UNIVERSITY OF CAMBRIDGE

EVALUATING RETINAL GANGLION CELLS IN INHERITED OPTIC NEUROPATHIES USING PERCEPTUAL TASKS AND FLAVOPROTEIN FLUORESCENCE IMAGING

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BACKGROUND

- Inherited optic neuropathies (IONs) are characterised by degeneration of retinal ganglion cells (RGCs) due to mitochondrial dysfunction.
- Different types of RGCs serve different visual functions. Midget RGCs subserve high acuity vision, and red-green chromatic sensitivity. Parasol cells are achromatic and associable with sensitivity towards high temporal and low spatial frequencies. Small bistratified cells are responsible for blue-yellow sensitivity.
- Flavoprotein oxidation is associated with increased reactive oxygen species production and is measurable using flavoprotein fluorescence (FPF).

AIM

- To assess patterns of RGC dysfunction in patients with IONs using perceptual tasks and FPF measurements.

METHODS

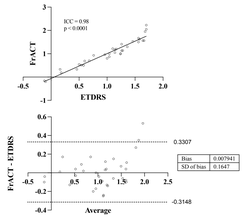
- Colour discrimination thresholds, and temporal and spatial contrast sensitivity functions were assessed.
- Best-corrected visual acuity (BCVA), optical coherence tomography (OCT), and retinal FPF intensity were measured.
- Colour discrimination was decomposed into two colour directions (red-green and blue-yellow) and grouped using k-means clustering. Contrast sensitivity was analysed with linear mixed models.
- Correlation between measures was assessed using linear regression and Pearson coefficients.

RESULTS

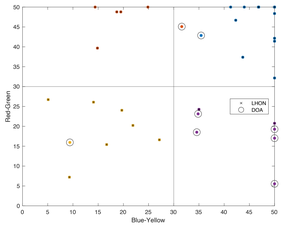
1. BASELINE DEMOGRAPHICS

Subjects, n	24
LHON, n	19
DOA, n	5
Age, mean y	36
Sex	
Male, n	16
Female, n	8
Duration since onset (LHON)	
<1 year, n	5
1 – 5 years, n	7
>5 years, n	7

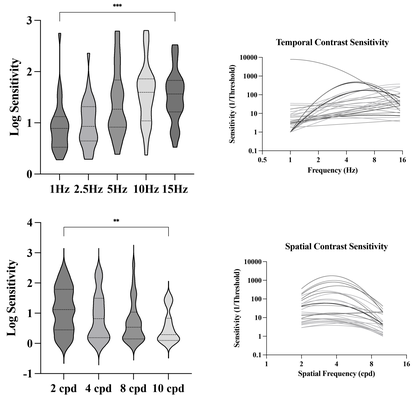
2. AGREEMENT BETWEEN FRACT AND ETDRS MEASUREMENT OF BCVA



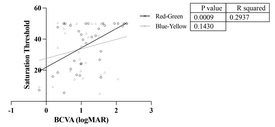
3. COLOUR VISION THRESHOLD CLUSTERS



4. SPATIAL AND TEMPORAL CONTRAST SENSITIVITY

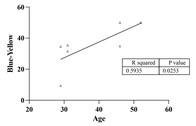


5. COLOUR AND ACUITY



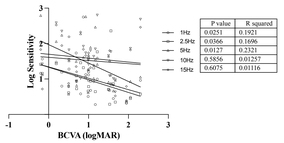
	P value	R squared
Red-Green	0.0009	0.2937
Blue-Yellow	0.1430	

6. COLOUR AND AGE IN DOA



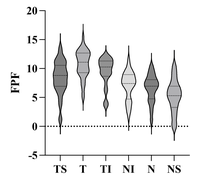
R squared	P value
0.5935	0.0253

7. TEMPORAL CONTRAST AND BCVA

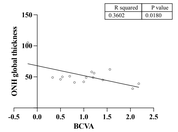


	P value	R squared
1Hz	0.0251	0.1921
2.5Hz	0.0366	0.1696
5Hz	0.0127	0.2321
10Hz	0.5856	0.01257
15Hz	0.6075	0.01116

8. OPTIC NERVE HEAD FPF



9. OPTIC NERVE HEAD OCT AND BCVA



R squared	P value
0.3602	0.0180

CONCLUSIONS

- Red-green colour sensitivity and low temporal frequency contrast sensitivity were correlated with visual acuity. These assessments reveal primarily midget cell status.
- Blue-yellow deficits were correlated with age in DOA—interestingly, 5 of the 7 eyes in the cluster with a primary blue-yellow deficit have DOA. This suggests a relationship between disease progression in DOA and small bistratified cell dysfunction.
- The relative preservation of sensitivity to coarse spatial and high temporal patterns in IONs supports a relative preservation of parasol cells.
- Psychophysical outcomes were not correlated with OCT measurements. Perhaps OCT cannot resolve type-specific structural deficits. OCT thinning of the optic nerve head is associated with BCVA.
- FPF was increased in the optic nerve head in IONs. This is most pronounced in the temporal sectors.
- These findings together support the further investigation of type-specific RGC deficits in IONs as a possible biomarker of disease status and subgroup. Surviving RGC types may also represent valuable therapeutic targets.

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