

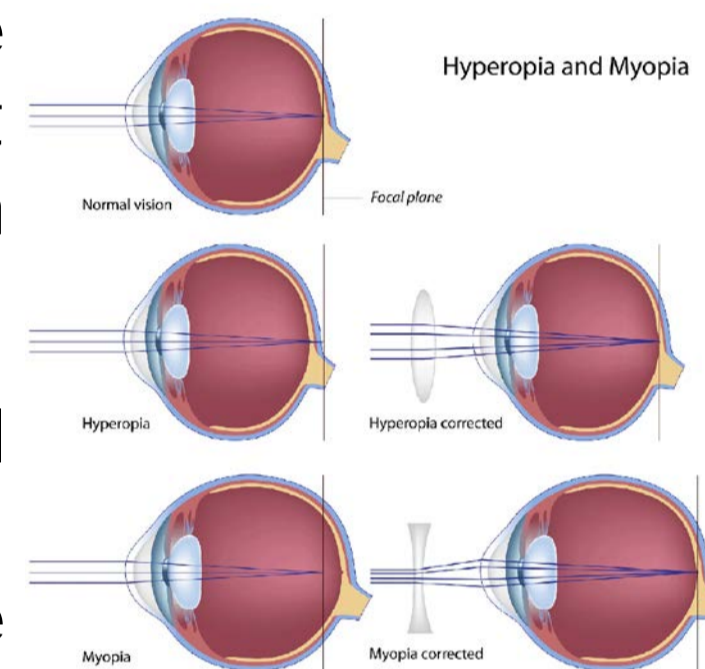
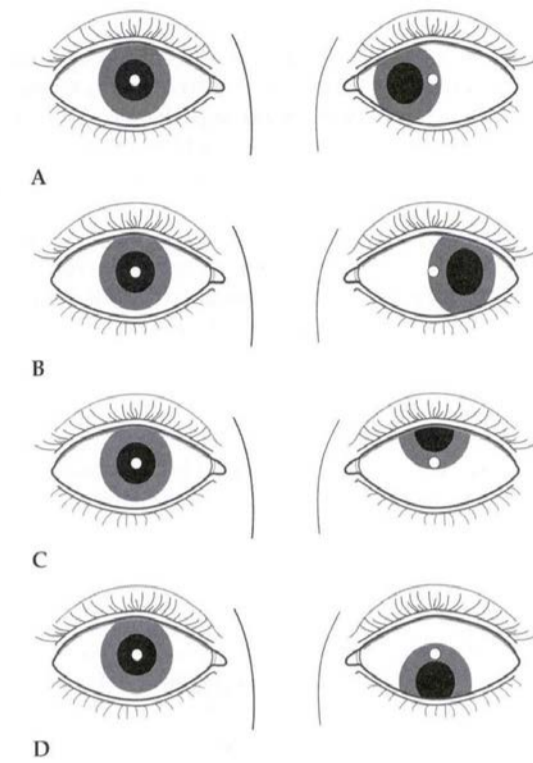
# Structural and functional effects of anisometropic amblyopia on ganglion cell development

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## BACKGROUND

- Amblyopia is the unilateral or bilateral loss or under-development of visual acuity, which is not accounted for by clinically presenting anatomic defects of the eye or visual pathways
- Two major causes of amblyopia are strabismus and anisometropia existing during the period of visual development in early life.
- Researchers have recently investigated anatomical changes in the retina following diagnosis of amblyopia, in particular through the assessment of retinal nerve fiber layer (RNFL) thickness using optical coherence tomography (OCT). Although some studies report significant RNFL thickness differences between amblyopic and fellow eyes, others do not.
- There is a dearth of research studying retinal functional changes in the case of amblyopia. Electroretinography (ERG) is a well-recognized mode of detecting functional abnormalities of retinal cells independent of the responses of the visual pathway and cortex. The ERG provides the photopic negative response wave (PhNR), which has been found to reflect retinal ganglion cell activity.
- PhNR amplitude may be a good functional correlate to assess, given the uncertainty in the literature regarding RNFL thickness changes in amblyopes. If the RNFL is indeed thicker in anisometropic amblyopes—suggesting an increased cell count, it would be logical to hypothesize that the PhNR amplitude would be larger in the ERG of the affected eye.
- In this study, we investigate the role of retinal structural and functional correlates in strabismic and anisometropic amblyopia in adults and children.



