Ultra-reflectivity as a novel ocular biomarker in mice models of Parkinson's and Alzheimer's diseases

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#ocularbiomarker #OCT #PD #AD #ultrareflectivity, #WomeninSTEM

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Abstract #: P383.03

Background & Purpose

- Early biomarkers for neurodegenerative diseases, such as Parkinson's disease (PD) and Alzheimer's disease (AD) are needed.
- Optical coherence tomography (OCT) has the capability to detect retinal nerve fibre thickness alteration in PD and AD.
- This study explores the possibility that in addition to changes in tissue thickness, toxic retinal alpha-synuclein (α-syn) and amyloid beta (Aβ) deposition may change OCT reflectivity or "ultra-reflectivity".

Materials & Methods: Dual mouse models

Parkinson's disease (PD) model:

- Transgenic a-synuclein deposition (hA53T; Tg(Prnp-SNCA*A53T)83Vle) and wildtype (WT) littermates.
- *In vivo* assessments: 6 & 14 months of age (n = 15-17 / group)

Alzheimer's disease (AD) model:

- Transgenic Aβ accumulation model of 5xFAD mice and WT littermates
- *In vivo assessment:* 3, 6 & 12 months of age (n = 11-12 / group)

General anaesthesia: ketamine: xylazine mix 80:10mg/kg, i.p.
Eye drops: 1% tropicamide (Mydriacyl, Alcon), eye gel lubricant (Systane)

Histology & Western Blot Protein Assay: Retinal cross-sections or snap frozen retinal tissue was processed with recombinant anti-phosphorylated α-syn (pSer129) & native anti-α-syn antibodies (Abcam®, Cambridge, USA, Cat#. Ab51253, ab138501) for immunohistochemistry and protein analysis, respectively.

Optical Coherence Tomography – Retinal Structure: Spectralis OCT2 Module, Heidelberg Engineering 768 A scan, 121 Bscan (8.0 x 6.8 mm axial depth). Retinal nerve fibre layer: RNFL, ganglion cell inner plexiform layer: GCIPL, inner nuclear layer: INL, outer plexiform layer: OPL, outer nuclear layer: ONL, total retinal thickness: TRT.

Statistical Analysis

- Two-way ANOVA with Bonferroni correction for multiple comparisons (Prism, GraphPad)
- Data expressed as average ± SEM; * p < 0.05, ** p < 0.01, *** p < 0.001, **** p < 0.0001

Results

A53T model: α-syn overaccumulates in cortical & retinal tissue

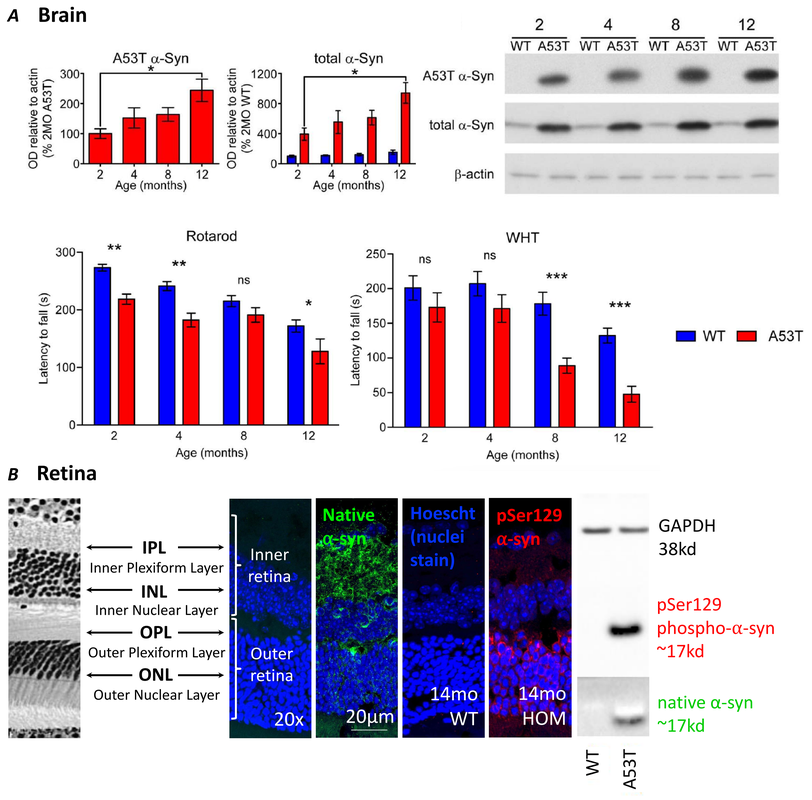

Fig 1. Immunohistochemical & protein assessment of A53T model. (***A***) A53T model shows a presence of α-syn accumulation in the brain with advancing age.[1] Behavioral assessment (rotarod; wire hang test, WHT) shows severity of motor impairment worsens with age. (***B***) A53T mice show elevated toxic phosphorylated (pSer129, red) & native α-syn (green) levels in the retina using immunohistochemistry & western blot analyses.

