ethnicity, and gender. RESULTS/ANTICIPATED RESULTS: We expect that a distinct host transcriptional profile is associated with the development of HIV-specific antibody neutralization breadth in early life. DISCUSSION/SIGNIFICANCE OF IMPACT: Identifying immune cell transcriptional profiles associated with neutralization breadth will lead to more targeted vaccine approaches for eliciting the appropriate B cell responses and provide an invaluable screening tool allowing early identification of vaccine candidates with the potential to induce bnAbs.

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Markers of blood–brain barrier impairment and inflammation in CAA-ri

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OBJECTIVES/GOALS: Cerebral amyloid angiopathy-related inflammation (CAA-ri) is a spontaneous inflammatory cerebral vasculopathy that mimics complications of Alzheimer's disease immunotherapies. Our objective is to evaluate imaging and cerebrospinal fluid (CSF) markers of blood–brain barrier (BBB) impairment and inflammation in CAA-ri. METHODS/STUDY POPULATION: We plan to enroll 20 patients total: 1) 10 patients with CAA-ri as defined by Auriel et al (JAMA Neurology 2016) (exposure group). 2) 10 patients with non-inflammatory CAA defined using Boston criteria 2.0 that do not also meet criteria for CAA-ri (control group). The primary outcome will be Ktrans, a parameter of BBB impairment calculated from dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) of the brain. Secondary outcomes will include DCE-MRI parameter VL, CSF albumin index, CSF fibrinogen, CSF sPDGFR-β, CSF MMP-2, CSF MMP-9, CSF C3, CSF IL1β, CSF IL6, IL8, and TNFα. Statistical comparisons between the exposure and control groups will be made using Wilcoxon rank sum test. RESULTS/ANTICIPATED RESULTS: We anticipate significantly higher levels of BBB impairment and inflammatory biomarkers from DCE-MRI and CSF in subjects with CAA-ri relative to control subjects with non-inflammatory CAA. DISCUSSION/SIGNIFICANCE OF IMPACT: Biomarkers are essential to characterize risk factors, pathophysiology, and possible treatment targets in CAA-ri. We plan to use the results of the current study to inform longitudinal studies that will test whether these markers are useful in identifying not only the presence of CAA-ri but also severity, progression, and response to treatment.

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Female rats show a greater behavioral response to heroin across self-administration and locomotor sensitization compared to males

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OBJECTIVES/GOALS: Men and women with opioid use disorder (OUD) show differences in their initiation, use patterns, and outcomes that may have biological underpinnings. Here we present data directly comparing adult male and female rats across heroin-induced behaviors in order to provide insight into the nuances of sex differences in OUD. METHODS/STUDY POPULATION: We first used a 6-hour intermittent access heroin self administration paradigm to quantify six distinct drug-taking and drug-seeking behaviors. Based on the sum of the z-scores for each behavior, we classified rats as having high- or low-severity phenotypes. In a separate group of rats, we adapted this classification system to a 10-minute continuous access self-administration paradigm to better represent the timeframe of use common in people. Finally, we examined locomotor sensitization following daily heroin injections in two groups of rats. The first were given 2 mg/kg/day i.p. heroin for 10 days and the second were given 0.55 mg/kg/day i.v. heroin for 20 days. RESULTS/ANTICIPATED RESULTS: In the 6-hour intermittent access, both sexes showed variability across individuals, but a greater proportion of females were classified as having a high-severity phenotype compared to males. This difference in severity distributions was also found in the 1-hour continuous access experiment. Consistent with the literature, in our sensitization experiments, we found that males had a lower baseline level of locomotion compared to females. Across sex and route of administration, rats treated with heroin initially decreased locomotion, but returned to baseline over the course of treatment. Females given i.v. infusions showed a rapid escalation of locomotion past baseline that was not seen in males or following i.p. injections. DISCUSSION/SIGNIFICANCE OF IMPACT: Our results indicate a consistent pattern of females having a greater behavioral response to heroin compared to males. This suggests a sex-based effect on OUD that may interact with gender-based influences. As such, future research needs to consider sex in the development of treatments for OUD and other substance use disorders.

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scRNA seq analysis of lower respiratory tract immune cells to uncover immuno-endotypes in SA-PARDS

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OBJECTIVES/GOALS: This study aims to uncover immuno-endotypes in sepsis-associated pediatric acute respiratory distress syndrome (SA-PARDS) by using single-cell RNA sequencing (scRNA seq) to analyze the immune cell populations of the lower respiratory tract of intubated pediatric subjects with SA-PARDS. METHODS/STUDY POPULATION: Inclusion criteria are age less than 18 years, admission to the PICU, diagnosis of SA-PARDS, and intubation. Both sepsis and PARDS will be defined using the most recent consensus definitions. Exclusion criteria include an order of limited resuscitation and clinician discretion. After informed consent is obtained, a tracheal aspirate and blood sample will be obtained on days 1, 3, and 7. Both samples will be processed for single-cell RNA seq via the HIVE platform per manufacturer protocol. cDNA libraries will then be sent for 150 base pair paired-end sequencing. Sequences will be aligned to a reference genome, and count matrices will be generated. The Seurat package in R will be used for cell-type annotation and analysis of differential gene expression. Clinical variables, labs, and outcomes will be recorded in REDCap. RESULTS/ANTICIPATED RESULTS: We expect to find

https://doi.org/10.1017/cts.2024.1042