Identification of functional visual field loss by automated static perimetry

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ABSTRACT.

Purpose: Diagnosis of functional visual field loss, that is, field loss lacking objective corollaries, has long relied on kinetic visual field examinations using tangent screens or manual perimeters. The modern dominance of automated static perimeters requires the formulation of new diagnostic criteria.

Methods: Retrospective review of automated perimetry records from 36 subjects meeting clinical and tangent screen criteria for functional visual field loss. Thirty-three normal eyes and 57 eyes with true lesions, including optic nerve compression, glaucoma, anterior ischaemic optic neuropathy and vigabatrin toxicity, served as controls.

Results: Standard automated perimetry statistics were unable to reliably discriminate organic versus non-organic visual field loss. Subjective evaluation of perimetric maps indicated that functional fields generally could be identified by the presence of severe and irregular contractions and depressions that did not conform to the visual system's neuro-architecture. Further, functional fields generally presented one or more isolated threshold 'spikes', that is, isolated locations showing much better than average sensitivity. On repeated examinations, threshold spikes always changed locations. Visual evaluation for spikes proved superior to an objective computational algorithm. Fairly reliable objective discrimination of functional fields could be achieved by point-wise correlations of repeated examinations: median intertest correlation coefficients equalled 0.47 compared with 0.81 for true lesions.

Conclusion: Functional visual loss can be identified by automated static perimetry. Useful criteria include severe and irregular contractions and depressions, the presence of isolated threshold spikes and poor intertest correlations.

Key words: functional visual field loss – optic nerve – perimetry – visual fields

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Introduction

Most instances of visual field loss have objective corollaries in one or more forms, for example, afferent pupil reflex defects, ocular fundus changes and neuro-imaging abnormalities. In a minority of instances, visual field loss not only lacks such objective corollaries but also presents features that are incompatible with current understanding of visual pathophysiology. Although long labelled 'hysterical', 'psychogenic', 'non-organic', or the like, there is little evidence for causal associations with psychological stress or psychiatric disease (Thompson 1985; Egan 2004; Lim et al. 2005; Pula 2012). The more neutral designation 'functional' has found increasing favour and will be used here.

Key features of functional field loss are peculiar dependencies on test conditions and particularly test distances and test durations. In the most common form, tunnel vision, functional field loss will change its spatial subtense with changes in test distance and the spatial subtense will decrease with time. For example, a functional central field remnant that subtends, say, 20° of angle at 1 m test distance typically will reduce its angular subtense to 10° on doubling the test distance and the remnant will shrink on prolonged examination.

Changing the test distance is easily performed at the old-fashioned tangent screen, but not in its successor, the kinetic perimeter. Instead, perimetrists have come to emphasize the fatigue effect, which typically produces interlacing and/or spiralling isopters (Thompson 1985; Egan 2004; Lim et al. 2005; Hsu et al. 2010; Pula 2012).

With the increasing dominance of automated static perimetry, the skills required for expert manual examinations are becoming increasingly hard to uphold. This may be advantageous in the sense that the ever-present risks of examiner bias are eliminated. On the other hand, automated static perimetry by its very nature cannot exploit the key aspects of functional field loss. Actually, when applied in the standard fashion, automated static perimetry has been held unable to support (or negate) a diagnosis of functional field loss (Smith & Baker 1987). Alternative indicators of functional field loss are clearly needed. The present report focuses on spatial distributions of functional field deficits in automated static perimetry, including a previously not described 'threshold spike sign', and various aspects of test–retest variability, in a retrospective review of 36 instances of functional field loss and appropriate controls, including 25 instances of optic nerve compression.

Methods

The local automated perimetry database was searched for subjects diagnosed with functional visual field loss. Thirty-six cases were identified and their full files were retrieved for retrospective review and validation of the diagnosis. All subjects initially had been referred for evaluation of field loss that had remained unexplained after extensive investigations, usually including neuro-imaging. The subjects were examined in the author's neuroophthalmology consultation service at Sahlgrenska University Hospital, a tertiary-care centre, paying particular attention to pupil reflexes and to results of visual acuity and tangent screen examinations made at minimum two test distances.

