Normal visual fields as assessed by computerized static threshold perimetry in patients with untreated primary hypothyroidism

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Abstract. In this prospective study, 25 consecutive patients with untreated primary hypothyroidism were tested with a highly sensitive perimetric technique, since a high prevalence of visual field defects has been described in this condition. All patients had clinical hypothyroidism, a serum TSH value > 20 mU/l (reference range 0.4–4.0) and decreased/low normal serum total T₄ concentration. Visual fields were tested with fully automated threshold-measuring computerized perimetry of the central 30 degrees field. Interpretation of fields included computer-assisted analysis provided by a perimetric statistical programme package. In 23 patients, conventional inspection and computer-assisted analysis showed no visual field defects. Two patients were excluded from the latter analysis: one patient who did not respond adequately at computerized perimetry and in whom manual field tests were entirely normal; one patient who had low sensitivity values in the uppermost parts of both visual fields owing to markedly swollen upper eye lids. In conclusion, although pituitary hyperplasia has been well documented in primary hypothyroidism, the present prospective study clearly indicates that visual field defects are not a common finding in patients with this disease.

It has been known for over a century that the pituitary fossa may be enlarged in patients with untreated primary hypothyroidism (1). Computed tomography has also shown that in this condition the pituitary gland often is enlarged, sometimes with suprasellar extension (2). There are some previous case reports (3–6) of visual field defects in patients with primary hypothyroidism, but such defects have not been considered common. Yamanoto et al. (7), using kinetic manual perimetry found visual field defects in 10 out of 14 patients with primary hypothyroidism. The aim of the present study was to investigate whether their findings could be confirmed in a prospective study using modern computerized perimetric techniques.

Material and Methods

Twenty-five patients (4 males, 21 females) with untreated primary hypothyroidism referred to the Department of Endocrinology were examined. The study material was gathered in a prospective way by including all patients with primary hypothyroidism except pregnant women and patients with known eye disease. Included patients had clinical hypothyroidism, serum TSH values over 20 mU/l (reference range 0.4–4.0), and decreased or low normal serum total T₄ concentrations (reference range 50–150 nmol/l) (Table 1). Anticipating that different severity and duration of hypothyroidism might be of importance for the occurrence of visual field defects, we divided the patients into two groups according to hypothyroid etiology. The hypothyroidism was due to autoimmune thyroiditis in 11 patients, and was of idiopathic origin in 2 patients (Group 1). The hypothyroidism followed radioiodine therapy because of hyperthyroidism in 12 patients (1 had previous toxic nodular goitre, the others had hyperthyroidism of Graves’ type) (Group 2). The minimum duration of hypothyroidism for each patient was roughly estimated from the patient’s history and any previous laboratory tests (Table 1).
Table 1.
Clinical and biochemical characteristics of the two groups of patients (median value and range).

<table>
<thead>
<tr>
<th></th>
<th>Males/</th>
<th>Age</th>
<th>Estimated</th>
<th>T₃ nmol/l</th>
<th>T₄ nmol/l</th>
<th>TSH mU/l</th>
<th>Prolactin</th>
<th>Reference range</th>
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<td>Autoimmune thyroiditis,</td>
<td>3/10</td>
<td>58</td>
<td>13</td>
<td>0.9</td>
<td>15</td>
<td>39</td>
<td>10</td>
<td>0.9–3.2</td>
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<td>idiopathic origin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>50–150</td>
</tr>
<tr>
<td>Following radioiodine</td>
<td>1/11</td>
<td>56</td>
<td>3</td>
<td>1.3</td>
<td>34</td>
<td>35</td>
<td>7</td>
<td>0.4–4.0</td>
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<tr>
<td>treatment</td>
<td></td>
<td></td>
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Fig 1.
One of the measured visual fields. Static differential light threshold values have been measured at 76 points in the central 30 degrees field resulting in the numerical values (in dB) of Fig. A. A grayscale representation of the sensitivities is also provided (B). Deviations of the measured threshold values from the age-corrected normal reference values are shown in C; the significances of these deviations are illustrated in D. In this field chart the deviation of the measured threshold reached statistical significance (at the 5% level) only at one point (marked by an arrow in Fig. D).
Visual fields were tested with fully automated threshold-measuring computerized perimetry. The 30-2 programme of the Humphrey Field Analyzer was used. This programme measures the differential light threshold at 76 points in the central 30° field (Fig. 1) using a repetitive up-and-down staircase technique with stimulus intensity steps of 0.4 and 0.2 log units (8).