## METHODS

- 16 adults and 6 children with strabismic or anisometropic amblyopia were examined. Clinical examination included best corrected visual acuity, refractive error, slit lamp exam, anterior segment exam, strabismic evaluation and IOP. RNFL was measured in the peripapillary region with the SLO/OCT (Optos Inc), using an average of 3 circular scans of 3.4 mm diameter. PhNR was recorded using brief 4 msec flashes of 640 nm wavelength at 5 cd-s/m<sup>2</sup> over a rod-adapting background (470 nm) at 10 cdm<sup>2</sup>. ERGs were recorded with DTL-Plus™ electrodes using Espion e<sup>2</sup> (Diagnosys LLC) with a 0.3 – 300 Hz bandpass and 50 sweeps of 150 msec duration were averaged. The peak latency and amplitude of the PhNR was determined through visual inspection
- The data obtained from both amblyopic and unaffected eyes of all patients were analyzed. Means of RNFL and PhNR were compared between the anisometropic and strabismic amblyopic eyes. Also, means of RNFL and PhNR were compared between the amblyopic and unaffected eyes in each of the study groups. Regression analysis was performed to determine correlation between RNFL and PhNR in strabismic and anisometropic amblyopic eyes.
- This study was approved by the Ottawa Health Science Network Research Ethics Board (OHSN-REB)

## RESULTS

- 16 adults and 6 children with strabismic (n=11) or anisometropic (n=11) amblyopia were examined.

	Anisometropic Amblyopic Eyes	Strabismic Amblyopic Eyes	Fellow Non-Amblyopic Eyes	All Eyes
Total Eyes	11	11	22	44
OD-OS Distribution	4-7	8-3	10-12	22-22
Adult-Child Distribution	5-6	11-0	16-6	32-12
Mean Age	31.545 ± 24.867	43.909 ± 15.267	37.727 ± 21.452	37.727 ± 21.202
Male-Female Distribution	9-2	3-8	12-10	24-20
Mean LogMAR Visual Acuity	0.745 ± 0.403	0.718 ± 0.549	0.041 ± 0.085	0.386 ± 0.483

Table 1. Patient Demographics.

