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Study Group: Vision Group

ABSTRACT

TITLE: Subretinal Aβ injections induce a localised, early CNV phenotype in C57BL/6 mice
ABSTRACT BODY:
Purpose: Amyloid β (Aβ) is associated with clinical hallmarks of Age-related macular degeneration (AMD), yet its potential role in AMD pathogenesis remains unknown. The purpose of this study was to test Aβ induced morphological/functional changes to the outer retina in situ by conducting non-invasive retinal imaging techniques in a mouse model.
Methods: Female C57BL/6 mice aged 117±4 days were subject to subretinal injection with 1.5µl 625nM human oligomeric $A\beta_{1-42}$(n=7), sham(n=6) or 625nM BSA(n=5). At 8 and 15 days post injection full-field electroretinography (ffERG) and optical coherence tomography (OCT) were performed to assess treatment effects compared to baseline. Scotopic ffERGs were conducted by stimulation with 1.5mm diameter, 6.8 cd-s/m^2 white LED light for 1ms in 2 sweeps with a 120s interval, from which average A-wave and B-wave amplitudes, and T(A) and T(B) implicit times were calculated. OCT images were acquired as 1.4mm volumetric scans (100 B-scans comprising 1000 A-scans). Scans were segmented at 24 locations using the InVivoVue 2.4 Diver software for Inner segments (IS), Outer segments (OS), Photoreceptor end tips (ETPRS) and the RPE, to assess treatment effects on layer thickness. One-way ANOVA with Tukey's post hoc test assessed statistical comparisons with individual mice as the statistical unit. Data is presented as mean ± SEM.
Results: Localised subretinal hyperreflective exudation (SHE) and subretinal hyper-reflective material (SHRM) were evident in OCT scans after $A\beta_{1-42}$ and BSA treatment at 8 and 15 days, with SHE/SHRM reduction associated with subretinal cystic spaces on day 15. No significant difference was seen in global thickness of the IS(p=0.46,p=0.80), OS(p=0.97,p=0.81), ETPRS(p=0.95,p=1.0) or RPE(p=0.95,p=0.28) compared to sham at 8 and 15 days respectively. Similarly, ffERGs saw no significant difference in the A-wave(p=0.94,p=1.00), B-wave(p=0.87,0.89), T(A) (p=0.43,p=0.19) and T(B) (p=0.94,p=0.82) between Aβ and sham at 8 and 15 days.
Conclusions: Aβ exposure induced pathology consistent with an early-CNV phenotype. However, this did not translate to a global reduction in IS, OS, ETPRS or RPE thickness, or retinal function, likely due to the localised nature of pathology observed. Nonetheless, our findings suggest a pro-angiogenic role for Aβ, where cumulative damage over time may cause statistically significant thickness/functional deficits.
(No Image Selected)

DETAILS

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AFFIRMATIONS

Affirmations: Affirmation that submission of this abstract has been approved by the Principal Investigator.
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