architecture underlying risk for CAA both in the context of significant AD pathology and without. Characterization of genetic variants and functional outcomes in the context of neuropathology may lead to new avenues of research aimed at identifying biomarkers and therapies to treat CAA

489

A retrospective analysis of varying thresholds of baseline lung allograft dysfunction in bilateral lung transplant recipients*

James McMenimen, Rodrigo Vazquez Guillamet, Ramsey Hachem, Jay Piccirillo, Tej Patel and Chad Witt
Washington University in St Louis

OBJECTIVES/GOALS: Baseline lung allograft dysfunction (BLAD) is defined as the failure to attain normal lung function after transplant and has been associated with impaired survival. BLAD has no consensus definition and assessment of varying thresholds of abnormality may identify an impact on survival or development of chronic lung allograft dysfunction (CLAD). METHODS/STUDY POPULATION: This is a retrospective cohort analysis of bilateral lung transplant recipients who were transplanted between 1/1/2012 and 12/31/2022 who have complete pulmonary function data posttransplant. Thresholds of BLAD including percent predicted levels of FEV1 and FVC at 80%, 75%, 70%, 65%, and 60% were assessed. Outcomes evaluated include survival, development of CLAD, and association of key risk factors with the development of BLAD including donor, recipient, operative, and postoperative characteristics. RESULTS/ANTICIPATED RESULTS: Totally, 680 bilateral lung transplant recipients were identified. Prevalence of BLAD ranged from 41.9% to 9.7% at specified thresholds. We anticipate performing survival analyses and evaluating development of CLAD in patients with BLAD at varying thresholds. We are assessing key donor, recipient, operative, and postoperative variables for association with BLAD. Preliminary analyses demonstrate significant associations of BLAD with recipient-donor height mismatch, prolonged mechanical ventilation time posttransplant, increased length of hospitalization posttransplant, the use of cardiopulmonary bypass intraoperatively and surgical allograft downsizing. DISCUSSION/SIGNIFICANCE OF IMPACT: A threshold of BLAD at 70% predicted FEV1 and FVC or lower suggests importance for developing CLAD. Key characteristics associated with BLAD suggest importance of height mismatch, operative complexity, frailty, and severity of disease at time of transplant and immediately postoperatively.

490

Characterizing water transfer rate in the young and elderly using diffusion prepared and multi-echo arterial spin labeling MRI

Yufei Zhu, Anjan Bhattarai, Barah Albuhwailah, Xingfeng Shao and Audrey Fan
University of California, Davis

OBJECTIVES/GOALS: Our study's overarching goal is to characterize the relationship between water transfer rate (Kw) across the blood–brain barrier (BBB) as measured by diffusion prepared (DP) and multi-echo (ME) ASL in two cohorts that have been shown to have regionally different water transfer rates due to underlying changes in BBB physiology. METHODS/STUDY POPULATION: Ten young, healthy participants (aged 21–30 years, 4f) and 12 elderly participants (aged 66–84 years, 8f) underwent MRI scans on a 3T Siemens Prisma scanner. Structural scans, along with DP and ME ASL, were acquired from each of the participants. The order of the DP and ME ASL sequences was reversed in half the participants to account for ordinal bias. FreeSurfer was used to segment the structural image into respective gray matter, white matter, and deep cortical gray regions to perform region of interest (ROI) analysis. RESULTS/ANTICIPATED RESULTS: We are still in the project's analysis phase. The anticipated result is that we will see different water transfer rate (Kw) patterns between the old and young groups and between the two sequence groups. DISCUSSION/SIGNIFICANCE OF IMPACT: The significance of the results is that we can answer two questions: 1) if there are any differences between water transfer rates in the two age groups and 2) whether there are any variations in performance differences between the sequences.

