SHORT REPORT

Spatial vision in visually asymptomatic subjects at high risk for multiple sclerosis

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Objective: To investigate the state of spatial vision in visually asymptomatic subjects at high risk for multiple sclerosis.

Methods: Fifteen subjects suffering a first neurological episode suggestive of multiple sclerosis in clinical presentation, immunological profile, and magnetic resonance imaging, were examined with a new, sensitive test of spatial vision, rarebit perimetry. None had symptoms or signs of optic neuropathy.

Results: Results of rarebit perimetry were significantly worse than those of 15 age matched normal controls ($p=0.01$); seven patients (47%) were outside normal limits. One patient only obtained abnormal results in high pass resolution perimetry.

Conclusions: Rarebit perimetry may help to close the sensitivity gap between clinical examinations and neuroimaging.

Advances in neuroimaging have highlighted an extensive involvement of the central nervous system at early stages of multiple sclerosis (MS), even at its very first manifestation. The first bout usually produces clinical signs attributable to a single lesion, most commonly in an optic nerve, in the brain stem cerebellum, or in the spinal cord. However, most of the lesions revealed in neuroimaging reside in the cerebral hemispheres, particularly in the periventricular regions, and are clinically silent. This silence points to the need for better tools for assessing neural function. Accurate assessment has become increasingly important with the advent of new treatment modalities.¹

When considering what functions and pathways might be best accessible for refined assessment, vision and the visual

pathways emerge as good candidates. Strong advantages include the possibility to probe function in small subsets of fibre bundles and the pathways' wide extension throughout the hemispheres, including the posterior periventricular regions. Although perimetry might seem ideal for the task, standard perimetry actually has a limited ability to detect small degree neural damage. Clinicopathological correlations have shown that neural channel losses must amount to 25% to 50% before standard perimetry returns consistently abnormal results. Experimental studies have revealed similar sensitivity gaps.² To meet the need for a more sensitive assessment, a new test principle, rarebit probing, has been developed and shown to have superior sensitivity in one model disorder—that is, chiasmal compression.³ Rarebit perimetry was used in this study of 15 subjects with a first, non-visual bout of focal, neurological disease. All had immunological and neuroimaging abnormalities predictive of MS.

METHODS

Patients were recruited sequentially from Sahlgren's Hospital's emergency neurological service where they had presented with a first neurological episode suggestive of MS. Those who had symptoms and/or signs of acute optic neuritis were excluded. Table 1 summarises key clinical data. Cerebrospinal fluid was assayed for oligoclonal banding. Magnetic resonance imaging (MRI) used a MS protocol.

Age matched normal controls were recruited among healthy blood donors and hospital staff. All subjects underwent a detailed clinical neuro-ophthalmological evaluation, including visual fields by high pass resolution perimetry

Abbreviations: MS, multiple sclerosis; MRI, magnetic resonance imaging; HRP, high pass resolution perimetry

Table 1 Summary of patient data

Case	Age (y)	Sex	Duration weeks	Symptoms	Hit rate (%)
1	22	m	1	sensory: hemi	97
2	22	f	1	motor: hemi	95
3	24	f	4	motor: legs	86
4	25	m	2	motor: arm	85
5	25	m	6	sensory: arm	77
6	26	f	1	sensory: legs	98
7	26	m	6	motor: face+arm	97
8	30	m	16	sensory: legs	87
9	31	f	2	sensory: legs	92
10	31	f	1	vertigo	91
11	34	f	1	sensory: leg	95
12	36	f	2	sensory: hemi	95
13	41	f	14	motor: arm	88
14	45	m	1	sensory: legs	98
15	49	f	1	vertigo, sens arm	93

depended on perimetric techniques that are now obsolete. Studies using modern, computer assisted perimetry have identified some abnormality in many fellow eyes.^{5 11–13} The Optic Neuritis Treatment Trial (ONTT) is the most representative by virtue of its size (448 subjects) and its strict quality controls. Keltner *et al* reported that 69% of the ONTT fellow eyes showed perimetric abnormalities.¹² These were labelled minimal in 62%. One quarter (26%) of all subjects had moderate or severe fellow eye abnormality. Most of the fellow eyes were found normal at a six month follow up.¹⁴ It may be that many of these subjects in reality had had truly bilateral neuropathy. There was evidence of chiasmal or retrochiasmal involvement in 3%. Therefore, the ONTT fellow eye study cannot clearly illuminate perimetry's capability to identify clinically silent lesions in early demyelinating disease. Furthermore, previous neurological episodes were not grounds for exclusion.

In a previous study of visual field defects from a variety of visual disorders, rarebit perimetry proved fully capable of accurate topographical diagnosis.³ However, it was unable to provide topographical information in this study, except for the single instance of a homonymous depression. The other subjects presented apparently randomly distributed losses of small areas and depths, without a central field preponderance. Hence, location(s) of injury cannot be pinpointed. This would be the expected outcome of a multiplicity of lesions along the visual pathways, where each lesion is small in relation to the pathways' cross section. Failure to identify homonymous components among the scattered depressions observed here cannot be taken as evidence against retrochiasmal lesions because homonymity cannot be taken for granted with lesions of small spatial extents.¹⁵ Furthermore, homonymity will be difficult to recognise if disseminated lesions involve the visual pathways bilaterally. The reasoning suggests that precise correlation with macroscopic MRI results cannot be expected. Indeed, none was found, except for the patient with the homonymous field depression.

An alternative interpretation of the observed deficits is that they are non-specific corollaries of disease and attributable to a general impairment in psychophysical performance. However, the internal test evidence points in the opposite direction. The rarebit test provides three indices of general performance level—that is, numbers of procedural errors, fixation stability, and reaction times. These indices indicated that the patients tended to perform somewhat better than did the controls.

Presumably, a large majority of the subjects studied here will with time accumulate an increasing number of lesions and present the picture of clinically definite MS.¹⁶ It will be interesting to see whether this expected course is associated with deteriorating rarebit perimetry results. If the test proves capable of reflecting progression of the disease, it might provide a prototype metric of functional neural channels in

MS. The low cost of the instrumentation, its simplicity of use, and the short duration of the test, would be important advantages in such a setting.

Rarebit perimetry software

The rarebit perimetry software (in Microsoft Windows format) is available free of charge from the author.

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