For comparisons with a representative variety of differential diagnoses, the perimetry database was searched for subjects diagnosed with unilateral sphenoid wing meningioma with optic nerve involvement, glaucoma, anterior ischaemic optic neuropathy (AION) or vigabatrin toxicity. Subjects who had had but one single examination were excluded as were subjects who had shown deterioration of their visual fields during follow-up. There remained 25 clinically stable instances of meningioma, 13 of glaucoma, nine of AION and 10 of vigabatrin toxicity. All the meningioma patients and all but one of the AION patients had

normal examination results in their non-involved eyes, which also were examined repeatedly as part of the clinical follow-up routine. These 33 non-involved eyes formed a normal control group.

All examinations adhered to the tenets of the Declaration of Helsinki. The study was approved by the institutional review board.

Perimetry

Primarily depended on high-pass resolution perimetry (HRP, HighTech Vision, Gothenburg, Sweden; ver. 3), a 5-min automated static threshold procedure employing so-called vanishing resolution targets, at 50 test locations inside 30° of eccentricity. HRP results are closely comparable with those of conventional, differential light sensitivity perimetry (Wall 1991; Martinez et al. 1995). Occasionally, Humphrey (Zeiss MediTec, Stockholm, Sweden) automated perimetry records were included in the original referral documents and thus available for review.

Statistical analyses

Least-squares linear regressions, product-moment correlation coefficients and receiver-operating characteristic (ROC) curves (MedCalc Software v 12.7.7.0, Ostend, Belgium).

Results

A demographic overview is provided in Table 1, together with means and standard deviations for standard perimetric indices. Most index values did not differ meaningfully between the various groups. The sole outstanding difference was the severity of field loss among the subjects with functional field loss. However, individual instances of equally severe field loss occurred in all the true lesion groups, indicating that the level of loss on its own is an unreliable indicator of aetiology. The same was true for the reproducibility, fixation stability and reaction time indices.

The vast majority (81%) of the functional field defects could be described as variants of tunnel fields. The remainder showed hemianopic patterns, of which two were altitudinal. More detailed descriptions would have been misleading as repeated examinations consistently presented different patterns. Figure 1 shows a typical example, where the initially dominant feature of tunnel vision changed into hemianopia on a second examination. Actually, hemianopia is a misleading description: the seeing hemifield is also severely affected. Most subjects (78%) had bilateral field loss. Figure 2 shows additional examples.

Scrutiny of visual field maps indicated that analysis of the spatial distribution of field loss should have a good potential for discrimination between organic and non-organic field loss. All functional loss maps belonging to the tunnel category showed severe and irregular depressions, and in most instances, ditto contractions (Figs 1– 2), whereas these features never were observed in the maps produced by subjects with true lesions. Unfortunately, irregular contractions and depressions cannot be captured objectively with existing analytical tools. However, another shape-related feature was identified during the visual scrutiny, namely isolated locations with better-than-average threshold levels, or threshold 'spikes'. Figure 3 presents an artistic rendition of three spikes occurring on an irregularly contracted and depressed threshold surface. In conventional grey-scale perimetric maps, interpolation commonly causes blunting of spikes, but they can be easily recognized in the accompanying

Table 1. Demographics and basic statistics on first examination: means (standard deviations).

| Diagnosis | No. cases | Age (years) | Male–female ratio | Overall deviation (dB) | Local deviation (dB) | $%$ deficient reproducibility | $%$ deficient fixation | Reaction time (second) |
|----------------|--------------|-------------|----------------------|---------------------------|-------------------------|----------------------------------|---------------------------|---------------------------|
| Normal | 33 | 54 (8.20) | 0.30 | $-0.2(0.76)$ | 0.7(0.13) | θ | 18 | 0.46(0.05) |
| Functional | 36 | 38 (14.5) | 0.39 | 6.0(0.52) | 1.6(0.44) | 33 | 19 | 0.53(0.13) |
| Meningioma | 25 | 56 (10.6) | 0.16 | 3.1(2.00) | 1.6(0.79) | 12 | 24 | 0.52(0.08) |
| Glaucoma | 13 | 57 (13.7) | 0.62 | 2.5(2.21) | 1.6(0.64) | 31 | 15 | 0.46(0.08) |
| AION | 9 | 53 (13.7) | 0.56 | 4.0(1.37) | 2.5(0.80) | 22 | $\mathbf{0}$ | 0.49(0.10) |
| Vigabatrin | 10 | 40(10.9) | 0.60 | 1.9(0.97) | 1.1(0.38) | 50 | θ | 0.51(0.07) |
| Pooled lesions | 57 | 53 (13.1) | 0.43 | 2.9(1.90) | 1.6(0.81) | 14 | 14 | 0.50(0.08) |

