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.

340

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.

341

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.

343

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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