The Role of Perimetry in the Diagnosis of Neuro-Ophthalmic Disorders and Its Implications to Neural Plasticity of Visual Perception

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Introduction

Formal visual field testing is commonly ordered in patients with neuro-ophthalmic disorders such as optic neuropathies or intracranial lesions involving the visual pathways. However, performing visual field tests may be a challenge in patients confined to a wheelchair, those who are unable to communicate, those with cognitive disorders, or patients with severely decreased vision. Manual Goldmann kinetic perimetry is classically considered to be the gold standard perimetry technique in patients with neurological disorders or very poor vision. However, not all centers have trained personnel capable of performing reliable GVF testing. Thus, there is a need for a faster, less technician dependent, standardized and commercially available test in neuro-ophthalmic practice. This is why in Study A we tested a new generation of perimetry strategy: SITA Fast in these patient populations in a large neuro-ophthalmic university referral center.

It is thought that the visual field improvement seen in approximately 50% of patients following homonymous hemianopia is likely due to brain plasticity. However, much less is known about diseases affecting the anterior afferent visual pathway such as optic neuritis or ischemic optic neuropathy. We do not know why there is improvement of visual function following optic
neuritis in certain patients and not others. Furthermore, why large percentage of patients following optic neuritis recover and there is usually no clinically significant improvement following ischemic optic neuropathy. To be able to answer these questions we first need to describe a perimetry technique for the functional assessment of visual cortical plasticity following optic neuropathy. Thus, in Study B we tested a novel technique, developed by our group on a neuro-ophthalmic patient.
Objectives

- The primary objective (Study A) is to assess the potential role of Swedish Interactive Thresholding Algorithm (SITA) Fast automated static perimetry, compared with that of Goldmann manual kinetic perimetry (GVF), for reliably detecting visual field defects in neuro-ophthalmic practice.

- The second objective (Study B) is to describe a novel objective perimetry technique: functional magnetic resonance perimetry (fMRI-perimetry) developed by us on a neuro-ophthalmology patient.

- The third objective (Study B) is to correlate standard automated perimetry with fMRI-perimetry findings in a patient with recurrent optic neuritis.
Methods

In Study A, we prospectively evaluated 64 consecutive patients seen with either severe neurological impairment (n=50 eyes) or severe vision loss (n=50 eyes) in the Neuro-Ophthalmology Unit at Emory University (Atlanta, Ga) between September 2000 and April 2001. Severe neurological impairment was defined by a score of 3 or 4 on the Modified Rankin Scale (MRS) (MRS 3 = moderate disability: requires some help, but able to walk without assistance; MRS 4 = patient unable to walk: requires permanent help). Severe vision loss was defined by a visual acuity of 20/200 or worse in at least one eye. The following patient inclusion criteria were applied: age 18 years or older, ability to understand instructions, motor ability to carry out a visual field examination (patient able to sit upright for at least half an hour and to press a button in response to visual stimulation). Patients not willing to have both GVF and SITA Fast perimetry on the same day were excluded. Visual field examinations were performed using the GVF and the Humphrey automated static perimeter with the SITA Fast algorithm. Both tests on both eyes were always performed on the same day, with the GVF examination performed first. The GVF was performed by the same skilled technician. Goldmann perimetry was then compared with the pattern deviation and the graytone printout from
the SITA Fast. The black spots on the pattern deviation and the
dark areas on the graytone printout of the SITA Fast correspond to
areas with decreased sensitivity.

**Study B** is an interventional case report of a patient with recurrent
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Unit. We chose the following primary outcome measures: fMRI-
perimetry, automated perimetry with the 24-2 SITA Standard
(MD) protocol and contrast sensitivity (Pelli-Robson chart at 1 m).
The secondary outcome measures were the following: retinal nerve
fiber layer thickness (RNFL), macular volume and thickness, cup-
to-disc ratio, visual acuity (retroilluminated Early Treatment
Diabetic Retinopathy charts at 3.2 m), color vision test, pattern and
mfVEP amplitude and latency. The following inclusion criteria
were applied: diagnosis of unilateral optic neuritis, visual field
defect involving the central 24 degrees, patient willing and able to
perform reliable fMRI testing and automated perimetry. We
considered the pilot patient to be an excellent candidate for fMRI
after performing reliable SITA Standard perimetry six times in his
affected eye within one hour with only one fixation loss in all of
these exams. In addition, he had 0 % false positive errors and only
once 1%. Exclusion criteria were the following: the patient is
unable or unwilling to perform the clinical and experimental testings.
Results

