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Extraordinary Claims Require Extraordinary Evidence: Centrally Mediated Preservation of Binocular Visual Field in Glaucoma is Unlikely

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We have read with interest the recent article by Sponsel et al.¹ There is much evidence that glaucomatous damage occurs at the optic nerve head,² and therefore we were surprised by the authors' conjecture that there may be a central mechanism that preserves the binocular visual field in advanced glaucoma.

If indeed there were some central mechanism responsible for "interlocking" monocular visual field defects to preserve binocular function, patients' binocular damage should, on average, be less severe than would be expected if the spatial pattern of damage in both fellow eyes were independent. We tested this simple hypothesis as follows: visual field pairs (24-2, Humphrey Field Analyzer; Carl Zeiss Meditec, Dublin, CA) from patients with glaucoma (mean deviation worse than -2.5 dB in both eyes) were taken from the datasets of previous studies. One dataset ($n = 246^3$) was from Halifax, Canada; the second ($n = 85^{4,5}$), from Rotterdam, the Netherlands, is freely available from <http://www.orgids.com/> (last accessed 7/31/2014). From both datasets, we selected the most recent pair of right and left visual fields from each patient. Similar to Sponsel et al.,¹ we calculated the integrated visual field⁶ as a proxy measure of the true binocular visual field for each of these patients (total $n = 331$). The greater of the two monocular sensitivities was used to represent the "binocular" sensitivity at each location, and the mean sensitivity (MS_{TRUE} , in dB) was derived as a summary index. Then, for comparison, we derived the distributions of the binocular sensitivities (MS_{RANDOM} , dB) that would have been obtained if the right visual field had been paired with the left visual field of 20

different patients who had left MS within ± 2.0 dB of the true left MS. This was possible for $n = 298$ patients.

By comparing MS_{TRUE} with MS_{RANDOM} , a distribution of differences ($MS_{TRUE} - MS_{RANDOM}$) is obtained for each individual patient. Under the null hypothesis of randomness, MS_{TRUE} will be similar to MS_{RANDOM} (mean difference ≈ 0). If indeed there

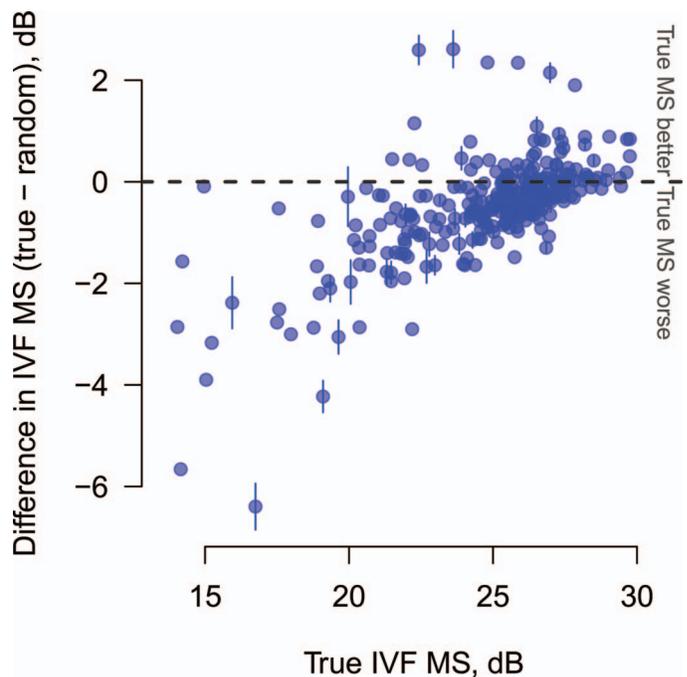


Figure 1. MS_{TRUE} versus mean difference in MS ($MS_{TRUE} - MS_{RANDOM}$) for 298 patients with glaucoma. Error bars representing ± 1 SEM are shown for 50 randomly selected patients distributed across the range of MS_{TRUE} . The data are not suggestive of binocular visual field preservation. A small tendency is shown for MS_{TRUE} to be worse than MS_{RANDOM} (median difference in MS -0.4 dB, interquartile range -0.8 to 0.0 dB).

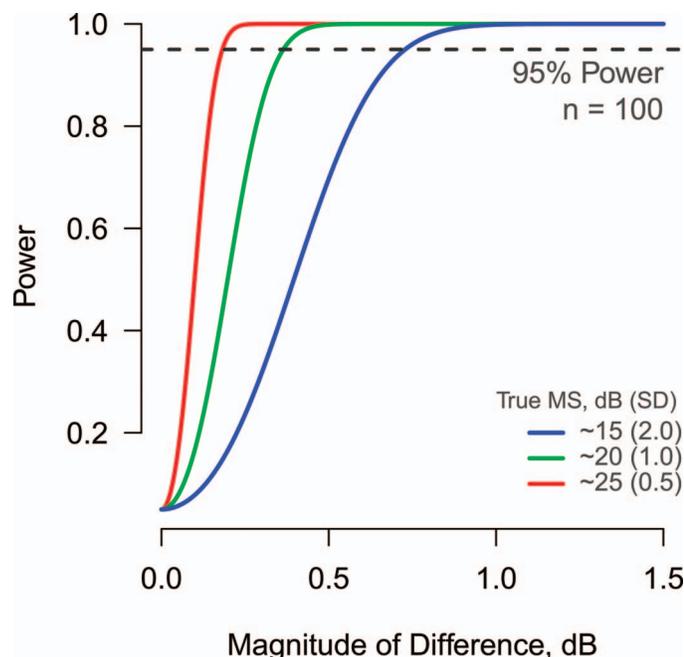


Figure 2. Power to detect differences between MS_{TRUE} and MS_{RANDOM} of varying magnitude when $n = 100$ and between-patient SD of differences is as shown, corresponding approximately to MS_{TRUE} of 15, 20, and 25 dB. A study of this size is powered to detect even a small amount of binocular visual field preservation, should it exist.

existed a central mechanism that minimizes binocular damage, the MS_{TRUE} should be systematically better than MS_{RANDOM} (mean difference > 0).

We found no evidence for such an effect (Fig. 1). In fact, true binocular visual fields were typically slightly worse than the integrated fields derived from randomly matched pairs (median difference between MS_{TRUE} and MS_{RANDOM} , -0.4 dB, Wilcoxon $P < 0.001$). This effect appeared to increase with visual field damage, and it is probably explained by the common disease process and predisposition of anatomically similar fellow eyes. Coexisting neurological damage (e.g., from strokes) would also cause homonymous visual field damage and contribute to this effect.

A power analysis (Fig. 2) suggests that, with our approach, samples of $n = 100$ would provide ample power to detect even small amounts (~ 1 dB) of binocular visual field preservation if such an effect had existed. Thus, the small effect in the opposite direction suggests that centrally mediated binocular visual field preservation is unlikely in glaucoma.

Extraordinary claims require extraordinary evidence. In a paper published nearly 10 years ago, Ioannidis⁷ explained “why most published research

findings are false”: hypotheses with a low prior probability of being true require strong evidence to generate a post-study probability of being true greater than that of being false, but many researchers are misled by hypothesis tests (P values) into overestimating the strength of their evidence.⁷ While we disagree on binocular visual field preservation in glaucoma, we thank Sponsel et al.¹ for a stimulating paper. The question of how, and when, visual field damage impairs real-world visual performance is one of the most important topics in glaucoma, and we hope that many other groups will contribute to this discussion.

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