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

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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.

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Molecular Signatures of Cocaine Toxicity in Postmortem Human Brain and Neurons

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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.

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Neural Network of the Cognitive Model of Reading†

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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