491

Safety and feasibility of transcranial magnetic stimulation in infants with perinatal brain injury: A step toward early clinical translation*

Kellie Collins[1], Cameron Casey[1], Ellen Sutter[1,2,3], Paige DeGrave[1], Danielle Gauthier[1], Ryan McAdams[3], Raghavendra Rao[4], Michael Georgieff[4], Bernadette Gillick[1,3,1] and Waisman
[1]University of Wisconsin Madison; [2]Department of Family Medicine and Community Health, University of Minnesota, Minneapolis, MN; [3]Department of Pediatrics, University of Wisconsin- Madison, Madison, WI, and [4]Department of Pediatrics, University of Minnesota, Minneapolis, MN

OBJECTIVES/GOALS: To determine the safety and feasibility of single-pulse transcranial magnetic stimulation (spTMS) for assessing corticospinal tract (CST) excitability and integrity in infants with perinatal brain injury, bridging foundational neuroscience to potential early diagnosis and clinical interventions during critical neuroplasticity periods. METHODS/STUDY POPULATION: Nineteen infants with perinatal brain injury underwent 1–3 spTMS sessions at three developmental time points: 3–6 months, 12 ± 1 month, and 18 ± 1 month. spTMS targeted the primary motor cortex to elicit motor-evoked potentials (MEPs), recorded via electromyography (EMG) from bilateral wrist flexor muscles. Safety monitoring included heart rate (HR), respiratory rate (RR), the Modified Behavioral Pain Scale (MBPS), and caregiver feedback. Feasibility was evaluated based on the ability to elicit MEPs, the number of trials that elicited MEPs, and procedure tolerability. Pre- and post-spTMS physiological and behavioral data were analyzed using linear mixed-effects models (LMEM) to account for repeated measures within subjects. RESULTS/ANTICIPATED RESULTS: Thirty-five spTMS sessions were conducted in 19 infants (mean age 8.75 ± 5.12 months) with perinatal brain injury, delivering 1936 pulses with a median inter-pulse interval of 24.7 seconds. Analysis with LMEM found no significant changes in HR (mean difference = 0.51 bpm, $p = 0.81$) or RR (mean difference = 0.69 breaths/min, $p = 0.66$). MBPS scores showed a small statistically significant increase (mean difference = 0.57, $p = 0.046$), but overall remained low (mean score change from 1.94 to 2.51 on 0–10 scale). The median change score was 0, and 18/35 sessions showed no change in MBPS, indicating low discomfort with TMS. No adverse events were reported during or after the sessions. The feasibility of eliciting MEPs in this population was confirmed, with 235 MEPs identified in 17/19 participants. DISCUSSION/SIGNIFICANCE OF IMPACT: Understanding neurodevelopment after injury is crucial for early diagnosis and targeted rehabilitation. Our study demonstrates that spTMS is a safe, feasible

https://doi.org/10.1017/cts.2024.1081

tool for assessing motor pathways in infants with early brain injury, highlighting its potential for clinical translation in neurodevelopmental disorders, and offering a pathway to improved care.

492

Characterizing clinical predictors of metabolic syndrome associated with second-generation antipsychotics in pediatric populations

Nihal El Rouby, Lisa J Martin, Leah C Kottyan, Cindy A Prows, Namjou-Khales, Jeffrey A Welge, Nancy Crimmins, Jeffrey R Strawn and Melissa P DelBello
University of Cincinnati

OBJECTIVES/GOALS: Second-generation antipsychotics (SGA) are used to treat mental disorders in youth but are linked metabolic syndrome (MetS). Most data on prescribing practices and risk factors are from short-term studies (6–12 months). We aim to characterize prescribing and identify clinical and genetic predictors of MetS using electronic health records (EHR). METHODS/STUDY POPULATION: EHR data were extracted from Cincinnati Children's Hospital Medical Center (CCHMC) for patients aged ≤21 years prescribed SGAs from 7/1/2009 and 7/1/2024, identifying prescribing prevalence. Next steps are to create an SGA-MetS case–control dataset 8 weeks after an SGA prescription. A case will be defined by meeting 3 of 5 criteria: 1) BMI ≥95th percentile for age/sex; 2) fasting glucose ≥100 mg/dL or use of anti-diabetics; 3) triglycerides ≥110 mg/dL; 4) HDL-C ≤40 mg/dL; 5) systolic/diastolic BP ≥90th percentile for age/sex or use of antihypertensives. The prevalence of SGA-MetS will be calculated by dividing SGA-MetS cases by total SGA users. Logistic regression will identify clinical predictors of MetS, and we will evaluate the association of polygenic risk scores (PRS) of BMI and type 2 diabetes with SGA-MetS risk. RESULTS/ANTICIPATED RESULTS: Our preliminary analysis identified 30,076 patients who were prescribed SGAs (mean age 12 years, SD = 4; 58.8% female; n = 17685). Most self-identified as non-Hispanic (95%, n = 28,595) and of White race (76%; n = 22,935), with 18.5% self-identifying as Black or African American (n = 5,579). The most commonly prescribed SGAs were risperidone (n = 12,382, 41.1%), aripiprazole (n = 9,847, 32.7%), and quetiapine (n = 5,263, 17.5%), with much lower prescribing rates of other SGA known of their low risk of MetS (e.g., ziprasidone 5.5%, lurasidone 1.4%, paliperidone (n = 316, 1.1%), or others cariprazine (n = 72), asenapine (n = 43), brexipiprazole (n = 39), iloperidone (n = 24), and clozapine (n = 20). DISCUSSION/SIGNIFICANCE OF IMPACT: Our analyses found that risperidone, quetiapine, and aripiprazole were the most prescribed SGA, with risperidone/quetiapine linked to a higher risk of MetS. We will present ongoing work identifying risk factors for SGA-MetS and examining the association with PRS. Our work has the potential to identify high-risk patients for personalized treatment.

