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.

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.

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...