A53T model: early outer retinal changes, late for inner retina

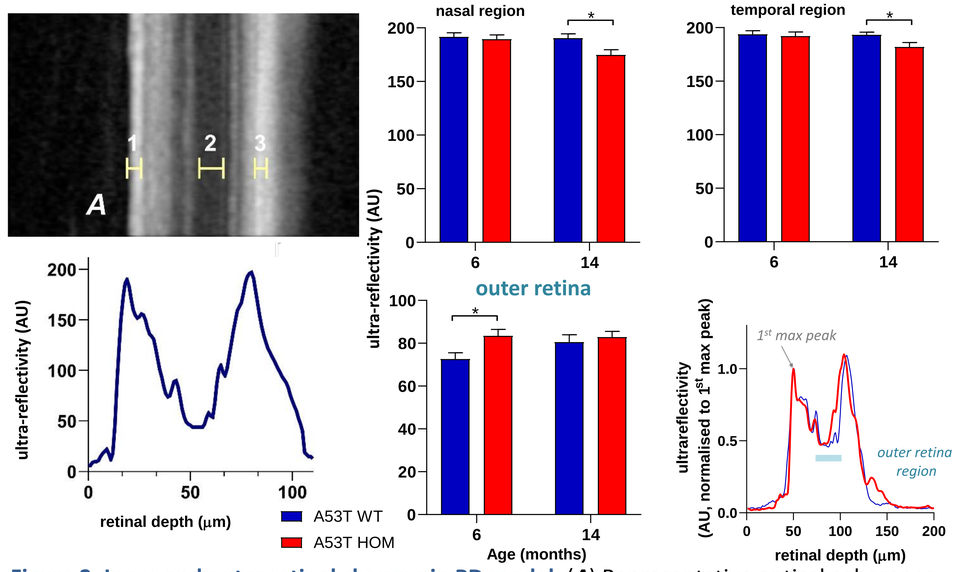

Figure 2. Inner and outer retinal changes in PD model. (***A***) Representative optical coherence tomography (OCT) image, with respective ultra-reflectivity profile (lower panel; 1: RNFL max peak, 2. outer retinal, and 3. ONL regions. Significant reduction in retinal nerve fibre (RNFL) reflectivity was found to be reduced (p = 0.011), particularly at 14 months of age in both nasal (p = 0.003) and temporal regions. Interesting, outer retinal reflectivity was elevated in A53T mice compared to WT-PD littermates (p = 0.026), particularly at 6 months of age.

5xFAD model: changes differ from A53T model

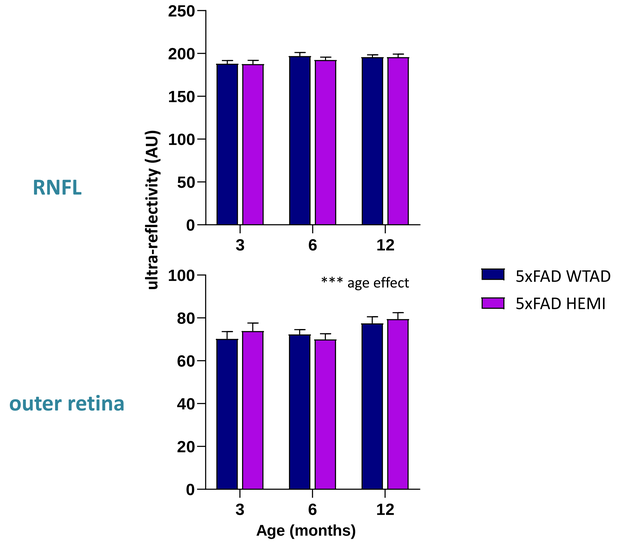

Figure 3. Ageing effect on reflectivity changes in AD model. There was no genotype effect in 5xFAD mice retina, however an ageing effect was present in the outer retina with retinal ultra-reflectivity analysis compared to the retinal nerve fibre layer (p < 0.0001)

Conclusions

Our study demonstrates that RNFL and outer retinal reflectivity are useful tools in following the neurobiological changes in disease progression. A53T mice exhibited changes in ultra-reflectivity measures whereas 5xFAD mice did not. Further studies are required to better understand these reflectivity changes in relation to α-syn related pathology and normal healthy aging.

Support Melbourne Neuroscience Institute Interdisciplinary Seed Fund (CTON, DIF, VHYW, JKHL), Australian Government Research Training Program (RTP) (KKNT); Australian Research Council Linkage (LP160100126, CTON, BVB)

References 1. Oaks et al. (2013) PLoS ONE. DOI: 10.1371/journal.pone.0060378

Commercial Disclosures:

none

NO – PHOTO / RECORD

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Australian Government Australian Research Council