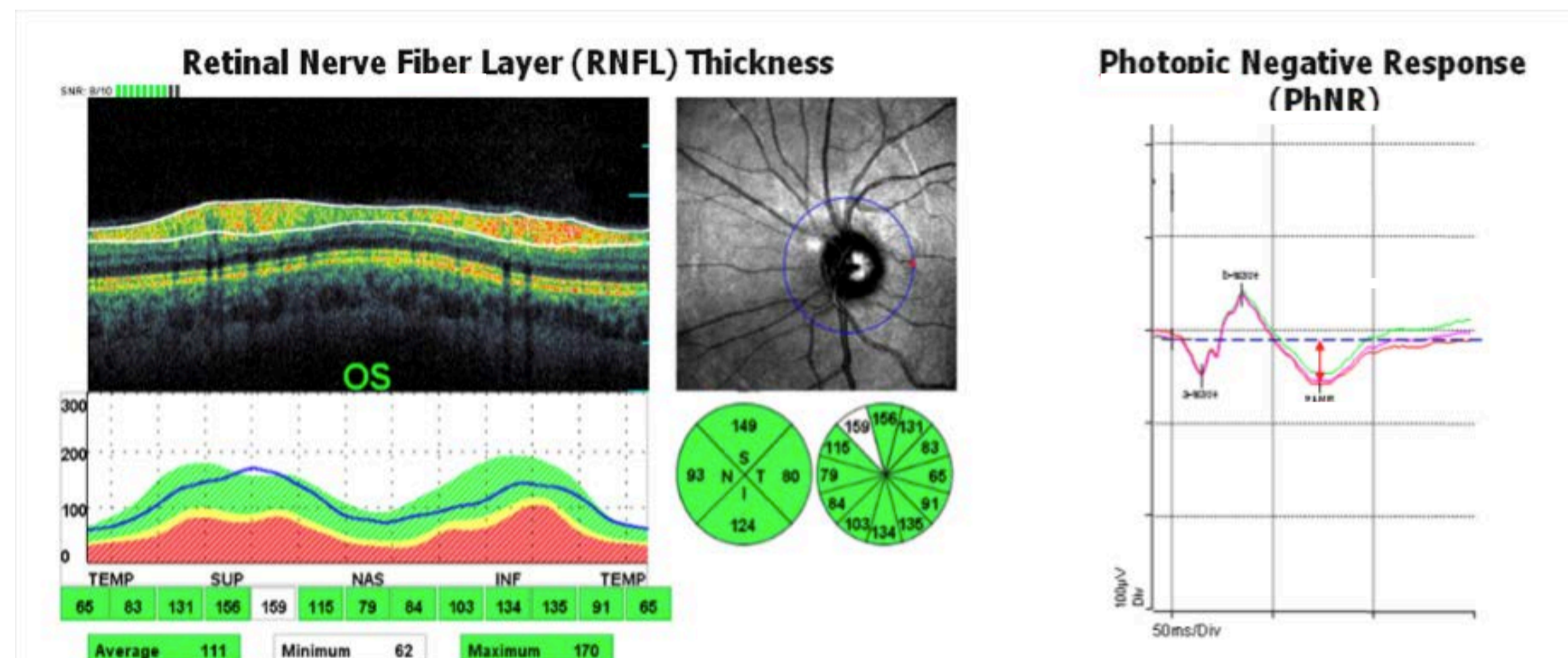


Figure 1. Peripapillary retinal nerve fiber layer thickness and full-field photopic negative response from a normal subject.

