Retinal hyperspectral changes in a mouse model of Parkinson's disease

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Abstract #: P383.02

Background and Purpose

- Retina is an accessible outpouching of the central nervous system (CNS)
- Hyperspectral imaging non-invasively images the retina has shown utility in Alzheimer's disease patients and animal models[1]
- We aim to examine whether hyperspectral imaging is altered in an animal model of Parkinson's disease

Materials & Methods

Parkinson's disease (PD) model

- Transgenic a-synuclein deposition (hA53T; Tg(Prnp-SNCA*A53T)83Vle) and WT littermates
- 6 and 14 months of age (n = 10-24 / group)

Histology/Western blot

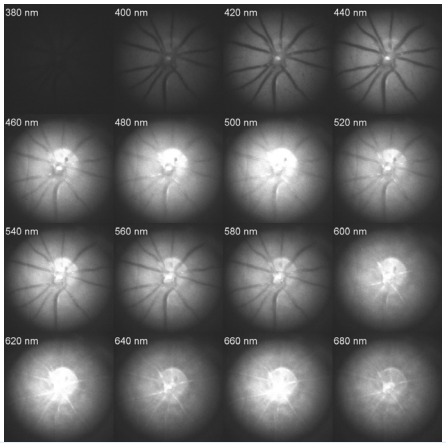
- Frozen sections of eye and brain tissues, tyrosine hydroxylase (TH) antibody (Chemicon® , Cat no. AB152)
- Western blot of TH (1:10,000; Millipore)

Hyperspectral imaging

- Customised retinal imaging platform: TILL Polychrome V light source, Andor Neo cMOS camera
- 320 to 680nm wavelengths scanned in 5 nm steps
- Images registered, blood vessels and optic nerve head masked

Statistical analysis

- Two-way ANOVA with Bonferroni correction for multiple comparisons (Prism, GraphPad)
- Principle component analysis (PCA; MATLAB, MathWorks)
- Data expressed at average ±95%CL. * p < 0.05



Results

Fig 1. A53T model: α-syn overaccumulates in cortical & retinal tissue

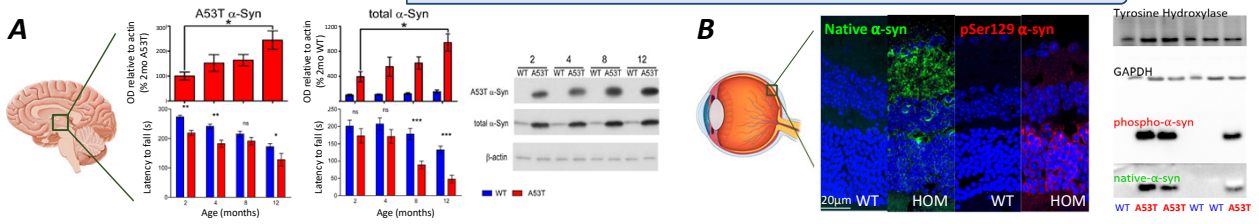
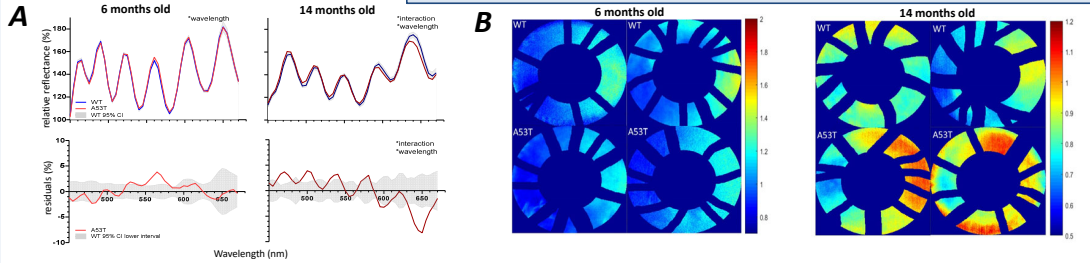


