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Retinal protein deposits identified using polarized light, as biomarkers of multiple neurodegenerative brain diseases

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Introduction: We have previously demonstrated, using polarized light, that we can image amyloid protein deposits in the retina without a dye. Postmortem, their numbers predict the load of amyloid in the brain and severity of Alzheimer's disease (AD). Here we differentiate retinal deposits of presumed amyloid beta, associated with AD, from presumed retinal deposits of alpha synuclein, associated with two other neurodegenerative diseases (multiple system atrophy, MSA and dementia of Lewy bodies, DLB). We also image precursors to these deposits.
Methods: Eyes and brains were obtained post-mortem in compliance with the Declaration of Helsinki from 10 donors with AD, and from 2 donors with MSA or DLB in whom alpha synuclein had been found in the brain. Individuals with multiple post-mortem brain pathologies were excluded from this study. Eyes were fixed in 10% formalin. Retinas were stained with 0.1% Thioflavin-S and counterstained with DAPI, flat mounted in quadrants and imaged using a microscope, custom fitted with a polarimeter. In each subject, deposits found in association with the neural retina as well as the surrounding retinal area were imaged. For each imaged region, 10 polarized light interactions were examined. The presence of interactions with polarized light was measured both in the deposits and surrounding tissue.
Results: Although their size distributions overlapped, retinal deposits were significantly smaller in retinas in which amyloid beta deposits were expected, compared with the size of the presumed alpha synuclein deposits. After correction for repeated measures, the averages and standard deviations of four polarimetric properties differed significantly between the presumed amyloid deposits and the presumed alpha synuclein deposits. Using machine learning (random forest and convolutional neural networks), we were able to separate the two deposit types with accuracies of >85%. Interactions with circularly polarized light were also detected.
Conclusions: Interactions with polarized light can separate deposits in the retina due to Alzheimer's disease from those due to diseases with alpha synuclein pathology (MSA and DLB), early in the disease. Polarized light also detects two circular signals which are presumed to be precursors to deposits. These findings could lead to earlier and simpler diagnosis and differentiation of multiple brain diseases.

Keyword-1

polarized light imaging

Keyword-2

retinal biomarker

Keyword-3

brain disease diagnostic

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