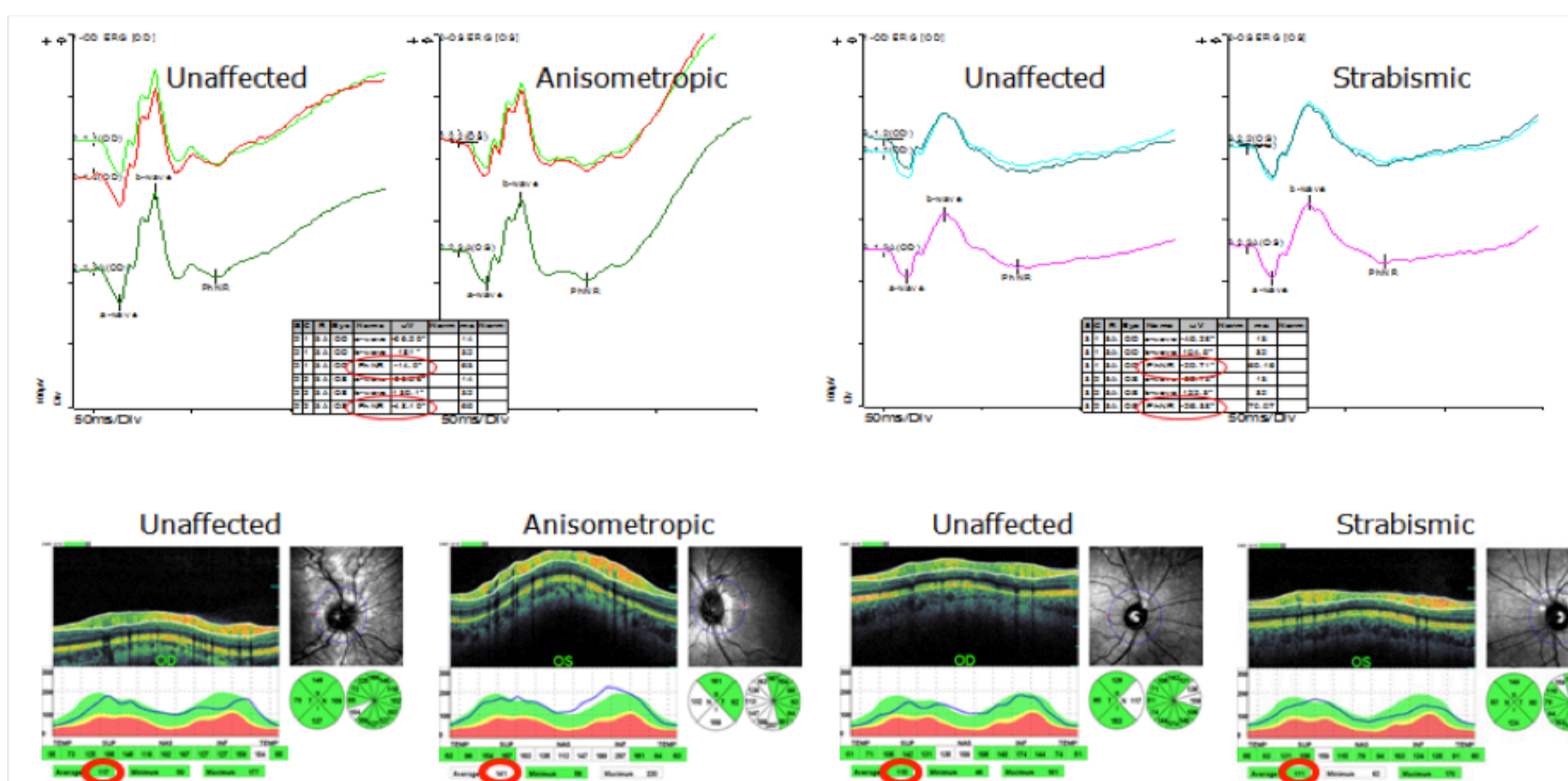


Figure 2. Photopic negative response and retinal nerve fiber layer thickness maps on two amblyopic patients.

Type of Amblyopia	Eye	RNFL Thickness Mean & sd	F-value	p-value	PhNR Amplitude Mean & sd	F-value	p-value
Anisometropic	Affected	123.5 ± 18.1			43.5 ± 11.9		
	Unaffected	108.9 ± 11.1	5.17	0.03	36.5 ± 11.5	1.95	0.18(ns)
Strabismic	Affected	110.3 ± 12.9			30.1 ± 9.0		
	Unaffected	118.9 ± 12.7	2.98	0.10(ns)	33.9 ± 18.2	0.38	0.54(ns)

Table 2. Photopic Negative Response and Retinal Nerve Fiber Layer thickness differences between amblyopic and fellow unaffected eyes.

