344

Polymer nanoparticles improve motor function after spinal cord injury in an injury severity-dependent manner*

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OBJECTIVES/GOALS: Previous studies of nanoparticles in a penetrating spinal cord injury demonstrated their ability to modulate immune responses to reduce secondary injury. This study investigated nanoparticles in contusion injury models, which is more common clinically, to quantify their efficacy as a function of injury severity. METHODS/STUDY POPULATION: Female C57BlJ/6 mice were anesthetized, and a T9/T10 laminectomy was performed to expose the spinal cord. A stereotactic setup with an Infinite Horizon impactor was used to position the spinal cord to receive a mild (30 kdyne), moderate (50 kdyne), or severe (70 kdyne) contusive injury. Within two hours of injury, poly(lactide-co-glycolide) nanoparticles, formed via a single emulsion with sonication protocol, or phosphate-buffered saline (PBS) vehicle were injected intravenously via tail vein injection. Nanoparticles (NPs) or PBS were administered daily for 7 days. Function was evaluated using the Basso Mouse Scale (BMS) test for hind limb function starting 3 days post-injury and repeated weekly thereafter, as well as a horizontal ladder beam test once they had recovered to at least occasional plantar stepping. RESULTS/ANTICIPATED RESULTS: In the moderate injury group, NP-treated mice had significantly higher BMS scores starting 6 weeks post-injury ($p=0.009$), with the NP-treated mice performing better than control to the end of the study. In the mild injury group, NP-treated mice scored significantly better on BMS starting at 3 days post-injury ($p=0.005$). This difference persisted through week 4, and then the vehicle-treated mice maintained a slightly lower score through the end of the study. In the severe injury group, no significant difference on BMS scores was observed between groups and animals did not recover enough function to be evaluated via ladder beam. Scoring of the ladder beam test for moderate and mild injury studies is underway. Animals treated with NPs are anticipated to have a significantly higher number of successful steps compared to control. DISCUSSION/SIGNIFICANCE OF IMPACT: Spinal cord injury consists of a primary injury and secondary injury caused by inflammation at the injury site. Nanoparticles present an opportunity to reduce secondary injury to improve functional outcomes of individuals with SCI. This study of NPs in a graded severity contusion model further illustrates the feasibility and utility of NPs in SCI.

345

Mammographic breast arterial calcifications in males

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OBJECTIVES/GOALS: Common mamographic findings, breast arterial calcifications (BAC), are a sex-specific biomarker for cardiovascular disease in women. While less common, BAC is frequently encountered on mammograms in males. This study aims to investigate BAC and its association with cardiovascular risk factors in men. METHODS/STUDY POPULATION: A retrospective single-institution study of male patients with mammography studies was performed between September 1, 2018, and September 3, 2025. Diagnostic mammographic images of male patients from a high-volume breast imaging facility were evaluated for the presence of BAC. BAC severity will be assigned a score based on the Canadian Society of Breast Imaging's grading system. Unique ICD-10 diagnosis codes from the electronic medical record that have been established as independent risk factors for cardiovascular disease will also be reviewed. Male patients who have a prior history of myocardial infarction, coronary revascularization, stroke, heart failure, peripheral vascular disease, breast cancer, dementia, or chronic dialysis/renal transplant were excluded. RESULTS/ANTICIPATED RESULTS: The study is in process of pulling male mammograms from our institution. Current volume of male mammograms at the institution is about 160 male mammograms performed per month. Therefore, we anticipate having around 13,600 male mammograms to analyze the BAC presence. Anticipated results include that patients with independent cardiovascular risk factors such as increased systolic blood pressure, increased LDL levels, and current smokers will have a higher prevalence of BAC presence. Additionally, those with a presence of BAC will be older compared to those that have an absence of BAC on mammography. If BAC is shown to be a significant risk factor for the development of cardiovascular disease, perhaps a mammogram might be recommended in men purely for cardiovascular risk assessment. DISCUSSION/SIGNIFICANCE OF IMPACT: A significant association between the presence of BAC and CVD risk factors may provide a supplementary assessment of CVD risk among men, offering a novel tool for risk stratification. Implementing a standardized BAC reporting model may allow for earlier identification of asymptomatic patients at high risk for adverse cardiac events.

346

Developing standardized, neurophysiologically informed EEG neurofeedback protocols: A translational neuroscience approach

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OBJECTIVES/GOALS: EEG neurofeedback is a promising neuromodulation approach for improving mental health outcomes but lacks standardized, neurophysiologically-grounded treatment protocols. This study uses high-density EEG (hdEEG) analyses to identify neural network patterns that inform development of evidence-based pediatric neurofeedback protocols. METHODS/STUDY POPULATION: This translational neuroscience project leverages resting-state hdEEG data and behavioral assessments from 600 six-year-old children in the Beginnings study (Arkansas Children's Research Institute; Andres, NCT00616395). Analyses will identify functional

