

Alzheimer's disease in the retina: imaging retinal A β plaques for early diagnosis and therapy assessment.

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Abstract

BACKGROUND: Definite Alzheimer's disease (AD) diagnosis at early stages is vital for targeting intervention, yet currently unavailable. Noninvasive detection of the pathological hallmark, amyloid- β protein (A β) plaques, is limited in the brain. However, the existence of A β plaques in the retina, possibly at presymptomatic stages, may improve early detection of AD.

OBJECTIVE: To summarize clinical and preclinical evidence showing that the retina, an accessible part of the central nervous system, displays abnormalities in AD, especially A β plaque pathology. The ability to monitor in vivo retinal plaque dynamics in response to immunotherapy is also assessed.

METHODS: Literature analysis of retinal AD pathology and imaging is provided. In our studies, systemic curcumin is administered to enable monitoring of retinal A β plaques in live APP(SWE)/PS1(Δ)(E9) transgenic mice by optical imaging.

RESULTS: Visual and retinal abnormalities, including early manifestation of retinal A β plaque pathology, have been documented in AD patients and animal models. In mouse models, retinal A β plaques accumulate with age and decrease in response to immunotherapy, consistent with brain pathology. Here, we demonstrate that retinal plaques can be individually monitored in real time following glatiramer acetate immunization.

CONCLUSION: Translation of noninvasive retinal-plaque imaging to humans could eventually facilitate early and accurate AD diagnosis and therapy assessment.

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Identification of amyloid plaques in retinas from Alzheimer's patients and noninvasive in vivo optical imaging of retinal plaques in a mouse model.

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Abstract

Noninvasive monitoring of β -amyloid (A β) plaques, the neuropathological hallmarks of Alzheimer's disease (AD), is critical for AD diagnosis and prognosis. Current visualization of A β plaques in brains of live patients and animal models is limited in specificity and resolution. The retina as an extension of the brain presents an appealing target for a live, noninvasive optical imaging of AD if disease pathology is manifested there. We identified retinal A β plaques in postmortem eyes from AD patients (n=8) and in suspected early stage cases (n=5), consistent with brain pathology and clinical reports; plaques were undetectable in age-matched non-AD individuals (n=5). In APP(SWE)/PS1(Δ E9) transgenic mice (AD-Tg; n=18) but not in non-Tg wt mice (n=10), retinal A β plaques were detected following systemic administration of curcumin, a safe plaque-labeling fluorochrome. Moreover, retinal plaques were detectable earlier than in the brain and accumulated with disease progression. An immune-based therapy effective in reducing brain plaques, significantly reduced retinal A β plaque burden in immunized versus non-immunized AD mice (n=4 mice per group). In live AD-Tg mice (n=24), systemic administration of curcumin allowed noninvasive optical imaging of retinal A β plaques in vivo with high resolution and specificity; plaques were undetectable in non-Tg wt mice (n=11). Our discovery of A β specific plaques in retinas from AD patients, and the ability to noninvasively detect individual retinal plaques in live AD mice establish the basis for developing high-resolution optical imaging for early AD diagnosis, prognosis assessment and response to therapies.

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