Short report

Effects of induced hyperthermia on visual evoked potentials and saccade parameters in normal subjects and multiple sclerosis patients

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SUMMARY A convenient method for raising body temperature has been developed and used to evaluate temperature effects on visual evoked potentials and saccade reaction time and velocity in five normal subjects and five patients with multiple sclerosis.

The value of visual evoked potential (VEP) recording^{1,2} and quantitative electrooculography (EOG)^{3–5} in the diagnostic evaluation of patients with multiple sclerosis (MS) is well-documented. Both techniques allow subclinical abnormalities to be detected in a significant number of patients. The symptomatic effects of changes in body temperature in MS also are well-known,^{6–9} and the effects of induced hyperthermia on central nervous system conduction in MS have been studied with various electrophysiological techniques. These include electronystagmography,¹⁰ double-flash discrimination¹¹ and VEP recording.^{12,13} We describe a method for raising body temperature which can conveniently be used for neurophysiological studies and present preliminary results of the effects of induced hyperthermia on the pattern VEP and on saccade parameters in normal subjects and MS patients.

Patients and methods

Five normal volunteers (three females, two males), aged 20 to 28 years, who denied any visual or neurological symptoms and five MS patients who were in a stable state were studied (table).

The subjects, wearing underclothes and hospital cotton gowns, were wrapped inside a "body-bag"

(fig 1) and sat in a dental chair. Heating was carried out over a 30 to 45 minute period by blowing hot air through the narrowed lower opening in the bag, using two commercial hair dryers. A combination of heating lamps and immersion in hot water were used for heating in two of the MS subjects (Cases 4 and 5). Oral temperatures were measured with a mercury thermometer at five to ten minute intervals during heating and prior to each test. Temperature rise was 0.7°–1.5°C in the normal subjects and 0.3°–1.1°C in the MS patients. The procedure was tolerated well but one MS patient complained of nausea and headache, and another of dizziness. None experienced deterioration of vision.

Pattern-reversal VEPs were recorded from an active midline electrode at Oz (10–20 system) during monocular central field (3° radius; 12' checks) stimulation.¹⁴ The latency and amplitude of the major positive component (P2 or P100) of the VEP were measured. The VEPs were recorded using a similar technique in Cases 4 and 5 who were studied at King's College Hospital, London.² Reaction times and peak velocities for abducting and adducting saccades were measured for each eye in the five normal subjects and three MS patients (Cases 1–3) using a technique described elsewhere.^{5,15} The VEP and saccade studies were performed before heating and again after completion of the heating procedure. Electrodes for recording the VEP and EOG were positioned securely at the beginning of the study using Grass electrode jelly or collodion.

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Table Details of the five MS patients studied

Case	Sex	Age (yr)	Duration of disease	Clinical category	Visual involvement	Eye movements	Other manifestations	Temperature sensitivity	VEP†
1 (PI)*	F	26	3 yr	CD	—	Bilateral INO	Spinal cord	+	Abnormal bilaterally
2 (SP)*	M	28	4 yr	CD	—	Nystagmus	Cerebellar and cord	—	Normal
3 (CP)*	M	52	4 yr	CD	—	R abducens paresis	Cerebellar and cord	—	Normal
4 (JH)‡	F	36	3 mth	EPL	R optic neuropathy; VA 6/18	Nystagmus	Cerebellar and cord	—	Normal
5 (IC)	F	61	3 mth	EPL	—	Nystagmus	Cord	—	Normal

CD —clinically definite MS

EPL —early probable or latent MS (McDonald & Halliday, 1977)²²

INO —internuclear ophthalmoplegia

* Patients in whom saccadic reaction times and velocities were measured.

† Visual evoked potentials prior to heating.

‡ Subsequently developed typical relapsing MS.

Fig 1 The "body-bag" used for heating.

