(*Col1A1), tissue inhibitor of metalloproteinase 1* (*TIMP1),* or *α-smooth muscle actin (ACTA2*). CDAHFD and SD pHSCs were then treated for 48 hours with increasing doses of BMS-22 or MVC (range: 0.3-120ng/mL) to determine (1) the degree of attenuation of the pro-fibrogenic response as measured by qPCR of fibrogenic genes (*Col1A1, TIMP1, ACTA2);* (2) enhancement of a fibrolytic response as measured by qPCR of *matrix metalloproteinases (MMP*) *2, 9* and *13* genes*;* and (3) pHSC migration using the scratch assay. Cell viability and CCR2 and CCR5 gene expression in response to escalating doses of antagonists were also measured. RESULTS/ANTICIPATED RESULTS: Plate- and TGF-b activated CDAHFD pHSCs had a 2-fold greater, dose-dependent attenuation of their pro-fibrogenic activity in response to BMS-CCR2-22 and MVC, when compared with plate- and TGF-b activated SD pHSCs, as measured by reductions in collagen 1α1 (*Col1A1*) and α-smooth muscle actin (*ACTA2*) gene expression. *TIMP1* gene expression was unaffected by drug treatment for 48 hours. Cell viability was not affected up to doses of 30ng/mL of each drug. pHSCs also demonstrated a dose-dependent increase in *CCR2, CCR5* and *MMP-9* gene expression in response to surface receptor antagonism. Migration assays comparing CDAHFD and SD pHSCs in response to escalating doses of MVC and BMS-22 are ongoing and expected to demonstrate a significantly decreased migratory capacity of CDAHFD pHSCs than SD pHSCs in response to therapy, reflecting the increased susceptibility of the "fat-exposed" pHSCs to anti-fibrotic therapy than normal pHSCs. DISCUSSION/SIGNIFICANCE OF IMPACT: Anti-fibrotic drugs that dampen pro-fibrogenic activities of "fat-exposed" pHSCs are urgently needed. CCR2 and CCR5 antagonists, BMS-22 and MVC, respectively, can selectively dampen the pro-fibrogenic response of fat-exposed pHSCs, and must be considered for future trials in human NASH. CONFLICT OF INTEREST DESCRIPTION: Dr. Jill Smith has a patent licensing agreement with Immune Therapeutics, Inc.

4492

The role of creatine in developmental myelination and remyelination†

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OBJECTIVES/GOALS: Oligodendrocytes (OL) are glial cells of the central nervous system (CNS) responsible for the energy demanding task of generating myelin sheaths during development and remyelination after demyelinating injury. One metabolite shown to significantly increase ATP production in OL is the nitrogenous organic acid, creatine. Creatine plays an essential role in ATP buffering within tissues with highly fluctuating energy demands such as brain and muscle. Interestingly, mature OL, which are the cells capable of myelin production, are the main cells in the CNS expressing the rate-limiting enzyme for creatine synthesis, guanidinoacetate methyltransferase (*Gamt)*. Patients with mutations in *Gamt* display intellectual disabilities, impaired myelination and seizures. Therefore, we hypothesize that creatine may be essential for developmental myelination and improve remyelination. METHODS/STUDY POPULATION: To investigate these hypotheses, we developed a new transgenic mouse model with LoxP sites flanking exons 2-6 of the *Gamt* gene where excision leads to expression of a green fluorescent tag allowing us to track the cells normally expressing *Gamt.* RESULTS/ANTICIPATED RESULTS: In this mouse model, we show a 95% (±0.47%, n = 3) co-localization of *Gamt* within mature OL during postnatal (P) day P14. Next, we show that knocking out *Gamt* leads to a significant reduction in OL in the major CNS white matter tract, the corpus callosum, at P14 and P21 (P14: 0.007, n = 3; P21: 0.04, n = 3). Here, we also investigate whether dietary creatine can enhance remyelination in the cuprizone model of toxic demyelination. DISCUSSION/SIGNIFICANCE OF IMPACT: These studies highlight the important role creatine plays in developmental myelination and investigate whether creatine can provide a therapeutic value during a CNS demyelinating insult.

