SIGNIFICANCE OF IMPACT: Patient uptake of LEAPED was high, which suggests that patient-report is a feasible method of evaluating diagnostic decision making and delivery to patients and yields insightful information beyond administrative data. The next steps are to validate the accuracy of patient-reported diagnostic error by comparing with administrative data.

4077

Listening with the HEAR-QL: Quality of Life in Children with Hearing Loss

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OBJECTIVES/GOALS: This study evaluates the utility of self-reported quality of life measure in children with hearing loss. We will compare self-reported HEAR-QL scores with parent-reported HEAR-QL scores. We will then test the relationship between HEAR-QL scores and scores on a standardized assessment of cognition, the NIH Cognition Battery. METHODS/STUDY POPULATION: We will administer the HEAR-QL questionnaire to children with hearing loss and their parents. We will then administer the NIH Cognition Battery to the child. We will include in our population children ages 7 to 14 with hearing loss of any severity or side. We will exclude those with intellectual disability, disorders of speech or language, or those who would be unable to complete the questionnaires for any reason. Children will be recruited from Otolaryngology clinics at St. Louis Children's Hospital based on ICD diagnosis of sensorineural hearing loss between 01/2015 – 03/2020. RESULTS/ANTICIPATED RESULTS: We will aim to recruit 44 patients in total, which is the sample size needed to detect a moderate correlation ($r = 0.4$) with a 1-sided $\alpha = 0.05$ and 1-$\beta = 0.8$. HEAR-QL scores and NIH Cognition Battery scores will be reported using descriptive statistics. Linear regression as well as correlation analysis between HEAR-QL scores and cognitive testing scores will be performed using a 1-sided $\alpha = 0.05$, with 1-$\beta = 0.8$. If recruitment is sufficient, we will adjust for demographics that are significantly correlated with the outcome on multivariate analysis. Finally, we will test for agreement between parent report and child report by calculating a Kappa statistic. DISCUSSION/SIGNIFICANCE OF IMPACT: There is little clarity on the necessity of amplification in children with hearing loss, yet the child's perspective is not routinely assessed in clinical practice. This study employs self-report in a pediatric population with hearing loss to find out if children provide new and reliable information.

4221

Lower Serum TWEAK Concentration is a Biomarker for Mortality in Community Acquired Pneumonia

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OBJECTIVES/GOALS: To determine the relationship among serum concentration of tumor necrosis factor (TNF)-like weak inducer of apoptosis (TWEAK) and mortality in community-acquired pneumonia (CAP) patients. METHODS/STUDY POPULATION: This is a multicenter 2-year cohort study in Spain, designed to better understand the role of sTWEAK concentrations in CAP patients. CAP patients were prospectively enrolled in two University hospitals and sTWEAK was measured within the first 24 hours of ICU admission. Samples were collected and stored for laboratory analyses. To detect sTWEAK in human samples, we used a commercially available ELISA kit following manufacturer's instructions. Demographic patients' characteristics and ICU mortality were prospectively collected. Descriptive statistics and logistical regressions were used to assess the proposed aims. RESULTS/ANTICIPATED RESULTS: A total of forty-three patients were included in the study (10 healthy users, 10 uninfected controls and 23 CAP patients). In comparison to healthy volunteers, patients admitted to the hospital (both, infected and non-infected) had lower level of sTWEAK. During hospital admission, 7 (17%) patients died. Patients whom died during ICU stay due to CAP, had significantly lower levels of sTWEAK when comparing with patients whom survived (Median [IQR]; 509.35 [357.49, 953.92] Vs 1103.03 [716.93, 1663.16]; $p = 0.015$). In contrast, patients that developed shock did not have different concentrations of sTWEAK (Median [IQR]; 1008.04 [531.87, 1390.80] Vs 1062.29 [575.24, 1598.83], $p = 0.84$). DISCUSSION/SIGNIFICANCE OF IMPACT: Community-acquired pneumonia (CAP) is the first cause of death in underdeveloped countries. CAP is a pulmonary infection that creates a proinflammatory environment not just locally but also systemically, secondary to upregulation of molecular cascades with a wide variety of proteins being released perpetuating this inflammation and tissue damage. Several of these molecules have been described and linked to a greater risk of inhospital complications, longer length of hospital stay and mortality. TNF-like weak inducer of apoptosis (TWEAK) is a member of the TNF-alpha superfamily, involved in immune response, cell growth, angiogenesis, NF-kB activation and apoptosis induction in tumor cells. It is known that serum-TWEAK plays a role in inflammatory processes, however, its behavior is unknown in patients with CAP. Therefore, this study aims to identify whether there is a relationship between serum concentration of TWEAK and prognosis in CAP patients. To our knowledge, this is the first study to shown that concentration of sTWEAK within the first 24 hours of ICU admission is lower in patients with CAP. Moreover, patients whom died during ICU admission due to CAP, have lower sTWEAK levels. This biomarker may identify patients at higher risk of dying due to CAP and may represent severe CAP. However, further studies are needed to confirm these findings.

4379

MARCKS protein is altered in naturally occurring model of asthma in horses

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OBJECTIVES/GOALS: Asthma is a significant health concern that affects people of all ages worldwide. EAS demonstrates many of the pathophysiological characteristics of nonatopic human asthma, which has led EAS to be used as naturally occurring model. Previous work from our lab determined that MARCKS (Myristoylated Alanine Rich C Kinase Substrate) protein is an essential regulator of cellular inflammatory functions. In the current study, we hypothesized that

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.

4141

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.

4488

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