Computerized threshold perimetry is a demanding type of visual field testing. Patients without previous perimetric experience frequently produce abnormal results, primarily characterized by decreased sensitivities in more peripheral areas, i.e., concentric contraction of the visual field (9). In subjects with normal fields these abnormalities gradually disappear on repeated testing. True field defects, on the other hand, do not disappear on re-testing. Therefore, fields which were not immediately classified as entirely normal were re-tested with the same protocol, and if necessary also with kinetic and static manual perimetry on the Goldmann perimeter.

In addition to conventional interpretation of the visual fields by the ophthalmologist, each field was subjected to computer-assisted analysis with a commercially available programme (10, 11), where measured differential light threshold values were compared with age-corrected normal values on a point-by-point basis. The age-corrected reference values are based on results from repeated examinations, performed at four different centres of several hundred normal subjects, which constitute a partially random selection from the normal population (11). Interpretation focussed on detection of even subtle differences between temporal and nasal hemifields, since in early phases, pituitary lesions characteristically affect the inferior crossing fibers in the chiasm thus producing relative field defects in the superior temporal quadrants. The defects first appear and are most pronounced in the central parts of the field (12–14).

The computer-assisted analysis (10, 11) shows the deviation of the measured threshold values from the age-corrected normal values (Fig. 1). This deviation at each point is expressed in dB, where 1 dB equals a difference of 0.1 log units. The mean deviation (MD) is a weighted average difference over all tested points in the visual field. Abnormal points have negative deviations from the age-corrected normal sensitivity levels, and abnormal fields thus have negative mean deviation values. The computerized interpretation programme also shows the significance of each measured deviation (Fig. 1). Significances are displayed on the 5, 2, 1 and 0.5% levels. A point where the measured sensitivity is significantly depressed at the 5% level shows a deviation from the age-corrected normal threshold value which occurs in less than 5% of normals.

The results of the computer-assisted analysis were used to assess the results in the following ways:

1. A frequency distribution showing the MD values of all eyes was plotted.
2. The average threshold deviation of all points in the temporal visual field minus the average deviation in the nasal hemifield was calculated for each eye. A frequency distribution was plotted showing these differences in all fields.
3. A similar frequency distribution was plotted where only points in the superior quadrants were included.
4. The mean number of significantly depressed points per field was determined. This was done at two levels; one analysis included points which were significant at the 5% level or higher, the second analysis included only points at the 1% level or higher. These observed means were compared with the theoretically expected numbers.
5. In each eye the number of significant points (at the 5 and 1% levels) in the nasal hemifield was subtracted from the number of such points in the temporal hemifield. The results from all eyes were displayed in two histograms, one for each level of significance.

These analyses were always performed on the last test in those eyes which had been subjected to re-testing.

Plain radiography of the sella turcica was performed and was interpreted according to Bonneville & Dietemann (15).

Serum T3 (reference range 0.9–3.2 nmol/l) and serum T4 concentrations were measured by radioimmunoassay. Serum TSH concentrations were determined by a sensitive immunoradiometric assay, Pharmacia TSH RIA 100, and serum prolactin concentrations (reference range <15 µg/l) by radioimmunoassay (Table 1).

The study was in accordance with the rules of the Ethical Committee of the Medical Faculty, University of Lund. Informed consent was obtained from all patients.

**Results**

Conventional inspection of the visual fields showed no patients with visual field defects except for an artifact in one in whom the differential light sensitivity was low in the uppermost parts of both visual fields. This was due to markedly swollen myxedematous upper eye lids. One patient did not respond adequately at computerized perimetry. His manual field tests were entirely normal. These two patients were excluded from the computer-assisted visual field analysis.

The results of the computer-assisted analysis of the remaining 23 patients showed:

1. There was no general reduction of differential light sensitivity in the study material. Instead MD values were small and distributed around 0 without any apparent negative skewness (Fig. 2). Mean MD was −0.23 dB (SD 1.3).
2. Measured threshold values did not differ more from the age-corrected normal values in the temporal field than in the nasal field (Fig. 3).
3. The frequency distribution of the differences between the upper two quadrants only was very similar to that shown in Fig. 3.

