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.

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

| 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.

Genetic influence on contrast sensitivity in young adults

Koen V. Haak

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

doi: 10.1111/aos.13955

© 2018 The Author. Acta Ophthalmologica published by John Wiley & Sons Ltd on behalf of Acta Ophthalmologica Scandinavica Foundation. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDe¬riva License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

### References

Ashworth B (1987): Chronic demyelinating optic neuritis: a reappraisal. Neuro Ophthalmol 7: 75–79.

Fisher JB, Jacobs DA, Markowitz CE et al. (2006): Relation of visual function to retinal nerve fiber layer thickness in multiple sclerosis. Ophthalmology 113: 324–332.

Khanifar AA, Parritis GS, Ehrlich JR, Acker GD, D’Amico DJ, Gauthier SA & Kiss S (2010): Retinal nerve fiber layer evaluation in multiple sclerosis with spectral domain optical coherence tomography. Clin Ophthalmol 4: 1007–1013.

Peterson JW, Bo L, Mork S, Chang A & Trapp BD (2001): Transected neuritis, apoptotic neurons and reduced inflammation in cortical MS lesions. Ann Neurol 50: 389–400.

Waxman SG (2005): Multiple sclerosis as a neuronal disease. Amsterdam: Elsevier Academic Press.

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

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 Electronic Visual Acuity (EVA) system (Arditi 2005) and visual acuity using the tomoe Project (Van Essen et al. 2013). Contrast sensitivity in a sample of middle-aged men.

The comparably moderate heritability of contrast sensitivity in early and middle adulthood suggests a strong influence of nongenetic, non-ageing-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.

Acknowledgement
Netherlands Organisation for Scientific Research (NWO-Veni 016.171.068).

Data were provided by the Human Connectome Project, WU-Minn Consortium (Principal Investigators: D.C. Van Essen and K. Ugurbil; 1U54MH091657) funded by the 16 NIH Institutes and Centers that support the NIH Blueprint for Neuroscience Research; and by the McDonnell Center for Systems Neuroscience at Washington University.

References
Almasy L & Blangero J (1998): Multipoint quantitative-trait linkage analysis in general pedigrees. Am J Hum Genet 62: 1198–1211.
Arndit A (2005): Improving the design of the letter contrast sensitivity test. Invest Ophthalmol Vis Sci 46: 2225–2229.
Baker DH. (2013): What is the primary cause of individual differences in contrast sensitivity? PLoS ONE 8: e69536.
Bartholomew AJ, Lad EM, Cao D, Bach M & Cirulli ET (2016): Individual differences in scotopic visual acuity and contrast sensitivity: genetic and non-genetic influences. PLoS ONE 11: e0148192.
Beck RW, Moke PS, Turpin AH et al. (2003): A computerized method of visual acuity testing: adaptation of the early treatment of diabetic retinopathy study testing protocol. Am J Ophthalmol 135: 194–205.
Cronin-Golomb A, Panizzon MS, Lyons MJ et al. (2007): Genetic influence on contrast sensitivity in middle-aged male twins. Vis Res 47: 2179–2186.
Owsley C, Sekuler R & Siemsen D (1983): Contrast sensitivity throughout adulthood. Vis Res 23: 689–699.
Van Essen DC, Smith SM, Barch DM, Behrens TE, Yacoub E & Ugurbi K; WU-Minn HCP Consortium (2013): The WU-Minn Human connectome project: an overview. NeuroImage 80: 62–79.

Persisting diplopia after periocular injection of parallel imported Kenalog® (triamcinolone acetonide)
Käre Clemmensen, Mette Slot Nielsen and Susanne Krag
Department of Ophthalmology, Aarhus University Hospital, Aarhus, Denmark
doi: 10.1111/aos.13960

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