4362

The Utilization of Polyethylene Glycol Fusion to Improve Facial Reanimation†

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OBJECTIVES/GOALS: This study's goal is to determine whether intraoperative treatment of facial nerves with polyethylene glycol (PEG) fusion technology improves facial paralysis outcomes. Improved facial nerve regeneration in facial paralysis patients would lead to improved recovery time and effectiveness. METHODS/STUDY POPULATION: 30 rats were utilized; 15 underwent facial nerve regeneration without PEG fusion, and 15 with PEG fusion. Facial paralysis was initiated on the left by transection of the buccal and marginal mandibular branches of facial nerve. The buccal branch was repaired though microsuture technique. Neurorrhaphy sites of rats in the PEG group were exposed to calcium free saline, methylene blue, and polyethylene glycol. Nerve continuity was assessed post-operative in 5 animals in each group through electron microscopy. Functionality was assessed in the other 10 per group by EMG and whisker analysis after surgery, and weekly for 8 weeks. At 8 weeks, nerves and distal muscles were histologically analyzed. RESULTS/ANTICIPATED RESULTS: PEG fusion technology immediately restored axonal continuity following surgery, demonstrated by electron microscopy. Electrophysiology was also similarly restored across the site immediately, determined through intraoperative nerve stimulation, in the PEG fusion group. The nonintervention group showed dramatically reduced functional recovery than the PEG fusion group following surgery, shown by lower whisking activity and poor electrophysiology outcomes. Furthermore, the PEG fusion group showed statistically significant higher fascicle counts, myelination diameter, axonal diameter, and distal muscle fibers histologically. DISCUSSION/SIGNIFICANCE OF IMPACT: This study demonstrates that polyethylene fusion technology may improve facial reanimation outcomes. PEG is already a FDA-approved drug, and thus the pathway to translational clinical application of this work may thus be streamlined, bringing new options to patients with facial paralysis.

4431

Utilization of swept source optical coherence tomography to optimize characterization of cystoid macular edema in preterm infants

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OBJECTIVES/GOALS: The goal of this study is to evaluate and optimize the characterization of cystoid macular edema (CME) using an investigational swept source (SS)-OCT system. Our knowledge of

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CME in preterm infants is limited; optimizing its characterization is a critical step in understanding its impact on vision. METHODS/STUDY POPULATION: In this IRB-approved protocol, 118 preterm infants were imaged in the Duke intensive care nursery (ICN) with a novel lightweight, hand-held, high-speed, SS-OCT system following routine clinical eye exams. SS-OCT images were deidentified, automatically segmented using custom software (DOCTRAP), measured for several retinal layer thicknesses, and reviewed by masked expert graders for the presence and severity of CME. Reliability of SS-OCT measures will be assessed, and the association between CME status and retinal layer thicknesses will be calculated using logistic regression modeling. RESULTS/ANTICIPATED RESULTS: The prevalence of CME overall and by severity will be calculated. The distribution of several retinal layer thicknesses will be reported and compared by infant CME status and, when edema is present, by CME severity. Reproducibility and repeatability will be reported for objective variables, and intra-grader and inter-grader agreement will be reported for subjective variables. Multivariate logistic regression coefficients and odds ratios will be calculated for each retinal layer thickness variable. DISCUSSION/SIGNIFICANCE OF IMPACT: This study will use a novel SS-OCT system to identify retinal thickness measures that may be objective markers of CME status. This will refine the characterization of CME and provide a framework for correlating CME with functional outcomes like visual acuity. CONFLICT OF INTEREST DESCRIPTION: SC and CT have unlicensed patents on relevant technologies. CT receives royalties from Alcon and Hemosonics and consultation fees from EMMES.

