including the serotonin transporter SLC6A4, and synaptic proteins SNAP25, SYN2, SYNGR3. Pathway analysis of our results revealed alterations in specific pathways involved with neuronal function including voltage-gated calcium channels, and GABA receptor signaling. In the future, we expect to see an enhancement in neuron-specific gene expression signatures in our sorted neuronal nuclei and our hiPSN model of cocaine exposure. The hiPSN model will help elucidate which effects are due to acute versus chronic exposure of cocaine. DISCUSSION/SIGNIFICANCE OF IMPACT: Neuronal signatures found with this analysis can help us understand mechanisms of cognitive decline in long-term cocaine users as well as the acute effects on the brain of cocaine taken in overdose. With this work and future proposed studies, we can discover novel clinical biomarkers for cocaine neurotoxicity in patients with cocaine use disorder and determine readouts for future therapeutic development on cocaine addiction and overdose.

4488

Neural Network of the Cognitive Model of Reading†

Joseph Posner[1], Vivian Dickens, Andrew DeMarco, Sarah Snider, Peter Turkeltaub, and Rhonda Friedman
[1]Georgetown - Howard Universities

OBJECTIVES/GOALS: A particularly debilitating consequence of stroke is alexia, an acquired impairment in reading. Cognitive models aim to characterize how information is processed based on behavioral data. If we can concurrently characterize how neural networks process that information, we can enhance the models to reflect the neuronal interactions that drive them. METHODS/STUDY POPULATION: There will be 10 unimpaired adult readers. Two functional localizer tasks, deigned to consistently activate robust language areas, identify the regions of interest that process the cognitive reading functions (orthography, phonology, semantics). Another task, designed for this experiment, analyses the reading-related

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functional-connectivity between these areas by presenting words classified along the attributes of frequency, concreteness, and regularity, which utilize specific cognitive routes, and a visual control. Connectivity is analyzed during word reading overall vs. a control condition to determine overall reading-related connectivity, and while reading words that have high vs. low attribute values, to determine if cognitive processing routes bias the neural reading network connectivity. RESULTS/ANTICIPATED RESULTS: The localizer analysis is expected to result in the activation of canonical reading areas. The degree of functional connectivity observed between these regions is expected to depend on the degree to which each cognitive route is utilized to read a given word. After orthographic, phonologic, and semantic areas have been identified, the connectivity analysis should show that there is high correlation between all three types of areas during reading compared to the control condition. Then the frequency, regularity, and concreteness of the words being read should alter the reliance on the pathways between these area types. This would support the hypothesized pattern of connectivity as predicted by the cognitive reading routes. Otherwise, it will show how the neural reading network differs from the cognitive model. DISCUSSION/SIGNIFICANCE OF IMPACT: The results will determine the relationship between the cognitive reading model and the neural reading network. Cognitive models show what processes occur in the brain, but neural networks show how these processes occur. By relating these components, we obtain a more complete view of reading in the brain, which can inform future alexia treatments.

4341

Neuroclinical fingerprints of risk for psychosis: Profiles of neurophysiology, symptom severity, and cognitive function

Keisha Novak[1], Sam Buck[1], Roman Kotov[2], and Dan Foti[1]
[1]Purdue University; [2]Stony Brook University