Fig. 1. Examples of different visual field maps from one and the same subject with functional vision loss in the left eye. Top left: Humphrey grey-scale; top right: resolution perimetry thresholds plotted to scale (crossed-out circles signify inability to see large targets [15 dB] used in initial probes for measurable vision, filled circles signify inability to see largest targets [14 dB] used during the remainder of examination). Lower panels show deviations in decibel from age-corrected reference values. Note that the two tests use different decibel definitions and sign conventions. Circles identify threshold spikes (see text for explanation). Note radically different locations of both spikes and measurable vision in the two examinations.

numerical deviation maps (Fig. 1). Spikes are amenable to objective numerical definition, for example, as isolated locations where thresholds deviate ≥4 dB above neighbouring, depressed locations. Application of this algorithm to the present data set resulted in the objective identification of spikes in 64% of the functional fields and in 21% of true field losses (Fig. 4). Inspection revealed that most spikes found in true field losses occurred in the border zones of localized field defects and reasonably could be regarded as normal features of border zones: there is no a priori reason to expect smooth threshold surfaces within border zones. With functional field loss, spikes consistently occurred in apparently random locations. Differentiation between border zone and random locations is more easily achieved by eye than by algorithm and allows a lowering of the minimum peak value to 3 dB. Subjective evaluation resulted in a decreased prevalence

of peaks in the lesion group (11%) and had the opposite effect in the functional group (97%).

Another characteristic aspect of functional field loss is the variability of results between examinations, as exemplified in Figs 1–2. When examined twice (or more) in the same way, intertest variability can be illuminated by scatter plots and regression analysis (Fig. 5). Ideally, test and retest results should be directly proportional and tightly clustered. Repeat examinations were available for 19 of the 36 subjects with functional field loss and for all other subjects. Correlation and regression coefficients were obtained both with and without origin constraints. Non-constrained correlation coefficients provided the best discrimination (Fig. 6). Contrasting correlation coefficients for functional and true field losses, receiver-operating characteristic analysis indicated a sensitivity of 100% and a specificity of 73% at the 0.69 criterion level; the area under the curve equalled 0.91. Inspection of paired maps revealed an even more striking aspect of variation, namely gross variations in threshold surface shapes and spike locations (cf. Figs 1–2).

Discussion

The term tunnel vision has long dominated descriptions of functional field loss, but it is a misnomer from several points of view. The term suggests a visual field limitation equivalent to looking down a smooth-bore tube, whereas the current study presents a picture of a vaguely delimited and perpetually swirling fog or veil of locally varying density, with clearer rifts here and there. These features are difficult to capture in static images (Figs 1–2) and in manual kinetic examinations, partly because of the crowded working conditions close by the fixation point. Affected subjects may well use the term tunnel vision themselves, presumably because of its intuitive appeal and colloquial usage, but in real life, they do not behave like subjects suffering true field contractions from organic disease.

Among the different features of functional visual field loss observed here, the spatial and temporal irregularities of the threshold surface may be the most striking (Figs 1–2). Although irregular contractions and depressions are easily recognized by the trained eye, both from their distinctive appearance and from their failure to conform to the visual system's anatomical architecture, objective identification remains desirable. Unfortunately, numerical descriptors of shapes of threshold surfaces are presently lacking. Analysis by artificial intelligence techniques, for example, neural nets (Andersson et al. 2013), might prove capable of discriminating functional and true visual field loss but cannot provide a single numerical shape index. Another shape feature is more easily accessible for objective evaluation, namely threshold spikes. Again, visual evaluation was found to be more effective (Fig. 4).

A different type of functional field deviation can sometimes be observed in the Humphrey visual field analyzer. This so-called cloverleaf pattern is characterized by relatively low threshold levels in the quadrant centres, with steeply sloping surrounds (Fig. 1, left panel). Because the exam-

Fig. 2. Examples of intra- and interindividual variations in functional vision loss in three subjects. Left panel shows initial results and right panel retest results. Inset: pointers to thresholds spikes.