## RESULTS

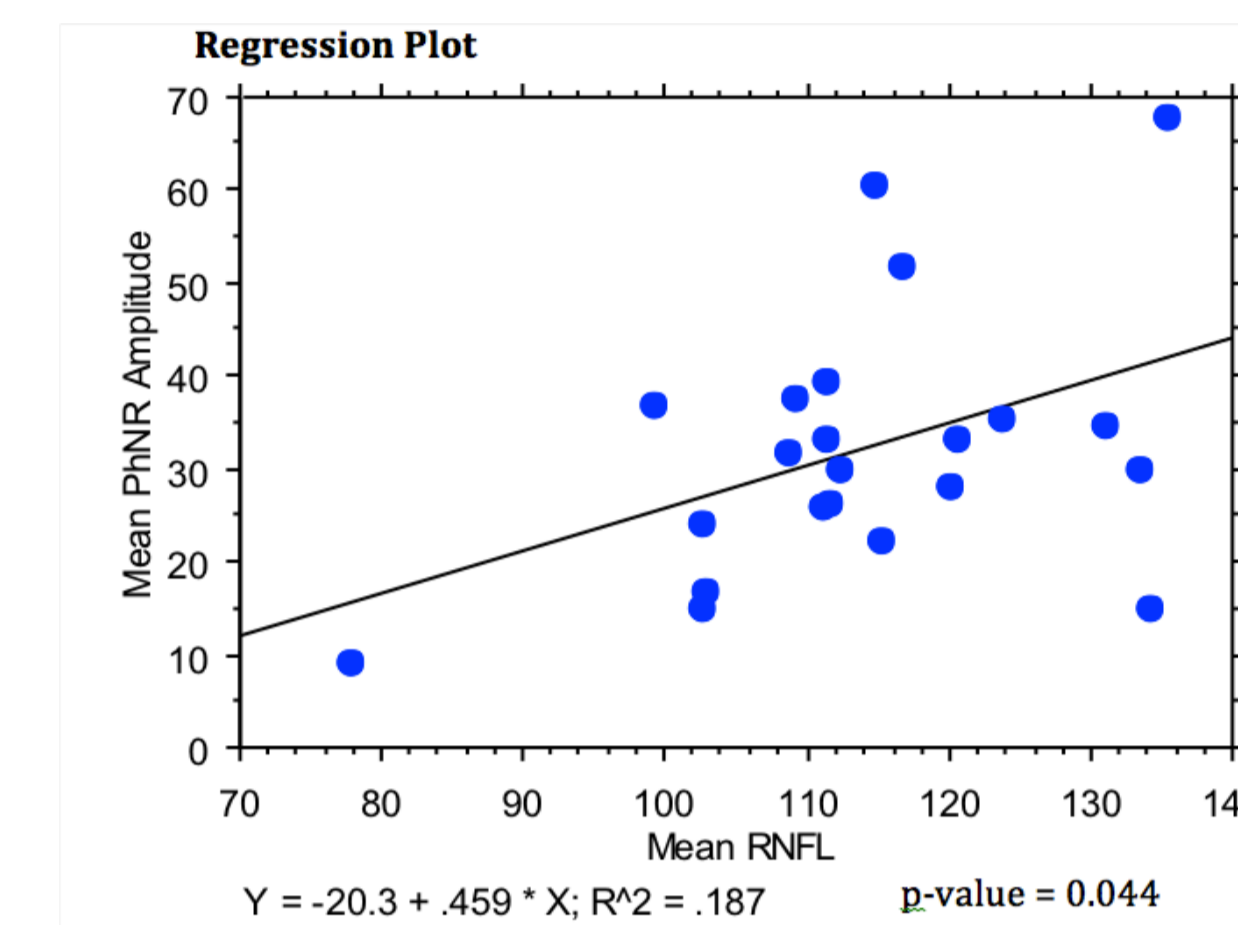


Figure 3. Mean photopic negative response amplitude versus mean retinal nerve fiber layer thickness regression plot of strabismic eyes.

