ANTICIPATED RESULTS: There was no observed difference in treated (n=20) versus placebo (n=12) longitudinal trends in trypsin levels when compared to baseline levels. However, responders to immunotherapy (n=4) had 6 month trypsin levels that were 114% of baseline whereas placebo subject 'responders' (n=2), placebo subjects (n=10), and non-responders to immunotherapy (n=15) had trypsin levels that were 81-93% of baseline (unpaired T test p=0.05). Overall, we found that serum trypsin, a marker of exocrine pancreatic function, had a normal upward trend in new-onset T1D subjects who responded clinically to immunotherapy but declined in subjects who did not respond or who were not treated. These results were bordering on statistical significance but did not reach significance, likely due to the small sample size. DISCUSSION/SIGNIFICANCE: An improvement in trypsin, a marker of exocrine function, after response to immunotherapy in new-onset T1D may be due to a direct impact on exocrine function versus an indirect effect from improved beta cell function. Future studies will be needed to confirm our findings in a larger sample and evaluate the mechanism for improved exocrine function.

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Machine Learning Segmentation of Amyloid Load in Ligamentum Flavum Specimens From Spinal Stenosis Patients†

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OBJECTIVES/GOALS: Wild-type transthyretin amyloid (ATTRwt) deposits have been found to deposit in the ligamentum flavum (LF) of spinal stenosis patients prior to systemic and cardiac amyloidosis, and is implicated in LF hypertrophy. Currently, no precise method of quantifying amyloid deposits exists. Here, we present our machine learning quantification method. METHODS/STUDY POPULATION: Images of ligamentum flavum specimens stained with Congo red are obtained from spinal stenosis patients undergoing laminectomies and confirmed to be positive for ATTRwt. Amyloid deposits in these specimens are classified and quantified by TWS through training the algorithm via user-directed annotations on images of LF. TWS can also be automated through exposure to a set of training images with user- directed annotations, and then application to a set of new images without additional annotations. Additional methods of color thresholding and manual segmentation are also used on these images for comparison to TWS. RESULTS/ANTICIPATED RESULTS: We develop the use of TWS in images of LF and demonstrate its potential for automated quantification. TWS is strongly correlated with manual segmentation in the training set of images with user-directed annotations ($R = 0.98$; $p = 0.0033$) as well as in the application set of images where TWS was automated ($R = 0.94$; $p = 0.016$). Color thresholding was weakly correlated with manual segmentation in the training set of images ($R = 0.78$; $p = 0.12$) and in the application set of images ($R = 0.65$; $p = 0.23$). DISCUSSION/SIGNIFICANCE: Our machine learning method correlates with the gold standard comparator of manual segmentation and outperforms color thresholding. This novel machine learning quantification method is a precise, objective, accessible, high throughput, and powerful tool that will hopefully pave the way towards future research and clinical applications.

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An intracranial EEG map of naturalistic images in the human brain*

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OBJECTIVES/GOALS: Our overall goal is to identify the processes used by the human visual system to encode visual stimuli into perceptual representations. In this project, our objective is (i) to collect a dataset of human neural activity in response to 1000 naturalistic color images and (ii) to determine how image parameters drive different parts of the human brain. METHODS/STUDY POPULATION: We recorded iEEG data in 4 human subjects who had been implanted for epilepsy monitoring. Each subject was presented 10 sets of 100 naturalistic stimuli, taken from the Natural Scenes Dataset (Allen et al., 2021), on a screen for 1 second each with 1 second rest intervals between stimuli. The subjects were instructed to fixate on a red dot at the center of the screen and were prompted to recall whether they had seen 3 additional test stimuli at the end of each set to encourage attentiveness. We calculated significant neural responses at each electrode by comparing evoked potentials and high frequency power changes during each stimulus vs. rest. Electrodes with significant responses were then mapped to anatomic locations in each subjects brain and then collectively to a standard brain. RESULTS/ANTICIPATED RESULTS: The natural image set elicited significant evoked potentials and high frequency responses at electrodes in each subject. Response latencies, from 80 to 300 ms after stimulus onset, portrayed the evolution of visual processing along the visual pathways, through key sites such as the early visual cortex, ventral temporal cortex, intraparietal sulcus, and frontal eye field. These responses differed significantly from those elicited by simple patterns, which drove early visual cortex but less so in later regions. DISCUSSION/SIGNIFICANCE: These data show that the human brain responds differently to more complex images. Determining the human brains response to naturalistic images is essential for encoding models that describe the processing in the human visual system. These models may further future efforts for electrical neurostimulation therapies such as for restoring vision.