Fig 1. a-syn in brain and retina of A53T mice A. Oaks et al. 2013[1] find A53T mice have increasing α-syn and behavioural motor dysfunction with advancing age. **B.** A53T mice show elevated phosphorylated & native α-syn levels in the retina using immunohistochemistry & western blot

Fig 2. Hyperspectral imaging alters with Parkinson's disease



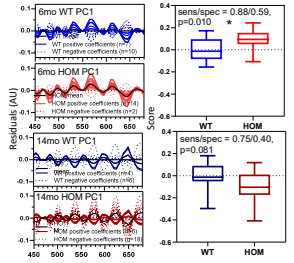
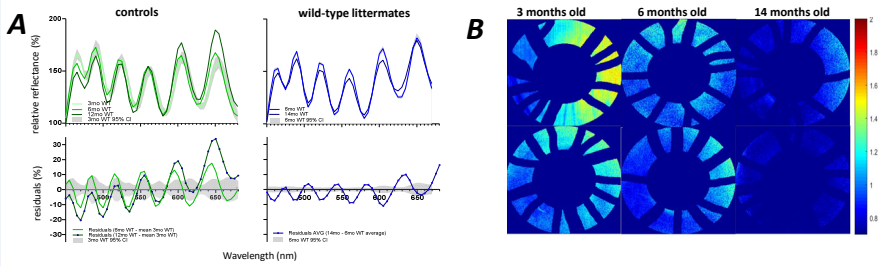


Fig 2A Hyperspectral changes are found in A53T mice compared with controls Significant A53T reflectance changes founds at 14mo but not at 6mo.

Fig 2B Retinal image heatmaps. Difference plots express image acquired at 475 nm relative to 670 nm. A53T mice exhibit warmer colors (higher ratio) compare to wild-type littermates (lower ratio) at 14 months old.

Fig 2C Principal component analysis shows sensitivity/specificity. Significant A53T differences found at 6mo but not 14mo

Fig 3. Healthy aging exhibits distinct changes to hyperspectral imaging



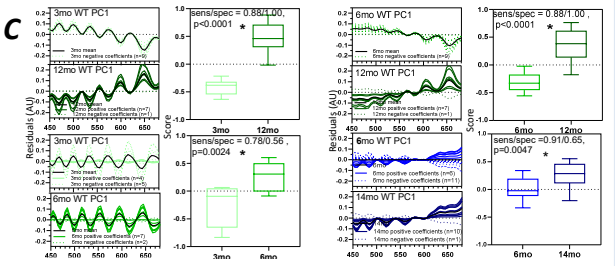


Fig 3A Advancing age manifests as an increase in longer wavelengths. Top panels control animals at 3,6, 12 months of age. Bottom panels, wild type littermates at 6, 14 months old.

Fig 3B Retinal image heatmaps. Difference plots express image acquired at 475 nm relative to 670 nm. With advancing age mice exhibit cooler colors (lower ratio) compared with younger mice (warmer colors, higher ratio)

Fig 3C Principal component analysis shows moderate sensitivity and specificity for hyperspectral imaging to differentiate ages. Significantly higher score were found for older animals compare with younger animals in both control and wild-type littermates.

Conclusions

- Transgenic mouse model of alpha-synuclein overexpression exhibits an alteration in spectral reflectivity of the retina at mid and advanced stages of PD.
- Hyperspectral signature exhibited with advancing alpha-synuclein deposition is distinct from normal healthy ageing
- Paves the way to determine whether translatable, inexpensive and non-invasive retinal measures can be useful preclinical biomarkers for drug discovery

References 1. Oaks et al. (2013) PLoS ONE. doi: 10.1371/journal.pone.0060378
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3. Nguyen et al. (2017). Pharm Ther. doi: 10.1016/j.pharmthera.2017.02.009

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NO – PHOTO / RECORD