A total of 64 patients were included in Study A. There were 36 men and 28 women with a mean age of 53 years (range, 18-92 years). Patients were divided into 2 groups, depending on their neurological status and visual acuity. Twenty-five patients (17 men, 8 women; mean age, 51 years [range, 18-86 years]) with severe neurological impairment (MRS 3 or 4) were included in the first group. All 25 patients were able to perform both visual field tests with both eyes, and all 50 eyes were included in the analysis. The mean MRS was 3.4 (range, 3-4), and the mean Barthel index was 52.4 (range, 25-85). Five patients with neurological deficits also had 8 eyes with poor visual acuity, ranging between 20/200 and hand motions. The other 42 eyes had a mean visual acuity of 20/30 (range, 20/20-20/100). Thirty-nine patients with severe vision loss (19 men, 20 women; mean age, 54 years [range, 18-92 years]) were included in the second group. Among these 39 patients (representing 78 eyes), 3 patients had 1 eye with a visual acuity of no light perception, and 25 patients had 1 eye with a visual acuity better than 20/200. These 28 eyes were excluded from the study, and the analysis was performed on the remaining 50 eyes. Visual acuity was extremely poor (20/400 or worse) in 34 of 50 eyes. Visual field examinations with GVF were reliable in 77%
of all eyes. Visual fields obtained with the SITA Fast strategy were also estimated to be reliable in 77% of all eyes. Overall, the 2 fields were similar (groups 1, 2, 3, and 4) in 75% of all eyes. Among the eyes of patients with neurological deficits, 35 (70%) of 50 eyes had similar visual field tests on both strategies. However, 11 (22%) of 50 eyes of patients with neurological deficits had normal visual fields (group 4). Excluding these 11 healthy eyes from the analysis, 24 (61.5%) of 39 eyes of patients with neurological deficits had similar visual field defects with both tests. Among the eyes with vision loss, 40 (80%) of 50 had similar visual field defects on both fields. The mean ± SD test time on the GVF perimeter was 7.97 ± 3.2 minutes per eye (range, 3-22 minutes). The mean ± SD test time on the SITA Fast perimeter was 5.43 ± 1.41 minutes per eye (range, 3.03-11.4 minutes). When asked which visual field test they would rather have on their follow-up examination, 58 (91%) of our 64 patients preferred GVF.

In Study B, the patient’s visual functions in his unaffected eye were entirely normal. In his affected eye his high-contrast central visual acuity as assessed by both the Early Treatment Diabetic Retinopathy Study charts and the Snellen chart was normal, except during the second visit when due to his macular star he had mildly decreased visual acuity to 20/25. However, his contrast sensitivity
as evaluated by the Pelli-Robson chart and expressed in log contrast was reduced from 2.25 to 1.65 at the second visit. This improved to 1.70 by the third visit. His color vision was measured by the Ishihara color plates and was reduced from 10/10 to 9/10 (slow). During all three visits he was observed to have a large right relative afferent papillary (RAPD) defect indicative of an optic neuropathy. SITA Standard static perimetry showed circular scotoma present outside ~12° eccentricity and intact central visual field in the right eye and entirely normal visual function in the left eye. He had greatly reproducible results and excellent reliability indeces without any fixation loss. Functional MRI-perimetry in Experimeriment 1 showed selective loss of signal intensity in the retinotopic regions corresponding to the right eye visual field scotomas. In Experiment 2, there was decreased psychometric performance of the affected right eye which corresponded to the performance seen on SITA Fast pattern deviation plot. In Experiment 3 we examined the activation patterns of simulated and pathological scotomas. There was marked difference observed in case of simulated scotoma as there was no significant BOLD activation in that part of V1 where the eliminated visual field was represented. However, in case of pathological scotoma there was gradual decrease of activation in V1 with increasing eccentricity,
and some remaining activation even in the part of V1 corresponding to the scotoma. Optical coherence tomography showed decreased peripapillary retinal nerve fiber layer in all four quadrants along with reduced macular thickness in the affected right compared with the unaffected left eye due to axonal loss. In addition, as a result of secondary peripapillary retinal nerve fiber layer loss there was decreased optic nerve head rim area with resultant increase in cup size.
Conclusions

Study A shows that SITA Fast computerized static perimetry, a new rapid perimetric threshold test, can be used to identify and localize visual field defects in most patients with neuro-ophthalmic diseases. Furthermore, our results suggest that for the general ophthalmologist or neurologist, visual field testing with SITA Fast perimetry might even be preferable to GVF (especially if the GVF is performed by a marginally trained technician) even in patients with severely decreased vision or who are neurologically disabled.

In Study B we used multiple stimuli to obtain retinotopic maps of the visual field quadrants, and described a novel technique developed by us for the mapping of perceptual and various neural visual field deficits provoked by neuro-ophthalmic disorders, so called fMRI-perimetry. This technique allows us to assess neural plasticity processes underlying spontaneous and induced (by rehabilitation and or medication) recovery. Functional MRI-perimetry was designed to be useful and relatively easily applicable in everyday clinical practice. We found that cortical activity in low-order (V1, V2, V3 and V3a) and high-order visual systems is reliably mapped by fMRI-perimetry and correlated well with performance on SITA Standard perimetry. In the future, we need to further validate this method on larger patient population.
Publications by the author pertinent to the dissertation:


Other publications and lectures by the author:


