

Supplementary Information for

Evoked potentials as a biomarker of remyelination

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This PDF file includes:

Figs. S1 to S4
Tables S1 to S2
Caption for movies S1

Other supplementary materials for this manuscript include the following:

Movies S1

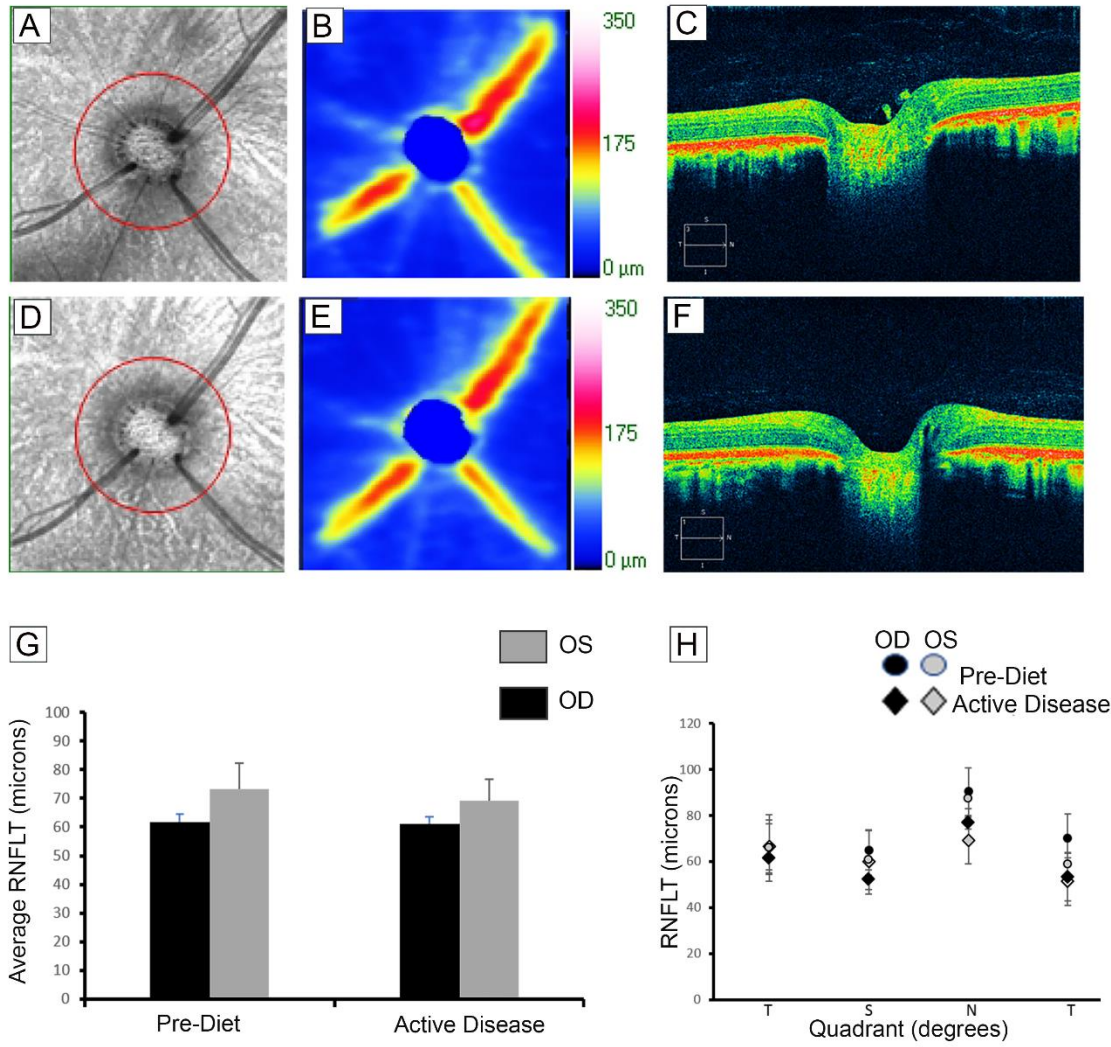


Fig. S1. Retinal nerve fiber layer (RNFL) remains intact during active disease.

Thickness of the RNFL is unchanged during FIDID. A) Pre-disease onset infra-red image of optic nerve the right eye showing location of peripapillary OCT scan. B) RNFL thickness measurement map (warm pseudo-colors (red, orange)=thicker); Retinal nerve fibers are concentrated along the blood vessels in the cat. C) Cross-sectional OCT raster scan through optic nerve. D-F: Scans through of the same location during clinically significant disease (D). The thickness map (E) and optic disk architecture and retinal layers (F) are unchanged during active disease. (G) Average RNFL thickness measurements (with standard deviations) obtained from optic nerve head peripapillary scan for each eye

from 6 cats with OCT scans pre-diet and 5 cats after the onset of FIDID. H) RNFLT at the standard 4 quadrant points from cats shown in G. There is no evidence of thinning of the retinal ganglion cell axons in active disease based on SD-OCT measures.