Fig. 3. Artistic representations of a typical visual field threshold surface in functional visual field loss (in front) and in normal vision (in back), as seen from a lower temporal aspect. The abnormal surface shows severe irregular contractions and depressions and isolated out-of-line spikes (white cones). The figure cannot capture the pronounced test–retest variability that characterizes functional loss of vision (cf Fig. 1).

ination begins in the quadrant centres and proceeds from there in a centrifugal manner, the steep slopes may be attributable to increasing fatigue effects. The cloverleaf pattern appears to be fairly uncommon: it was observed once among five examinations in the present study and in none of the 16 examinations presented by Smith & Baker (1987). Again, objective identification remains elusive.

All automated perimeters provide several numerical indices. Perhaps surprisingly, no standard index has been found capable of reliable identification of functional visual field loss (Smith & Baker 1987). From a statistical group perspective, the present subjects did not deviate radically from normals or subjects with true lesions, except for the magnitude of threshold elevation (Table 1). Occasional instances of sim-

Fig. 4. Relative frequencies of threshold spikes among the diagnostic groups as judged by eye (open bars) and by computer algorithm (hatched bars).

ilar elevations occurred in the control groups. Similar overlaps occurred for the reliability and fixation statistics and for reaction times. Hence, standard indices offer little help in the diagnosis of functional field loss. Scrutiny of numerical deviation maps for threshold spikes is more informative.

Automated perimetry offers yet another opportunity for numerical analysis, namely statistical correlation of results from two (or more) examinations of one and the same subject. Considering the fairly demanding nature of perimetric examinations, it is unrealistic to expect perfect correlations. Nevertheless, the statistical distribution of results from subjects with functional field loss showed but little overlap with those from subjects with true lesions (Fig. 6). The observation that normal eyes generated intermediary correlation levels is of little concern from a differential diagnostic point of view as normal eyes can be recognized from their normal threshold surfaces (Fig. 3).

The present analysis of test–retest correlations can be viewed as a modern counterpart to the classical kinetic approach to functional field loss, which essentially seeks to demonstrate that test–retest variability exceeds expected bounds. A possibly crucial difference concerns target movement: movement might uncover an aspect of functional field loss that is hidden to static perimetry. Unfortunately, this issue is clouded in more than one sense. One concerns the difficulties of adhering to all the rules of expert kinetic perimetry and the other concerns the even less tangible aspects of suggestion and suggestibility. Subjects with functional field loss have long

Fig. 5. Scatter plots of test versus retest thresholds from a control subject (left), a subject with optic nerve compression (centre) and a subject with functional visual loss (right). Datum points have been randomly jittered up to 0.2 dB to minimize overlapping. Inset, linear regression parameters and correlation coefficients. Ideally, datum points should cluster on the diagonal from below left to above right.

Fig. 6. Box-and-whisker plots of correlation coefficients among diagnostic groups. The outlier belongs to a subject with optic nerve compression combined with functional overlay.

been held to have excessive suggestibility. Suggestion and suggestibility may be particularly detrimental in the second major approach of classical testing for functional visual field loss, namely changing the test distance. An interesting alternative way of varying angular subtense is to do an automated kinetic examination, which is possible in some modern bowl perimeters, with and without a field-expanding telescope (Pineles & Volpe 2004). Incidentally, the perimeter used here has the unique features of allowing variation in test distance at will while retaining full control over the stimulus values of its resolution-type targets. These features open a new avenue to static examinations under controlled conditions.

Over the years, investigations of functional field loss have involved a

large number of different examination techniques. The topic seems to have attracted a more modest interest during latter years, presumably because of dwindling access to old-time equipment and uncertainty about the applicability of modern examination techniques. The true prevalence of functional field loss is not well known. Drawing a cautious parallel with the reported prevalence of functional deficits in the field of neurology (Edwards & Bhatia 2012), it appears that the occurrence of functional visual field loss may well be severely underreported. The modes of analysis developed here may help to clarify the situation and to illuminate novel pathophysiological hypotheses (Vuilleumier 2005; Edwards et al. 2012).

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