OBJECTIVES/GOALS: The study aims to utilize event-related potentials (ERPs) coupled with observable reports of symptoms to comprehensively understand neurological and symptomatic profile of individuals at risk for developing psychosis. The study is a short-term longitudinal design which allows for examination of course as well as structure of illness. METHODS/STUDY POPULATION: This study uses a combination of well-validated ERPs (P300, N400, ERN) and symptom data to predict variation in symptoms over time. We parse heterogeneity within a high-risk group to create innovative profiles and predict variation in course of symptoms. Data collection is ongoing (n = 35; target N = 100). Methods include a battery of ERP tasks tracking neural processes associated with attention, language processing, and executive function (P300, N400, ERN), along with assessment of symptom type and severity. Analyses include how ERPs correlate with severity of risk and symptom dimensions (positive, negative, disorganized). We examine whether individual versus global ERP aberrations (P300, N400, ERN) predict individual versus global symptom domain severity (positive, negative, disorganized), or vice versa. RESULTS/ANTICIPATED RESULTS: Symptom domain scores were elevated compared to general population on positive ($M = 1.65$, $SD = .36$), negative ($M = 1.9$ $SD = .42$), and depressive ($M = 1.94$, $SD = .40$) domains. Small to medium effect sizes emerged for P300 profile (r's = −.001 to −.41) and ERN profile (r's = −.03 to −.37), though small effect sizes for N400 profile (r's = −.06 to .29). Analyses were run to determine the degree to which profiles of risk were similar: P300/ERN (r = −.09), ERN/N400 (r = −.39), and N400/P3 (r = −.20). Additional analyses suggest potential mediating effects of cognition on neural activity and symptoms. DISCUSSION/SIGNIFICANCE OF IMPACT: We use a combination of well-validated ERPs (i.e. P300, N400, ERN) with behavioral and symptom data to predict variation in symptoms over time. A "fingerprint" physiologic aberration may be exhibited within high-risk individuals and can be used as biomarkers to identify those at risk even before onset of observable symptoms.

4532

Pancreatic Cyst Risk Stratification for Early Detection of Pancreatic Cancer Using Quantitative Radiomics and Activity-Based Biomarkers

Sophia Hernandez[1], Andre Luiz Lourenco, Evan Calabrese, Tyler York, Alexa Glencer, Spencer Behr, Zhen Jane Wang, Eugene Koay, Charles Craik, and Kimberly Kirkwood
[1]University Of California, San Francisco

OBJECTIVES/GOALS: Pancreatic cysts are comprised of both precancerous mucinous lesions and non-mucinous lesions with minimal malignant potential. Our goal is to improve our ability to classify the type of cyst using a combination of novel radiomic features and cyst fluid proteolytic activity. METHODS/STUDY POPULATION: Preoperative pancreatic protocol CT images from 30 patients with proteolytic assay characterization, followed by surgical resection with a pathologically confirmed pancreatic cyst diagnosis between 2016-2019 will be used in this study. We will contour images using the widely available software 3D Slicer, and extract radiomic features using IBEX software. We will analyze area under the ROC curves to identify the radiomic features that best differentiate mucinous from non-mucinous cysts, and identify features to be cross validated. The predictive ability of identified radiomic features combined with proteolytic assay will be determined by performing multiple logistic regression analysis and comparing AUROC analysis. We will determine sensitivity and specificity for individual, as well as combinations of, analytes to determine the optimal classifier. RESULTS/ANTICIPATED RESULTS: We anticipate that the predictive ability, sensitivity, and specificity of utilizing radiomic features combined with proteolytic assay data will exceed the performance of any individual test. DISCUSSION/SIGNIFICANCE OF IMPACT: This work is designed to provide a predictive radiomic model that will enable us to better identify mucinous cysts that require further evaluation, and potentially prevent unnecessary surgery in other patients. Ultimately, we would like to improve the accuracy of noninvasive radiographic evaluation using radiomic markers. CONFLICT OF INTEREST DESCRIPTION: Dr. Charles Craik is a co-founder of Alaunus Biosciences, Inc.

4340

Piloting Implementation and Dissemination of Best Practice Guidelines Using BPM+Health

James McClay, MD, MS, FACEP, FAMIA[1], and Pawan Goyal[2]
[1]University of Nebraska Medical Center - Great Plains IDeA-CTR; [2]American College of Emergency Physicians

OBJECTIVES/GOALS: Clinical translational studies inform clinical practice patterns through dissemination of clinical practice guidelines (CPG). In EM practices change to rapidly for timely local EHR implementation. We test the OMG BPM+Health specification for rapid deployment of best practices relevant to EM. METHODS/STUDY

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