4190

White Matter Integrity in Hemodialysis Patients

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OBJECTIVES/GOALS: The purpose of this study is to understand how hemodynamics during dialysis in End-Stage Renal Disease (ESRD) patients on hemodialysis (HD) affect white matter health and how those effects cause cognitive impairments. METHODS/STUDY POPULATION: We collected demographic data, comorbidities, intradialytic measurements of blood pressure and cerebral oximetry, cognitive measures in several domains using NIH Toolbox Cognition Battery, diffusion-weighted and anatomical MRIs for 20 participants on HD. Specific tracts were identified using tractography and were used to calculate the average DTI measurements in each tract. Regression analysis was used to examine the relationship between mean DTI measurements of white matter integrity and cognitive performance scores. In addition, we compared diffusion MRI and T1 anatomical images of 16 healthy age-matched controls from a previous study. RESULTS/ANTICIPATED RESULTS: In our cohort 18 participants had imaging data that could be used in the analysis. We found widespread decreases in DTI white matter integrity compared to healthy age-matched controls, mean whole-brain fractional anisotropy was .3218 in the HD cohort and .3472 in controls $p = .0018$. Decreased integrity was found in most of the tracts identified but more decreased in tracts implicated in cognition. Partial regression analysis identified significant relationships between the white matter integrity of the left superior longitudinal fasciculus and overall fluid cognitive performance, $R = .5525$, $p = .0174$ before multiple comparisons correction when controlling for differences due to age. DISCUSSION/SIGNIFICANCE OF IMPACT: We found a widespread decrease in white matter integrity and significant correlations between cognitive performance and specific tract integrity in our HD cohort using regions identified by tractography imaging analysis. This analysis shows that HD patients have decreased white matter health and identifies several tracts that are important for cognitive performance in HD patients.

Precision Medicine

4228

A latent class analysis of seriously ill adults with multiple chronic conditions receiving palliative care

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OBJECTIVES/GOALS: The purpose of this secondary data analysis was to identify latent subgroups of seriously ill adults based on multiple chronic conditions and mortality risk using the CCI. This study was conducted by performing a secondary analysis of data from a randomized controlled trial of seriously ill patients receiving palliative care. METHODS/STUDY POPULATION: A cross-sectional analysis of baseline CCI data was conducted. 381 seriously ill adults receiving palliative care were in the original study. Latent subgroups were identified based on the CCI by conducting a latent class analysis in MPlus. The LCA was modeled on each of the 19 disease items as binary latent predictor variables, an additional binary variable representing presence of any disease not accounted for by the CCI, and a final categorical variable representing the total CCI score divided based on clinically significant cutoffs including zero, low (>=1-<2), moderate (>=2-<5), and high CCI (>=5). RESULTS/ANTICIPATED RESULTS: Three distinct latent subgroups were identified based on the CCI. Latent subgroup 1 included those with a low-moderate CCI consisting of MCC and non-Metastatic Cancers (n = 178), with 45% of this group having chronic obstructive pulmonary disease. The second two subgroups included individuals with a high CCI or a score greater than or equal to 5. Latent subgroup 2 (n = 64) was comprised of individuals with MCC and non-metastatic cancer. Latent subgroup 3 (n = 139) included individuals with metastatic cancer. DISCUSSION/SIGNIFICANCE OF IMPACT: In a sample of seriously ill adults with MCC, latent subgroups were identified consisting of individuals with low, moderate, or high CCI. The low to moderate CCI group consists of individuals with chronic conditions including COPD, congestive heart failure, myocardial infarction, cardiovascular disease. There were two subgroups with high CCI scores and the differentiating factor between the two subgroups was the presence of metastatic cancer in latent subgroup 3. The identification of latent subgroups sets the groundwork for further analyses to compare differences in symptom burden, quality of life, and functional status between groups. The findings have the potential to inform future studies seeking to better characterize seriously adults with MCC based on their disease burden and mortality risk.

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