Influence of ageing on visual field defects due to stable lesions

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Br J Ophthalmol 2007;**91**:1276–1278. doi: 10.1136/bjo.2006.112508

Background: Knowledge about the effects of ageing on visual field defects is very sparse.

Methods: Long-term follow-up records were examined from 28 patients with light-to-moderate visual field defects remaining after surgery for pituitary tumours. All were proven free from tumour recurrences and complicating disorders. Hence, all had isolated, stable lesions of the chiasm. Follow-up periods ranged over 4–18 years (median 9). Using high-pass resolution perimetry, results were analysed from the central-most test locations in the upper temporal and upper nasal quadrants. The former typically bear the brunt of damage whereas the latter are least affected. Each patient contributed results from one eye only. Fixation stability and reproducibility were uniformly good.

Results: Measuring values from the nasal quadrants remained essentially constant throughout the follow-up periods. Results from the temporal (T) quadrants were contrasted with those from the nasal (N) quadrants by calculating the T/N ratios, which were then individually regressed over follow-up periods. Hence, each patient was his or her own control. The absolute majority of regression coefficients (25 out of 28) did not significantly differ from 0.

Conclusion: The rate of age-related loss of neural channels appears to be identical in normal and abnormal visual field areas in subjects with stable mid-chiasmal lesions.

Virtually all tests of vision show a deterioration of performance with increasing age. This also applies to different forms of perimetry.^{1–4} However, there is very little information available on the effect of ageing on visual field defects.⁵ This is due to the fact that most patients undergoing follow-up examinations do so because they suffer progressive disorders. A unique opportunity to evaluate the effect of ageing on non-progressive visual field defects is provided by patients who have been operated on for pituitary tumours and can be proven free from recurrence by neuro-imaging. These patients typically have bitemporal visual field defects of varying severity, with more or less normal nasal hemifields. In this retrospective longitudinal study we addressed whether ageing has different effects on nasal and temporal hemifields.

PATIENTS AND METHODS

Patients

Records from patients who regularly had been followed up after surgery for pituitary tumours were retrieved from the database at the neuro-ophthalmology unit at Göteborg University. Every patient underwent a yearly neuro-ophthalmological examination, including an automated visual field examination. Neuro-imaging was usually performed at 3-year intervals. Patients with asymmetrical chiasmal syndromes were excluded. A suspicion or proof of tumour recurrence or the start of any complicating disorder that could influence visual fields were also grounds for exclusion. A minimum of four examinations and four years of follow-up was required. Further, visual field

thresholds had to be measurable in all test locations, meaning that all subjects with absolute field defects, for example temporal anopia, were excluded.

Perimetry

Visual fields were examined by high-pass resolution perimetry (HRP) (HighTech Vision, Göteborg, Sweden; Version 3). HRP has been described in full detail previously.⁶ In brief, HRP uses different-size ring-shaped targets, of constant contrast, displayed on a cathode ray monitor under computer control. Each target contains a bright core, delimited by darker bands. The core and band proportions are balanced so that their luminances, 25 and 15 cd/m², produce a space-average luminance of 20 cd/m², equal to background luminance. These conditions bring detection and resolution thresholds to near coincidence, making for a simple test task. Exposure time is 165 ms. Using targets stepped by 0.1 log unit in size, the smallest discernible size is determined in 50 test locations between 6 and 28 degrees of visual field radius. Eccentricities smaller than 6 degrees could not be tested, because of computer graphics limitations. Thresholds are defined in minutes of arc. The test was performed in a standardised manner by the same perimetrist. HRP is known to be closely comparable to conventional, differential light sensitivity perimetry in cases with chiasmal syndromes.^{7,8}

Data analysis

To avoid statistical dependencies between eyes, results were analysed for one eye only for each subject. The eye selected was the right eye, unless this eye had a complicating condition like amblyopia or defective motility.

In typical midchiasmal lesions, the upper temporal quadrants are most affected and the upper nasal quadrants are least affected. For that reason, and to avoid any glass rim effects, we selected the three central-most test locations in the upper nasal and temporal quadrants for analysis (fig 1) and calculated the geometric mean values to obtain mean resolution thresholds. Linear least square regressions were calculated over age for the nasal and temporal threshold values separately. For comparison of the nasal and temporal hemifields, we calculated a temporal over nasal ratio for each examination (T/N ratio). For example, a ratio of 2 means that the patient needs twice as much target to reach threshold in his or her temporal field compared to the nasal field. If age affects both hemifields in equal measure, this ratio will remain essentially constant during follow-up. In case of accelerated ageing of one of the hemifields, the T/N ratios should change with time.

