Table 1. Global and sectorial RNFL thickness in the control, MS without ON and MS with previous ON groups.

RNFL thickness (μm) Region	Control Mean (SD)	MS – without ON Mean (SD)	MS – with ON Mean (SD)
Global	104.3 (9.1)	93.6 (13.3)*	79.8 (15.9)*
Temporal	76.0 (11.5)	63.7 (14.2)*	48.9 (14.8)*
Superior temporal	141.6 (19.2)	126.7 (24.9)*	113.0 (25.1)*
Inferior temporal	146.5 (17.6)	132.3 (23.3)*	107.3 (30.2)*
Nasal	81.1 (12.7)	75.2 (14.7)	65.2 (16.9)*
Superior nasal	112.9 (19.4)	99.5 (25.4)*	88.4 (24.0)*
Inferior nasal	118.6 (20.7)	108.6 (25.5)	98.9 (24.6)*

MS = multiple sclerosis; ON = optic neuritis; RNFL = retinal nerve fibre layer; SD = standard deviation.
* Statistically significant difference (p value < 0.01; adjusted for age) when compared to the control group.

ophthalmological examination, and spectral-domain optical coherence tomography (OCT; Spectralis OCT, software v. 4.0, Heidelberg Engineering, Dossenheim, Germany) imaging to measure RNFL thickness. Subjects were excluded from the study if any of the following were present: glaucoma, optic neuropathy, high ametropia (refractive error spherical equivalent more severe than ±5 dioptres), history of ocular or neurological trauma, or other relevant retinal and/or optic nerve disease.

Fifty-six subjects with treated MS and 35 healthy subjects were included. Mean global (MS: 89.6 ± 15.4 μm, control: 104.3 ± 9.1 μm; $p < 0.001$) and sectorial RNFL thicknesses were significantly less in the MS group than in the control group (Table 1). Global RNFL thickness was thinnest in MS subjects with a history of ON (79.8 ± 15.9 μm), followed by MS subjects without a history of ON (93.6 ± 13.3 μm), and thickest in the control group (104.3 ± 9.1 μm; all $p < 0.001$). Additionally, the Spearman rank correlation coefficient (rs) between the number of ON episodes and RNFL thickness was −0.41 in the MS group ($p < 0.001$). Therefore, MS subjects that had more ON episodes had a thinner RNFL thickness. The area under the receiver operating characteristic curve (AUROC) for global RNFL measurements was 0.83 (95% confidence interval [CI]: 0.66–0.94) for discriminating between healthy subjects and those with MS. Sectorial RNFL thickness measurements had the highest AUROC (0.83, 95% CI: 0.67–0.93), and subsequently the best accuracy, in the superior temporal sector. That means that the superior temporal parapapillary sector is the most affected in MS.

Interestingly, subjects with a higher number of ON episodes had larger RNFL changes than subjects with a lower number of ON episodes. This finding indicates that serial OCT monitoring of patients with MS may provide useful information on disease status, disease activity and treatment efficacy. However, caution should be used to not overlook RNFL changes in eyes classified as 'within normal limits', because the software database is made for glaucoma, not for demyelinating disease. Serial testing is always helpful for comparison to baseline values obtained at the beginning of a disease process.

In conclusion, MS subjects without a history of ON had a thinner RNFL than normal subjects. Additionally, RNFL thickness was negatively correlated with the number of prior ON episodes, indicating a larger amount of RNFL damage. Therefore, we recommend that all patients with MS, and not just those with a history of ON, undergo regular RNFL thickness measurement with OCT during the diagnostic process and follow-up.

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Correspondence:
Ivan M. Tavares, MD
Department of Ophthalmology and Visual Sciences
Universidade Federal de São Paulo
Paulista School of Medicine
Rua Botucatu
821 – 2nd floor
Sao Paulo 04023-062
Brazil
Tel: +55 11 5576 4981
Fax: +55 11 5576 4981
Email: im.tavares@unifesp.br

Genetic influence on contrast sensitivity in young adults

Koen V. Haak[1,2]

[1]Donders Institute for Brain, Cognition and Behaviour, Centre for Cognitive Neuroimaging, Radboud University, Nijmegen, The Netherlands; [2]Department of Cognitive Neuroscience, Radboud University Medical Centre, Nijmegen, The Netherlands