4. The mean number of significant points were low and very close to the expected mean in normals. The average number of points at the 5% level or higher was 4.3 per field as compared with the theoretically expected number of 3.7 (5% × 74 points). The observed mean at the 1% level was 0.6 points; theoretically expected 0.7 points per field (1% × 74 points).

5. The differences between the number of significant points in the two hemifields were low; the rather few points were symmetrically distributed with no preponderance for the temporal or nasal side (Fig. 4).

In Group 1, radiography was normal in 9 patients, showed enlargement of the sella in 2, and double-contoured bottom in 2. In Group 2, the radiographic findings were normal in all patients. There was no correlation between the findings at radiography and the prolactin values.

Discussion

In the present material there was no evidence of visual field loss. The distribution of MD values was the same as that expected in a randomly selected normal population. Furthermore, there was no sign even of a subtle preponderance of temporal field disturbances in the material. This is in con-
trast with the results of Yamamoto et al. (7) who found a very high incidence of field defects in their material of 14 patients.

Even one eye with a moderately pronounced temporal field defect would have appeared as an outlier in the histograms of Figs. 2–4. A complete hemianopsia would result in an MD value of approximately -13 dB; the difference between the temporal and nasal hemifields or upper quadrants would be approximately 26 dB. The number of significant points (both at the 5 and 1% levels) would be around 36.

The first question then obviously is whether the conflicting results may be explained by differences in perimetric techniques. Yamamoto and coworkers used manual kinetic perimetry on the Goldmann perimeter, but the exact technique is not reported in their article. The outcome of manual perimetry depends on the perimetrists. This type of examination may be sensitive if performed by a skilled operator, but unfortunately it is a subjective procedure. The examiner’s error is added to the inevitable error of measurement introduced by the patient. Fully automated computerized static threshold perimetry is less subjective; the influence of examiner’s bias has been significantly reduced. It is also usually a more sensitive technique than manual kinetic perimetry, regularly identifying field loss at an early stage where the defects often are missed on manual perimetry (16–18). The comparison with age-corrected normal threshold values facilitates the interpretation of the perimetric test results and makes a numerical and objective analysis of the field test results possible (19,20). Thus, any true field defects would have a considerably higher chance of being detected by our techniques of testing the visual field and interpreting the test results, than by the method used by Yamamoto et al. (7).

Are there then any non-perimetric differences in the two studies, which may explain the conflicting results? There may be differences in severity of disease in the two materials. It may be noted, however, that in the material of Yamamoto et al. (7), the extent of visual field change did not correlate with the volume of the sella turcica or total pituitary TSH reserve. In this context, it could be mentioned that in addition to pituitary enlargement there might be other potential mechanisms of visual changes in hypothyroidism, e.g. nerve conduction defects (21) and as indicated by the presence of TRH receptors in the retina (22). The duration of hypothyroidism before diagnosis is of course very difficult to estimate. Although the patients were unselected in the Japanese study the duration of the disease was estimated to a median of 5 years (7), whereas in the present consecutive series the median estimated minimum duration was 13 months in Group 1 and 3 months in Group 2. This possible difference in duration may be of importance, even though it has been observed that hypothyroidism need not be severe or of long duration to induce pituitary enlargement (23,24). Furthermore, normal visual fields were found also in those five patients of the present study in whom the minimum duration of the disease was two years or more.

To the best of our knowledge no other prospective studies have been published where patients with hypothyroidism have been subjected to visual field examination. Smallbridge (25) recently reviewed the clinical features of 159 patients with primary hypothyroidism and radiologic enlargement of the pituitary gland. Sixty patients had undergone testing of visual functions, and defects had been found in 22. These patients obviously represent a highly selected group; not only did they all have enlarged pituitary glands, but many of them were possibly tested because of visual symptoms.

In our prospective non-selected series we could find no patients with field loss despite the use of highly sensitive perimetric techniques. The fact that we examined consecutive patients makes us believe that our results are fairly representative for Western countries. We conclude that, although pituitary hyperplasia has been well documented in primary hypothyroidism, the present prospective study clearly indicates that visual field defects are not a common finding in patients with this disease.

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References


References


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