Glaucomatous Retinal Nerve Fiber Layer Thickness Loss Is Associated With Slower Reaction Times Under a Divided Attention Task

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• PURPOSE: To examine the relationship between glaucomatous structural damage and ability to divide attention during simulated driving.
• DESIGN: Cross-sectional observational study.
• METHODS: SETTING: Hamilton Glaucoma Center, University of California San Diego. PATIENT POPULATION: Total of 158 subjects from the Diagnostic Innovations in Glaucoma Study, including 82 with glaucoma and 76 similarly aged controls. OBSERVATION PROCEDURE: Ability to divide attention was investigated by measuring reaction times to peripheral stimuli (at low, medium, or high contrast) while concomitantly performing a central driving task (car following or curve negotiation). All subjects had standard automated perimetry (SAP) and optical coherence tomography was used to measure retinal nerve fiber layer (RNFL) thickness. Cognitive ability was assessed using the Montreal Cognitive Assessment and subjects completed a driving history questionnaire. MAIN OUTCOME MEASURES: Reaction times to the driving simulator divided attention task.
• RESULTS: The mean reaction times to the low-contrast stimulus were 1.05 s and 0.64 s in glaucoma and controls, respectively, during curve negotiation ($P < .001$), and 1.19 s and 0.77 s ($P = .025$), respectively, during car following. There was a nonlinear relationship between reaction times and RNFL thickness in the better eye. RNFL thickness remained significantly associated with reaction times even after adjusting for age, SAP mean deviation in the better eye, cognitive ability, and central driving task performance.
• CONCLUSIONS: Although worse SAP sensitivity was associated with worse ability to divide attention, RNFL thickness measurements provided additional information. Information from structural tests may improve our ability to determine which patients are likely to have problems performing daily activities, such as driving. **(Am J Ophthalmol 2014;158:1008–1017.**

Glaucoma is a progressive optic neuropathy that may result in significant vision-related morbidity.[1] As glaucomatous neural loss is irreversible, the central aim of disease management is to slow progression and reduce the risk of patients developing visual impairment and reduction in vision-related quality of life. Visual function in glaucoma is traditionally evaluated using standard automated perimetry (SAP). Although SAP provides a means to quantify glaucomatous damage, the true clinical significance of SAP depends on how well it is able to predict the impact of disease on ability to perform activities of daily living, and an understanding of this relationship remains elusive.[2,3] In fact, as SAP attempts to minimize visual distractions during testing, it may be limited in its ability to measure visual impairment related to real-world tasks.[4] Visual distractions are present during most daily activities, including during driving and navigation while walking, tasks that require the ability to divide attention or "multitask."[3,5–8]

Divided attention specifically requires processing and/or responding to information from one task while simultaneously conducting another.[8] In the case of driving, divided attention involves continuously monitoring information from the roadway to control the vehicle, while simultaneously maintaining awareness of potential hazards surrounding the vehicle. This requires attention to be distributed across the driving scene.[9,10] As the cognitive system has a limited amount of attentional resources, the quality and efficiency of performance of a particular task may be compromised if performed under a divided attention situation.[11] The ability to divide attention is therefore intrinsically related to the ability to perform tasks such as driving, with failures of divided attention a leading cause of motor vehicle collisions.[5,7,10,12,13]

The purpose of the present study was to evaluate the ability to divide attention during a simulated driving task and to determine the relationship between ability to divide attention and an objective measure of glaucomatous neural loss, namely, retinal nerve fiber layer (RNFL) thickness measured using spectral-domain optical coherence tomography

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(SD OCT). The contrast characteristics of the visual stimuli presented during driving simulation were varied in order to impose different demands on the visual system, and also to assess damage to the magnocellular pathway, which has been hypothesized as preferentially damaged in glaucoma.[14]

METHODS

THIS WAS A CROSS-SECTIONAL OBSERVATIONAL STUDY involving participants from the Diagnostic Innovations in Glaucoma Study (DIGS), a prospective longitudinal study designed to evaluate optic nerve structure and visual function in glaucoma. The study was conducted at the Hamilton Glaucoma Center at the Department of Ophthalmology, University of California San Diego (UCSD). Methodological details have been described previously.[15] Written informed consent was obtained from all participants, and the institutional review board and human subjects committee at University of California San Diego prospectively approved all methods. All study methods adhered to the tenets of the Declaration of Helsinki for research involving human subjects and the study was conducted in accordance with the regulations of the Health Insurance Portability and Accountability Act. The study was registered at ClinicalTrials.gov with registration number NCT00221897.