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and effective connectivity patterns across major brain networks – Default Mode (DMN), Salience (SN), and Central Executive (CEN) – using graph theoretical metrics, phase-locking values, and multivariate analyses. Identified network patterns will be linked with neuropsychological measures, including the Child Behavior Checklist (CBCL), to inform development of standardized neurofeedback protocol recommendations grounded in developmental neuroscience. RESULTS/ANTICIPATED RESULTS: We anticipate identifying distinct patterns of functional connectivity that predict variation in children's emotional and behavioral functioning. Findings are expected to highlight network patterns – particularly within emotion regulation and executive control circuits – that can guide neurofeedback protocol design. Anticipated products include neurophysiologically informed recommendations for standardized frequency bands, target networks, and protocol parameters to support future clinical trial development. This project represents a key T1 translational step toward establishing a neuroscience-based framework for EEG neurofeedback treatment protocols. DISCUSSION/SIGNIFICANCE OF IMPACT: By integrating neurophysiological and behavioral data to guide protocol development, this work addresses a critical translational gap in the EEG neurofeedback literature. Findings will establish a foundation for standardized, evidence-based neurofeedback interventions that could improve accessibility and efficacy in clinical settings.

351

From pixels to pathology: Excitation-scanning hyperspectral imaging for rapid colorectal cancer detection

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OBJECTIVES/GOALS: Colorectal cancer (CRC) disproportionately affects the U.S. Deep South. Socioeconomics, genetics, and healthcare access contribute to increased incidence and mortality. A next-generation endoscope with improved contrast and automatic detection may boost early detection and narrow expertise gaps between top centers and rural clinics. METHODS/STUDY POPULATION: We implemented excitation-scanning hyperspectral imaging (Ex-HSI) to discriminate normal and cancerous mouse colorectal tissues by detecting changes in autofluorescence. Ex-HSI permits detection of all emitted light above a cutoff wavelength. Ex-HSI reduces acquisition time and improves signal-to-noise ratio compared to traditional emission scanning. We used azoxymethane/dextran sodium sulfate (AOM/DSS) to induce colitis and nodule formation in the mouse CRC model. Ex-HSI data was complemented with transmitted light and confocal images. Histology sectioning with H&E staining was obtained for "gold standard" validation. RESULTS/ANTICIPATED RESULTS: Inflammation and bleeding were observed, consistent with AOM/DSS treatment. Nodules were visible using 4x and 20x objectives. Background-subtracted Ex-HSI data was corrected to a flat spectral response. Excitation spectra were extracted from select regions within each field of view. Excitation spectra displayed multiple peak excitation wavelengths, suggesting multiple autofluorescent molecules present. Further investigation will utilize spectral unmixing, principal component analysis, and neural networks to interpret image data. DISCUSSION/SIGNIFICANCE OF IMPACT: A hyperspectral endoscope that detects early-stage cancers and precancers would enhance CRC screening in the Deep South. This research is supported by NIH P01HL066299, NIH UL1TR00141, S10RR027535, S10OD02860, NSF MRI1725937, CCTS T32TR004767, and the Center for Lung Biology, University of South Alabama.

352

Macrophage regulation of inflammation in type 2 diabetes

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OBJECTIVES/GOALS: Type 2 diabetes is a metabolic disease characterized by non-resolving inflammation. Our objective is to investigate how macrophages contribute to this dysregulation. We hypothesize that diabetic macrophages have impaired response mechanisms and are more sensitive to metabolic flux, limiting their ability to effectively resolve inflammation. METHODS/STUDY POPULATION: To study this, we isolated and cultured bone marrow-derived macrophages from WT and db/db mice *in vitro* and stimulated them with maturation, inflammatory, and resolving cues. We also isolated human monocytes from PBMCs from patients with type 2 diabetes and age-matched healthy controls and stimulated them *ex vivo* and cultured them *in vitro*. We assessed their timeline of maturation through changes in cell surface markers, their functional inflammatory response through phenotypic marker changes and cytokine release, and their sensitivity to metabolic flux by culturing in the presence or absence of extracellular glutamine. Together, these responses can allow us to understand intrinsic defects in diabetic macrophages' ability to regulate inflammation. RESULTS/ANTICIPATED RESULTS: Notably, diabetic and healthy macrophages display distinct maturation timelines. Overall, diabetic macrophages lag behind healthy macrophages in expression of CD45 and F4/80 but eventually acquire a similar level of mature cell surface markers by day 7-8 in culture. In addition, diabetic cells have a higher proportion of Ly6Chi cells earlier in culture, cells that are generally more poised to be pro-inflammatory. Both healthy and diabetic mature macrophages displayed similar levels of inflammatory response cytokines, inflammatory gene expression changes, and phenotypic marker expression. Interestingly, stimulating these macrophages in the absence of glutamine revealed underlying impairments in their response to inflammatory and resolving cues. DISCUSSION/SIGNIFICANCE OF IMPACT: Patients with diabetes suffer significant complications, such as susceptibility to infections and non-healing wounds, driven by impairments in resolution of inflammation. This research begins to explore the cell-mediated inflammatory aberrations in type 2 diabetes and may reveal targetable mechanisms to improve patient outcomes.

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