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Editor,

Contrast sensitivity, the ability to detect small luminance differences, is an important independent aspect of visual function that can vary more than fourfold across normal individuals (Baker 2013). Little is known about the degree to which this variation is determined by genetic and environmental factors. The only study to date was based on a sample of male military veterans with an age range of 52–60, and estimated the heritability of contrast sensitivity (i.e., the portion of phenotypic variance accounted for by genetic factors)

between 14% and 38%; much lower than might be expected of a core, biologically-based visual function (Cronin-Golomb et al. 2007). However, due to the relatively homogeneous sample of middle-aged men, it is unclear whether these estimates reflect environmental influences on development or the rate of age-related decline, which normally begins at age 40–50 for higher spatial frequencies (Owsley et al. 1983). Here, therefore, I estimated the genetic influence on contrast sensitivity in a sample of healthy young adults of both sexes between 22 and 36 years of age, who can be considered to represent the population at large with respect to ethnic and socio-economic diversity, and whose visual contrast sensitivity should be fully developed but not yet aged.

The sample contained 149 monozygotic (MZ) and 94 dizygotic (DZ) twin pairs of the WU-Minn Human Connectome Project (Van Essen et al. 2013) whose twin-status was confirmed by genetic testing. The mean (SD) age was 29.3 (3.4) and the sample included 295 females (174 MZ, 121 DZ). Inclusion and exclusion criteria are detailed elsewhere (Van Essen et al. 2013). Contrast sensitivity was assessed binocularly using the Mars Letter Contrast Sensitivity test (Arditi 2005) and visual acuity using the Electronic Visual Acuity (EVA) system running the *e*ETDR protocol (Beck et al. 2003). Both tests involved corrected vision, if applicable. Contrast sensitivity was calculated as the log contrast sensitivity value at the final correct letter minus the number of errors prior to the final correct letter times 0.04. The EVA scores were converted to logMAR using the formula $-\log_{10}(A)$, where A is the ratio between the EVA nominator and denominator scores.

The heritability of contrast sensitivity, $h^2 = \sigma_g^2/\sigma_p^2$, was estimated using SOLAR (Almasy & Blangero 1998) with covariates visual acuity, age and sex. SOLAR estimates the genetic and environmental variances, σ_g^2 and σ_e^2, by comparing the observed phenotypic covariance matrix with the covariance matrix predicted by genetic relatedness (i.e., $\Omega = 2\Phi\sigma_g^2 + I\sigma_e^2$, where Φ encodes the pair-wise genetic relatedness among all individuals) and determines the statistical significance of the heritability estimates by a chi-squared test comparing the log-likelihood of the model in which σ_g^2 is constrained to be zero to that in which σ_g^2 is estimated. Continuous traits were normalized using the inverse normal transformation.

The mean (SD) log contrast sensitivity across all twin pairs was 1.80 (0.06) and the mean (*SD*) visual acuity was −0.14 (0.12) logMAR. There were no significant differences between the monozygotic and dizygotic groups in contrast sensitivity, visual acuity, age (all $p > 0.58$), or the proportion of males/females ($\chi^2 = 1.72$, $p = 0.19$). Contrast sensitivity was moderately heritable, with additive genetic effects explaining 27% of the phenotypic variance ($h^2 = 0.27$, SE = 0.07, $p = 1.2 \times 10^{-4}$), which is consistent with the prior estimates for peak contrast sensitivity in middle-aged men.

The comparably moderate heritability of contrast sensitivity in early and middle adulthood suggests a strong influence of nongenetic, nonageing-related factors. While these influences may partly reflect measurement error, variations in cognitive ability and/or task engagement, a large proportion likely involves individual-specific environmental experiences during childhood and adolescence (Cronin-Golomb et al. 2007; Baker 2013; Bartholomew et al. 2016). Identifying these experiences is an important direction of future research, as they may be altered to improve visual function in adulthood.

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Correspondence:
Koen V. Haak, PhD
Donders Centre for Cognitive Neuroimaging
Radboud University
Kapittelweg 29, 6525EN
PO Box 9101
6500HB Nijmegen
The Netherlands
Tel.: +31243668064
Fax: +31243610652
Email: k.haak@donders.ru.nl

Persisting diplopia after periocular injection of parallel imported Kenalog® (triamcinolone acetonide)

Kåre Clemmensen, Mette Slot Nielsen and Susanne Krag

Department of Ophthalmology, Aarhus University Hospital, Aarhus, Denmark

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Editor,

We report four cases with persisting diplopia as an unusual complication after periocular steroid injections with Kenalog Orifarm.

Case 1 A 20-year-old man with bilateral idiopathic pars planitis complicated by cystoid macular oedema (CME) in his left eye. Immediately after a periocular injection with Kenalog Orifarm, the patient developed painless diplopia, which initially was thought to be caused by the