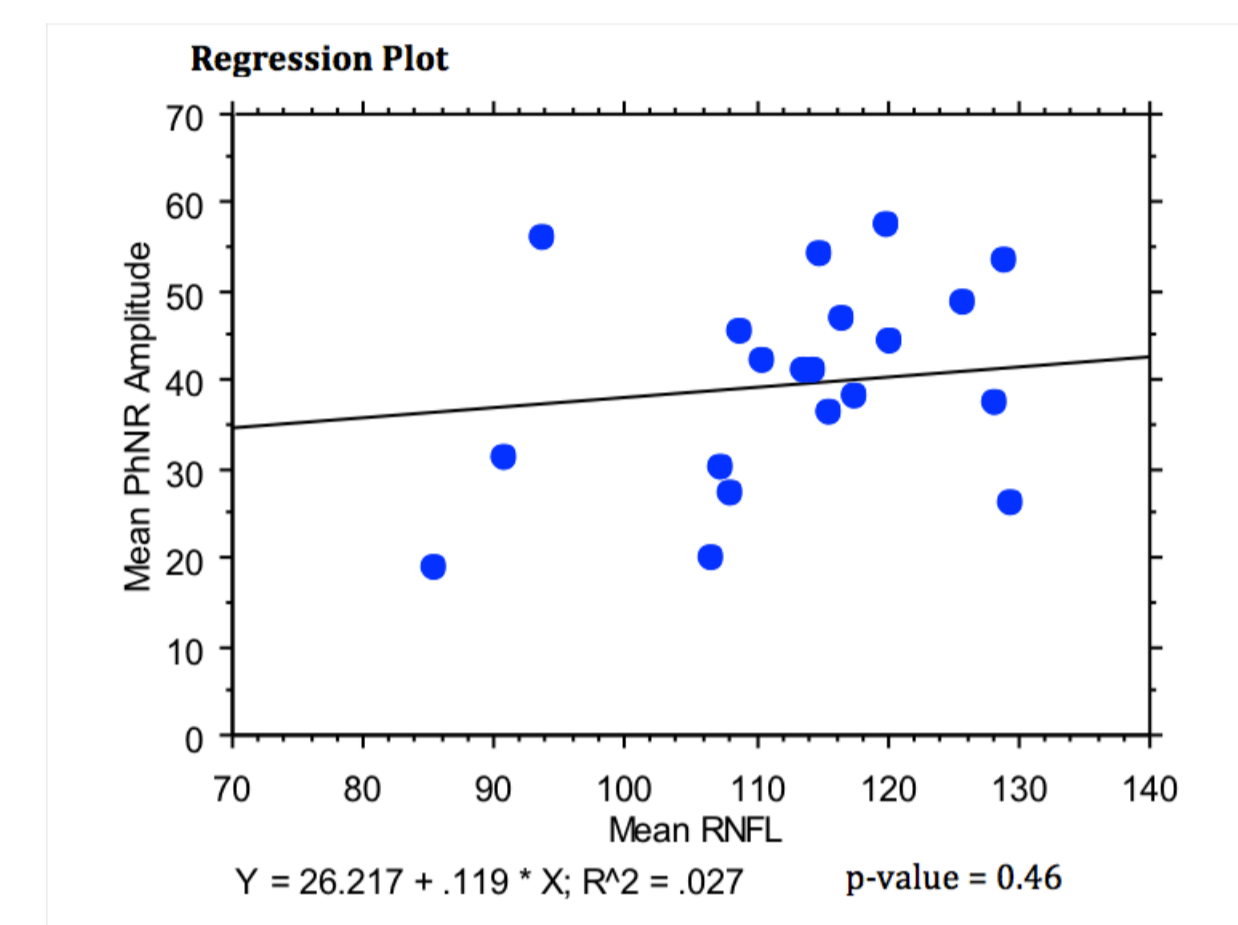


Figure 4. Mean photopic negative response amplitude versus mean retinal nerve fiber layer thickness regression plot of anisometropic eyes.

Figure 3 (n=22) indicates a significant, positive correlation between mean RNFL thickness and mean PhNR amplitude in strabismic eyes. Figure 4 (n=22) indicates a positive but statistically non-significant correlation between mean RNFL thickness and mean PhNR amplitude in anisometropic eyes.

## DISCUSSION

- The greater RNFL thickness in anisometropic eyes suggests a larger ganglion cell population. This supports Yen et al.'s findings, since insufficient apoptosis due to anisometropia during postnatal development could lead to an inability to reduce cell count number.
- Therefore, sharply focused objects may be required as appropriate stimuli to activate apoptosis. The ganglion cell count in a normal eye is down regulated rapidly between 18 and 30 weeks gestation and eventually is reduced from approximately 2.5 to 1.5 million cells by two or three years of age.
- Interestingly, we failed to find that PhNR amplitude correlated with increased RNFL thickness in anisometropic amblyopic eyes. Given the thicker RNFL in anisometropic amblyopic eyes versus normal, we had expected a greater PhNR amplitude as well in these eyes; however, this did not prove to be the case.
- It is possible that ERG is not a sensitive enough test to detect mild changes in function for a small—but significant—change in RNFL thickness. It is also possible that although the RNFL thickness is greater, the abnormally retained ganglion cells may be dysfunctional resulting in little to no increase in PhNR amplitude. It can be speculated that these ganglion cells do not receive or respond to input from the outer retina hence they do not contribute to the PhNR amplitude following light stimulation.

## CONCLUSION

- Increased RNFL thickness might reflect the disruption of normal retinal ganglion cell apoptosis during postnatal development suggesting that the process requires sharply focused objects as appropriate stimuli. Full-field PhNR did not correlate with RNFL thickness in anisometropic eyes, contrary to what we had hypothesized, which suggests that these abnormally retained ganglion cells are dysfunctional, or that these functional changes may be undetectable by ERG.

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