RESULTS

Twenty-eight patients met all inclusion criteria. The mean age at the time of study entry was 48.3 years (SD 14.9). The median number of examinations was 6 (range 4–12) and the follow-up periods ranged from 4.3 to 18.5 years (median 9). Figure 1

Abbreviations: DLS, differential light sensitivity; HRP, high-pass resolution perimetry; N, nasal; T, temporal

Figure 1 Examples of follow-up results from four individual patients. Circles and crosses represent mean resolution thresholds in the nasal and temporal study locations, respectively. Lines represent least square regression. Inset: studied test locations (black circles).

shows four examples of individual follow-up results, where both temporal and nasal mean thresholds are plotted against age at examination. Omitting the individual measuring points for better clarity, fig 2 shows regression lines for all 28 patients. The temporal hemifields show larger interindividual variations and larger overall averages, as expected. However, the regression coefficients were not significantly different from 0 in 23 out of 28 nasal hemifields and 24 temporal hemifields ($p < 0.05$). Figure 3 shows the trend for each patient's T/N ratio. Overall, gradients were usually quite small and statistical significance was present in only three instances. The mean T/N ratios at the start and end of follow-up were identical (1.9; SD 0.7 and 1.0). Hence, the overwhelming majority of patients showed no significant change with age in either nasal or temporal hemifields or in the T/N ratios.

DISCUSSION

Primed with the knowledge that virtually all tests of vision show changes with age, we were surprised to find that neither normal nor abnormal visual field areas in our 28 patients with stable chiasmal lesions showed any meaningful deterioration

Figure 2 Regression lines for all subjects, for temporal (above) and nasal hemifields (below), omitting individual measuring points.

Figure 3 Regression lines for the T/N ratios for all subjects. Asterisks identify 3 subjects whose regression coefficients differed significantly from 0.

over a median of 9 years of follow-up. The cause of the lack of change is not immediately obvious. It cannot relate to a poor sensitivity of HRP because the normal HRP database shows a decline with age that is closely similar to other forms of perimetry (fig 4, upper chart). Furthermore, resolution perimetry allows the estimation of the number of functional retino-cortical neural channels and the observed normal age change in HRP agrees very well with the observed age-related decline in optic nerve axons.²⁻⁹ Errors of instrument calibration can be ruled out because calibration was carefully checked on a daily basis and a drift was never observed.

It is important to consider learning or training effects. Most perimetrically naive subjects obtain better results on repeated examinations. In the case of HRP, a minor learning effect is expected between the first two examinations.¹⁰ Consecutive examinations within the next months are expected to be stable.¹¹ All our patients had been examined with HRP prior to surgery and shortly after surgery, that is, before entering the present study. Thus, our patients were well trained. However, long-term learning might take place in a small minority of subjects. Interestingly, the three patients who did present significantly increasing T/N ratios showed improved nasal hemifields rather than deteriorated temporal hemifields.

An important difference between the present study and other studies of age effects in perimetry concerns modes of subject selection. Prior studies were all cross-sectional, that is, each subject contributed one measurement only. Hence prior studies cannot inform on any individual changes with time. Instead, their results may primarily reflect so-called cohort effects. The present study, on the other hand, followed subjects longitudinally. Cohort effects can be shown to occur also among our observations, by converting to a cross-sectional presentation. Then, each patient contributes one result only, for example, from the entrance into the study. When plotted against age, the familiar age-related decline reappears (fig 4, lower chart). Moreover, results from the nasal test locations are well comparable to those of the normal HRP database. A possible explanation for these seemingly disparate observations is that any age-related changes taking place during follow-up periods that are brief in relation to normal life-spans are obscured by normal perimetric variability (BC Chauhan, personal communication, 2006).

Our results appear to run counter to those reported by Kim *et al.*⁵ These authors reported on three subjects with optic atrophy acquired at an early age, who after decades of apparent stability showed a pronounced deterioration of central visual acuity. In the absence of identifiable causes, the deterioration was attributed to a superposition of age-related neural channel losses on a severely depleted neural substrate. There may be

Figure 4 Data from the HRP normative database (above), showing mean of threshold level in studied test locations. Cross-sectional representation of results from present study (below). Here, each patient contributes the nasal threshold at the time of entry into study.

several explanations for the discrepancies between the two studies, including differences in the duration of follow-up, diagnostic accuracy, severity of deficits, measurement techniques and measurement scales. In the case of acuity measurements, severity of involvement may be particularly important, because the relationship between optotype acuity and the fraction of functional neural channels has a quadratic format.¹³ It may be that we might have observed some age-related changes if we had been able to include patients with more severe field defects. Unfortunately, instrumental limitations made such an extension impossible.

HRP differs from conventional differential light sensitivity (DLS) perimetry in several ways and the two methods might provide different perspectives on ageing effects. Data allowing a comparison of ageing effects on stable visual field defects are presently lacking. In DLS, variability of measurements within field defects is known to depend on defect depth. This is not the

case in HRP,¹² suggesting that the latter might provide the clearer picture.

ACKNOWLEDGEMENTS

Data from this article were presented at the International Perimetric Society meeting in Portland, OR, USA, 2006. TR was supported by an IPS travel grant.

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Competing interests: None declared.

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Accepted 1 March 2007

Published Online First 27 March 2007

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