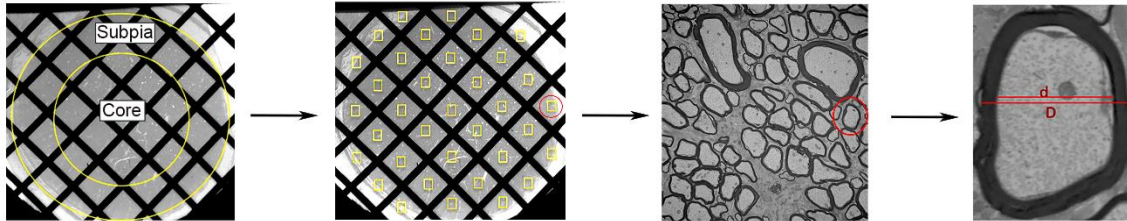


Fig. S2. Schematic image showing g-ratio quantification method in optic nerve.

An electron microscope image was taken from the center of each grid and g-ratio (d/D) of all axons were quantified. d =axon diameter, D =axon+myelin sheath diameter.

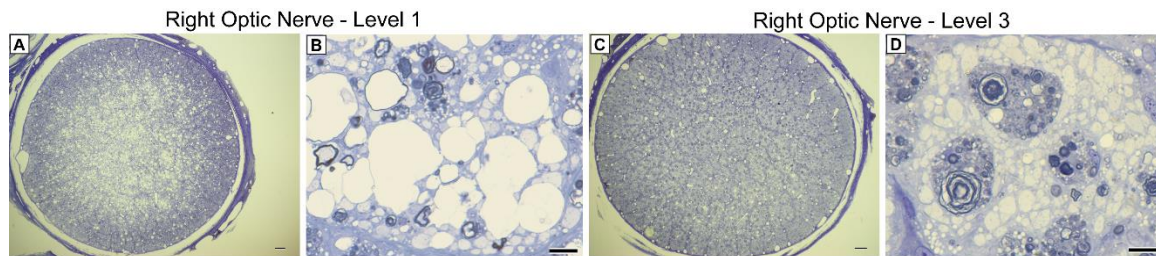


Fig. S3. Extensive myelin vacuolation and demyelination without axon degeneration causes vision loss.

In the cat which lost vision, there was extensive myelin vacuolation at level 1 (A) and level 2. However, this led primarily to extensive demyelination and not degeneration (B). At level 3 (more proximal) (C) the nerve was extensively demyelinated with little evidence of

vacuolation. The majority of axons in the core of the nerve were demyelinated with numerous myelin-debris filled macrophages (D). Remyelinated axons were also present in the subpia.

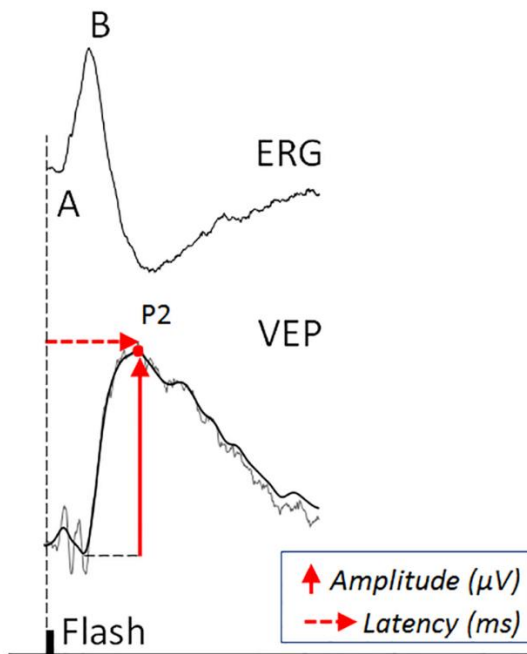


Fig. S4. Scoring of the feline VEP 'P2' wave.

Bottom traces: Gray trace: VEP minimally processed with low-pass filter with a cutoff of 500 Hz, illustrating the high-frequency components consisting of wavelets preceding the P2 wave. Black trace: For scoring, the wave is low-pass filtered at 100 Hz to remove high-frequencies and facilitate peak determination (red dot) from which amplitude and peak-latency measurements are calculated. Top trace shows relationship to simultaneously recorded ERG.

Table S1. Statistical test, *p* value, number of myelinated axons measured and animals used in each experiment.

	VEP Latency and amplitude	Myelin status %	g-ratio	g-ratio gradual changes	VEP/Myelin status correlation
Statistical test	One way ANOVA Tukey's multiple comparison post-test	Two-way ANOVA Tukey's multiple comparison post-test	Multiple linear regression	Multiple linear regression	Simple linear regression
<i>p</i> value	<0.01	0.0002	<0.0001	<0.0001	0.006
Myelinated axons (n)	NA	NA	~11,951	~4,100	NA
Active disease (n)	15	5	2	0	4
Fully recovered (n)	6	3	3	3	3
Partially recovered (n)	0	0	0	2	0
Control (n)	25	0	3	0	0

Table S2. VEP latency changes in recovered animals

Recovered animals	Absolute VEP latency (msec)		Δ VEP latency (msec)	Average g-ratio at level 3 after recovery	Clinical score at recovery
	Active disease	Recovery			
Animal 1	90.1	72.2	-17.9	0.84	0
Animal 2	104.6	87.1	-17.5	0.87	0
Animal 3	91	77.4	-13.6	0.86	+
Animal 4	96.5	60	-36.5	NA	0/+
Animal 5	93.5	85.5	-8	NA	0
Animal 6	112	75.5	-36.5	NA	0

Movie S1. Video showing myelin status across the optic nerve. Light microscope image scanning of the entire section of the control optic nerve, active disease, and recovery.