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Brain-derived Extracellular Vesicles: A Novel Biomarker of CNS Metals Load with Applications in Identifying Neurodegenerative Diseases

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OBJECTIVES/GOALS: This study aims to develop a method to examine whether blood-borne CNS-EV metal cargoes can serve as reliable biomarkers of CNS metal load and reveal a link between metal load and ALS development (i.e., neurodegenerative disease development). METHODS/STUDY POPULATION: CNS-EVs were

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isolated from human blood and plasma samples via direct immunoprecipitation using biotinylated antibodies for proteins known to be expressed in neurons (Contactin-2, i.e.) and astrocytes (glial-glutamate-aspartate-transporter, i.e., GLAST). Once isolated, protein concentrations in the EV samples were analyzed via ELISA assay, EV abundance was measured using ViewSizer Nanoparticle Tracking analysis, and EVs were visualized via Transmission Electron Microscopy. EVs were then analyzed for metal contents using a Perkin-Elmer NexION 350S via an ICP-MS/MS dynamic reaction cell method. RESULTS/ANTICIPATED RESULTS: Preliminary results demonstrate that it is feasible to quantify the metal contents of these CNS-derived EVs, particularly in terms of toxic metals known to be associated with neurodegenerative disorders, including copper, zinc, lead, aluminum, manganese, and iron. DISCUSSION/SIGNIFICANCE: CNS-derived EVs isolated from peripheral blood draws show promise as a potential biomarker of real-time metal load in the brain and spinal cord, with promising applications in predicting future development of neurodegenerative disorders (i.e., ALS) among patients with relevant elevated CNS metal loads.

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Interest in and Perceived Effectiveness of Contingency Management Among Alcohol Drinkers Using Behavioral Economic Purchase Tasks*,†

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OBJECTIVES/GOALS: The purpose of this study was to develop behavioral economic purchase tasks to assess interest in CM as a function of treatment cost and perceived effectiveness of CM as a function of abstinence incentive size in alcohol drinkers. Additionally, these purchase tasks are being assessed for their clinical utility in an ongoing clinical trial. METHODS/STUDY POPULATION: Alcohol drinkers recruited from Amazon Mechanical Turk completed behavioral economic purchase tasks measuring demand for CM based on targeted abstinence intervals and treatment effectiveness and alcohol use disorder severity assessments. Nonlinear mixed effects modeling was used to fit demand curves and assess the relationship between individual characteristics and demand metrics for CM. Ongoing analyses involve administering the same behavioral economic purchase tasks in heavy alcohol users in the ongoing clinical trial, which is aimed at reducing alcohol use through remotely implemented CM. RESULTS/ANTICIPATED RESULTS: Mechanical Turk participants reported higher probability of abstinence when offered larger incentives and required larger incentives when duration of abstinence required to earn the incentive was increased. Additionally, willingness to pay for treatment increased as effectiveness of treatment increased. It is anticipated that these patterns will be observed in the clinical trial participants. DISCUSSION/SIGNIFICANCE: Abstinence interval and treatment effectiveness are important features to consider when developing effective CM for widespread use, as these variables affected participants likelihood of being abstinent and their interest in treatment. We are currently working on verifying the results of these assessments in clinical trial participants.

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Resting state fMRI connectivity in individuals with aphasia and the role of the inferior frontal gyrus

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OBJECTIVES/GOALS: This poster will explore lesion-symptom mapping and resting state functional magnetic resonance imaging (rsfMRI) in participants with aphasia. This analysis aims to reveal the behavioral impact of distinct lesions to the left inferior frontal gyrus (LIFG) and the potential for rsfMRI to provide evidence of cortical reorganization. METHODS/STUDY POPULATION: The analyses will be conducted on a small sample of approximately six participants with post-stroke language impairment (i.e., aphasia) recruited as part of an ongoing study. Lesion load in the anterior LIFG (aLIFG), consisting of the orbital (BA 47) and triangular (BA 45) parts, and the posterior LIFG (pLIFG), consisting of the opercular part (BA 44) will be correlated with performance on tasks of semantic and phonological processing. Functional connectivity will be determined between regions of interest (i.e., anterior superior temporal, posterior middle temporal, angular, and supramarginal gyri) in the left and/or right hemispheres based on rsfMRI data. RESULTS/ANTICIPATED RESULTS: Lesion load in the aLIFG is expected to correlate to performance on the semantic task, whereas lesion load in the pLIFG is expected to correlate to performance on the phonological task. For participants whose behavioral performance exceeds expectations based on lesion load (e.g., larger aLIFG lesion load, yet better semantic task performance), rsfMRI connectivity is expected to be greater (e.g., between the posterior middle temporal and angular gyri), suggesting cortical reorganization. DISCUSSION/SIGNIFICANCE: If our hypotheses are supported, our results will corroborate evidence of a functional spectrum (i.e., semantic-phonological) in the LIFG. Future work will compare rsfMRI connectivity to neurotypical controls and sites of connectivity may be used as targets in studies of non-invasive brain stimulation as an adjuvant to behavioral therapy.

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Investigating the Architecture of Speech Processing Pathways in the Brain

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OBJECTIVES/GOALS: Speech production requires mapping between sound-based and motor-based neural representations of a word – accomplished by learning internal models. However, the neural bases of these internal models remain unclear. The aim of this study is to provide experimental evidence for these internal models in the brain during speech production. METHODS/STUDY POPULATION: 16 healthy human adults were recruited for this electrooculography speech study. 20 English pseudowords were designed to vary on confusability along specific features of articulation (place vs manner). All words were controlled for length and voicing. Three task conditions were performed: speech perception,

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