Automated Morphometry of the Visual Pathway in Primary Open-Angle Glaucoma

Aditya T. Hernowo,1,2 Christine C. Boucard,3 Nomdo M. Jansonius,4 Johanna M. M. Hooymans,4 and Frans W. Cornelissen1

Purpose. To establish whether primary open-angle glaucoma (POAG) is associated with a change in volume of the visual pathway structures between the eyes and the visual cortex.

Methods. To answer this question, magnetic resonance imaging (MRI) was used in combination with automated segmentation and voxel-based morphometry (VBM). Eight patients with POAG and 12 age-matched control subjects participated in the study. Only POAG patients with bilateral glaucomatous visual field loss were admitted to the study. The scotoma in both eyes had to include the paracentral region and had to, at least partially, overlap. All participants underwent high-resolution, T1-weighted, 3-T MRI scanning.[b] Subsequently, VBM was used to determine the volume of the optic nerves, the optic chiasm, the optic tracts, the lateral geniculate nuclei (LGN), and the optic radiations. Analysis of covariance was used to compare these volumes in the POAG and control groups. The main outcome parameter of the measurement was the volume of visual pathway structures.

Results. Compared with the controls, subjects with glaucoma showed reduced volume (P < 0.005) of all structures along the visual pathway, including the optic nerves, the optic chiasm, the optic tracts, the LGN, and the optic radiations.

Conclusions. POAG adversely affects structures along the full visual pathway, from the optic nerve to the optic radiation. Moreover, MRI in combination with automated morphometry can be used to aid the detection and assessment of glaucomatous damage in the brain. (Invest Ophthalmol Vis Sci. 2011;52: 2758–2766) DOI:10.1167/iovs.10-50682

In the developed world, glaucoma is one of the most notorious causes of visual field defects. Typically, over the course of the disease, the visual field becomes narrower, but foveal vision remains relatively intact. The pathogenesis of the disease is not well understood, and that hampers early diagnosis and advances in treatment.

Degeneration of retinal ganglion cells (RGCs) is currently thought to play a key role in the pathogenesis of glaucoma. The resulting damage to the RGC axonal projections is reflected by thinning of the retinal nerve fiber layer (RNFL). Analysis of RNFL thickness has thus become a primary tool for investigating volumetric changes in the most anterior part of the visual pathway.

Moreover, growing evidence suggests translation of the RGC degeneration to more distal parts of the visual pathway. In mice, the loss of RGCs is followed by a reduction in the thickness and area of the optic tract. In nonhuman primates, an experimentally induced increase in intraocular pressure led to RGC loss and to the degeneration of the lateral geniculate nucleus (LGN) cell layers. In humans, magnetic resonance (MR) studies have shown that patients with glaucoma, compared with healthy individuals, have smaller optic nerves, a smaller optic chiasm, and smaller LGNs. A diffusion tensor imaging (DTI) study found marked, disease-stage-correlated changes in the optic nerves and weak changes in the optic radiations when comparing glaucoma patients and healthy controls. Finally, the visual cortex was shown to decline in volume in glaucoma, as revealed in one postmortem study by Gupta et al. and in a recent in vivo MR study from our group. The degeneration in these central portions of the visual pathway in humans may also be a sign of transsynaptic neuronal degeneration, which is provoked by the death of the RGCs.

Thus far, MR-based measurements of the size of the human prefrontal portion of the visual pathway have all been performed manually. Besides being time consuming, this manual assessment can result in subjective measurement bias. To overcome these disadvantages, in a recent study, our group used an automated morphometric technique that can objectively compare anatomic changes at all locations in the brain simultaneously. Using this new approach, we found MR evidence of gray matter density loss in the primary visual cortex in individuals with a long-standing visual field defect due to primary open-angle glaucoma (POAG). This, together with the DTI findings mentioned earlier, implies that the optic radiation that carries visual information from the LGN to the visual cortex may also be affected in POAG. To our knowledge, morphologic changes have not yet been reported for these structures.

If morphologic changes in the visual pathway can be reliably measured, it could assist a clinician in deciding on the diagnosis, prognosis, and further management of individual patients. In the present study, we investigated volumetric changes along the entire afferent visual pathway in individuals.