Results

Visual evoked potentials In the normal subjects the P2 latency fell by 2 to 6 ms after heating in six eyes, increased by 2 ms in one eye and remained unchanged in three eyes (fig 2A). The P2 amplitude fell by 4% to 26% in eight eyes, increased by 12% in one eye, and remained unchanged in one eye after heating (fig 2B).

The VEPs were normal in four of the MS subjects before heating. After heating in these four cases, the P2 latency fell by 2 to 6 ms in five eyes, and increased by 3 ms in one eye (fig 2A). P2 amplitude fell by 13% to 60% in seven eyes and increased by 26% to 50% in three eyes (fig 2B). In each patient the response remained within normal limits after heating. In the fifth patient (Case 1), who had bilaterally delayed VEPs before heating, the right eye latency increased by 8 ms, while the amplitude of the right eye response fell by 28% and that of the left eye response by 66% after heating. **Saccadic studies** Reaction times and velocities were within the normal range (Mastaglia *et al* 1979)⁵ in each of the normal subjects before heating and showed only minor changes after heating. Reaction times fell by 1%–9% in four patients and rose by 2% in one patient, while velocities showed changes of 0.1%–0.4% in four patients. Reaction times were abnormal in one of the three MS patients studied (Case 1) and showed increases of 0.5%–4% after heating. Velocities did not change significantly after heating in Case 2, but fell in Cases 1 and 3. In Case 1, previously normal abducting velocities fell by 27% and adducting velocities, which were considerably reduced before heating, fell by a further 10%. In Case 3, adducting velocities were normal before heating and fell by 46% after heating.

Discussion

The "body-bag" method for heating offers advantages for electrophysiological studies over other methods such as the heat cradle,¹⁰ humidified "hot-box"⁸ and hot water immersion.^{11 16} The method allows ready access to any part of

Fig 2 (A) Latencies of the P2 component of the visual evoked potential before (open circles) and after heating (full circles) in normal subjects and MS patients. (B) Amplitude of the P2 component of the visual evoked potential before (open circles) and after heating (full circles) in normal subjects and MS patients.

the body and allows the subject greater freedom of movement.

While the changes in VEP latency in normal

subjects after heating were less than 10% and were not statistically significant, amplitude changes were more marked (reductions of up to 26%) as was found by Matthews *et al.*¹³ Whether such changes are the result of alterations in skin resistance or stimulus perception resulting from temperature effects on the skin or ocular mediae, or result from physiological changes in impulse conduction in the visual pathways remains to be determined. A temperature-induced reduction in nerve fibre action potential amplitude has been shown in the squid giant axon¹⁷ and the possibility that an increase of temperature may alter the temporal pattern of impulse transmission or cause conduction block in some nerve fibres in the visual pathway has been considered.^{13 18}

Our VEP findings in the MS subjects agree with those of Matthews *et al.*¹³ who also found a fall in P2 amplitude without significant latency changes after heating. In the present study an appreciable increase in latency occurred in the patient whose VEPs were already delayed before heating, and only minor changes occurred in the other four patients with normal responses. Unlike Matthews *et al.*¹³ who found a comparable reduction in P2 amplitude in their normal and MS patients, we found considerably greater amplitude reductions after heating in two of the MS patients than in any of the control subjects. Reduced P2 amplitude and increased latency after heating may be due to changes in conduction in demyelinated nerve fibres in the visual pathway. It is known from experimental work in the peripheral nervous system that conduction in demyelinated fibres is extremely temperature sensitive.^{19 20} Amplitude reduction without latency change would be more readily accounted for by reversible conduction block in demyelinated nerve fibres than by slowing of conduction, which would be more likely to cause a delayed response. Transient VEP amplitude reduction without latency change has also been shown to occur after exercise in some MS patients.²¹

Temperature effects on saccade parameters have not been reported previously. The finding of substantial reductions in saccade velocities after heating in two of the MS patients suggests that conduction in the ocular motor pathway in demyelinating disease is also affected by temperature increase, as in the visual pathway and peripheral nervous system. Reduction in saccadic velocity after heating may result from failure of high-frequency repetitive firing in saccade generator neurones.

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