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Classification of Retinal TDP-43 and Amyloid beta Deposits as Biomarkers of Differing Neurodegenerative Diseases

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Introduction: We have used polarized light to image and differentiate protein deposits as biomarkers of different neurodegenerative diseases and their severity; including amyloid deposits in Alzheimer's disease (AD) and alpha synuclein deposits found in other brain diseases. Here we differentiate, with polarized light, retinal deposits of amyloid beta, associated with AD, from TDP-43 deposits found in the neurodegenerative diseases Frontotemporal Lobular Dementia (FTLD) and Amyotrophic Lateral Sclerosis (ALS). Our retinal imaging could be the first differential diagnostic of neurodegenerative diseases.
Methods: Post-mortem eyes and brains were obtained from 2 individuals with ALS, including 1 who also had FTLD, and 4 individuals with only FTLD, including 1 with Type C. Brain TDP-43 was present, except in the ALS case and some had brain age-related tau. 10 individuals had brain amyloid beta and tau and a moderate to high likelihood of AD. Flat-mounted retinas were imaged using a polarimeter. Polarimetric properties of deposits were analyzed for 270 presumed amyloid beta deposits in those with AD, and 138 presumed TDP-43 deposits in those with FTLD and/or ALS. In 1 case of ALS with concurrent low values of brain amyloid and 1 of FTLD-Type C, only thioflavin negative deposits were classed as potential TDP-43 deposits. Random forest, an ensemble learning method, was then used to differentiate amyloid beta from TDP-43 deposits.
Results: Thioflavin positive deposits in the retina with FTLD type C had interactions not different from AD deposits, consistent with a recent report of protein fibrils which combine TDP-43 and the amyloid protein ANXA11. The deposit means and/or standard deviations of nine different polarized light interactions were significantly different between the other TDP-43 retinal deposits, found in ALS and FTLD, and amyloid deposits found in AD. We achieved a classification accuracy of 83.9± 0.5% using random forest and utilizing only 6 of these interactions.
Conclusions: Polarized light imaging can differentiate retinal deposits associated with Alzheimer's disease from those linked to ALS and FTLD, with a relatively high accuracy. This first differential diagnostic of Alzheimer's disease from TDP-43 related diseases, is early, non-invasive and inexpensive and would reach underserved populations.

Keyword-1

neurodegenerative diseases

Keyword-2

biomarkers

Keyword-3

retinal protein deposits

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