495

DNA targeting autoantibody for brain tumor therapy*

Olivia Turk and James E. Hansen
Yale School of Medicine

OBJECTIVES/GOALS: Nucleoside transport by ENT2 facilitates transit of the lupus anti-DNA autoantibody Deoxymab into cells and across the blood–brain barrier into brain tumors. This work examines the Deoxymab-nucleoside interactions that contribute to membrane crossing and apply them in brain tumor therapeutics. METHODS/STUDY POPULATION: Deoxymab interactions with individual nucleosides, nucleobases, and pentose sugars are examined by surface plasma resonance (SPR) and cell penetration assays in a panel of cell lines including glioblastoma, breast cancer, and normal breast epithelial cells. Deoxymab-conjugated gold nanoparticles are generated and tested for binding to normal human astrocytes and glioma cells, and the impact of supplemental nucleosides on this binding is determined. Deoxymab-gold nanoparticles are tested for brain tumor localization by systemic and local administration in mice bearing orthotopic glioblastoma brain tumors and enhancement of laser interstitial thermal therapy (LITT) examined. RESULTS/ANTICIPATED RESULTS: Individual nucleosides significantly increase the efficiency of cell penetration by Deoxymab in all cell lines tested. In contrast, component nucleobases and pentose sugars significantly suppress the uptake of the autoantibody into cells. Deoxymab-conjugated gold nanoparticles bind DNA in vitro and to astrocytes in culture and are anticipated will enhance the efficacy if LITT in vivo by associating with DNA released by necrotic tumors and/or by locally administered nucleosides in brain tumor environments and subsequently act as heat sink to amplify LITT impact. DISCUSSION/SIGNIFICANCE OF IMPACT: Deoxymab is a DNA-targeting, cell-penetrating autoantibody. These findings establish nucleosides as the components of DNA that promote autoantibody membrane crossing through ENT2 activity and indicate potential for use of Deoxymab-gold nanoparticles in combination with LITT for brain tumor therapy.

496

The genetic risk assessment with mobile mammography (GRAMM) project: Providing genetic counseling referrals in tandem with mobile mammography for at-risk Black women

Versha Pleasant, Kiyah Mills, Audrey Widner, Kara J. Milliron and Sofia Merajver
University of Michigan

OBJECTIVES/GOALS: The overarching goal of the GRAMM study is to address racial health disparities by increasing access to genetic counseling and testing among the Black community. Specific objectives are to determine patient acceptability of risk assessment at time of mammography and to evaluate subsequent access to and uptake of genetic counseling and testing. METHODS/STUDY POPULATION: All women presenting for screening mammography at the Ypsilanti Health Center under the University of Michigan were invited to enroll. After providing written informed consent, study participants entered family cancer and personal health information in the InheRET software tool which links to the National Comprehensive Cancer Network genetic testing guidelines. Upon completion, each participant was informed immediately if they did or did not meet the criteria to meet with a genetic counselor. For those who met the criteria, referral to genetic counseling was provided. All enrollees were invited to complete a post-assessment survey on acceptability of the service and genetics knowledge. Patients will be followed over time for completion of genetic counseling and testing. The study was approved by the Umich IRB. RESULTS/

https://doi.org/10.1017/cts.2024.1081