Glaucoma was defined by the presence of 2 or more consecutive abnormal SAP tests or evidence of progressive glaucomatous optic disc changes based on masked assessment of stereophotographs. Suspect glaucoma was defined by the presence of a suspicious appearance of the optic disc (neuroretinal rim thinning, excavation, or suspicious RNFL defects) or elevated intraocular pressure (IOP) (>21 mm Hg). Healthy subjects were recruited from the general population and had IOP of 21 mm Hg or less with no history of raised IOP, and normal SAP testing. Categorization was based on the diagnosis in the worse eye.

At each visit, subjects underwent comprehensive ophthalmologic examination including review of medical history, visual acuity, slit-lamp biomicroscopy, IOP measurement, gonioscopy, dilated funduscopic examination, stereoscopic optic disc photography, SD OCT RNFL imaging (Spectralis; Heidelberg Engineering, Dossenheim, Germany), and SAP using the Swedish interactive threshold algorithm (SITA Standard 24-2; Carl Zeiss Meditec, Inc, Dublin, California, USA). Only subjects with open angles on gonioscopy were included. Subjects were excluded if they presented with a best-corrected visual acuity of less than 20/40, spherical refraction outside ±5.0 diopters or cylinder correction outside 3.0 diopters, or any other ocular or systemic disease that could affect the optic nerve or the visual field.

• **IMAGING AND STANDARD AUTOMATED PERIMETRY:** Spectralis SD OCT (software version 5.4.7.0) was used to obtain average circumpapillary RNFL thickness measurements. Details of its operation have been described elsewhere.[16] RNFL thickness measurements were acquired from a 3.45-mm circle centered on the optic disc consisting of 1536 A-scan points. All images were reviewed by the UCSD Imaging Data Evaluation and Analysis Center to ensure that the scan was centered, that the signal strength was >15 dB, and that there were no artifacts. Scans that were inverted or clipped or those that had coexistent retinal pathologic abnormalities were excluded. The RNFL segmentation algorithm was also checked for errors and corrected according to standard protocols.

SAP was performed using the Humphrey Field Analyzer II (Carl Zeiss Meditec). All visual fields were evaluated by the UCSD Visual Field Assessment Center.[17] Visual fields with more than 33% fixation losses or false-negative errors, or more than 15% false-positive errors, were excluded. The only exception was the inclusion of visual fields with false-negative errors of more than 33% when the field showed advanced disease. An abnormal SAP test was defined as a visual field with a pattern standard deviation with $P < .05$ and/or a Glaucoma Hemifield Test outside normal limits.

• **DRIVING SIMULATOR:** For the purposes of this study, ability to divide attention was assessed by measuring reaction times to stimuli presented during a divided attention protocol during simulated driving. The driving simulator consisted of a typical driving seat, a steering wheel, brake and accelerator pedals, and a 40-inch screen (Supplemental Figure, available at AJO.com). The position of the seat, wheel, and pedals could be adjusted for comfort but the distance between the subject's head and the center of the screen was set at 43 inches. The screen width was 35 inches, resulting in a driving scene with a 45-degree horizontal field of view. Software for the driving simulator was developed at the Hamilton Glaucoma Center, UCSD.

The driving simulator tested the ability to attend simultaneously to 1 of 2 central visual tasks of driving (adjusting speed while following another car that varies its speed and staying in a lane on a winding road) and to a peripheral visual task of perceiving a projected stimulus and responding by pushing a button on the steering wheel. The peripheral stimuli were presented at about 20 degrees of visual angle in the upper right and upper left of the driving simulator screen and at 3 different contrasts (low, medium, and high). The contrast of the stimulus was altered using alpha blending techniques to achieve symbol transparencies of 0.1, 0.4, and 0.9. Therefore, in the case of 0.1 symbol transparency, the symbol intensity and color that the driver perceived was 10% of the symbol intensity and color and 90% of the background intensity and color. The equivalent Michelson contrasts were 0.04, 0.14, and 0.27 for low-, medium-, and high-contrast stimuli, respectively. At maximum screen intensity the divided attention stimulus symbols were pure white, while the background was constant and consisted of a cloudy sky. There were an average