

Short report

Pattern visual evoked responses in hereditary spastic paraplegia

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SUMMARY Pattern visual evoked responses were studied in 13 patients from nine families with dominant hereditary spastic paraplegia and in seven sporadic cases. The responses were normal in all the dominantly inherited cases but abnormal in three of the seven sporadic cases.

Hereditary spastic paraplegia (HSPP) or Strümpell-Lorraine disease is characterised clinically by progressive lower limb spasticity¹ and pathologically by degeneration of the corticospinal tracts and (to a lesser degree) of the posterior columns and spinocerebellar tracts.^{2,3} The condition is usually dominantly inherited but recessive and X-linked forms also occur.⁴⁻⁶ Reduced visual acuity and optic atrophy have been reported¹⁻⁵ but there is little data on the frequency of visual involvement in the different genetic forms of HSPP.⁷⁻⁹ We studied the visual evoked response (VER) to pattern reversal in a group of patients with HSPP with normal vision to determine how frequently subclinical involvement of the visual pathway occurs.

Patients

Fourteen patients (eight males and six females, cases 1-14, table) from Newcastle upon Tyne and six from Perth, Western Australia were studied. Their mean age was 43.9 years; mean duration of symptoms 19.8 years. All had slowly progressive lower limb spasticity without relapses or remissions and none had visual symptoms. All had mild pyramidal weakness of the lower limbs with pathologically brisk tendon reflexes and extensor plantar responses; three also had spasticity and hyperreflexia in the upper limbs. Six had bilateral pes cavus. In 12 cases there was reduced appreciation of vibration sense in the lower

Table Summary of clinical and neuro-ophthalmic findings in 20 patients with progressive spastic paraplegia

Case	Sex and age (years)	Duration of symptoms (years)	Family history	Visual acuity*		VER
				R	L	
1	F, 33	8	+	6/9	6/6	N
2	M, 10	6	+	6/5	6/5	N
3	M, 53	10	+	6/9	6/6	N
4	M, 56	36	+	6/6	6/6	N
5	M, 54	24	+	6/9	6/9	N
6	M, 46	15	+	6/5	6/5	N
7	F, 56	30	+	6/9	6/9	N
8	F, 31	23	+	6/6	6/6	N
9	M, 14	4	+	6/5	6/5	N
10	M, 30	20	-	6/5	6/5	N
11	F, 47	5	-	6/6	6/6	R delayed
12	M, 52	12	-	6/9	6/9	N†
13	F, 52	14	-	6/6	6/6	N
14	F, 61	20	-	6/9	6/9	R & L delayed
15	M, 55	35	+	6/36	6/5	R absent†
16	M, 29	8	+	6/6	6/6	N
17	F, 56	50	-	6/9	6/6	N
18	F, 54	33	+	6/12	6/9	N
19	M, 52	22	+	6/5	6/5	N
20	F, 37	27	-	6/5	6/5	N

*Corrected for refractive errors. †Post-traumatic visual loss.
‡Normal P2 latencies but increased inter-ocular P2 latency difference.
N=normal.

limbs without impairment of other sensory modalities. Apart from case 15 who had unilateral post-traumatic visual loss, the visual acuity, colour vision, visual fields and optic discs and retinae were normal in all cases.

The 13 familial cases came from nine families, each with affected members in at least two successive generations indicating autosomal dominant transmission. Cases 1 and 2 were mother and son, and cases 3, 4, 5 and 6 were brothers.

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Method

VERs were recorded from Ag/Ag Cl₂ disc electrodes during monocular pattern stimulation. The active electrode was at Oz, reference electrode at Cz or Pz (Perth study) (10–20 system). In the Newcastle study a television pattern generator was used for stimulation.¹⁰ The frequency of reversal of the frame-locked pattern was 2 Hz (transient VER) or 12 Hz (steady state response). The transition time for frame pattern reversal was 20 ms. At the viewing distance of 1.7 metres the screen subtended angles of 17° 12' and 13° at the eye; each check had a visual subtense of 50'. Maximal contrast was used, luminance was kept constant; 128 responses were averaged using a Medelec DAV 6 digital averager triggered by each pattern reversal. In the Perth cases pattern stimulation was carried out using the rotating mirror system; full details of the technique are given elsewhere.¹¹ Subjects fixated on a central spot on the screen and those with refractive errors wore corrective lenses. The latencies of the major positive component (P2 or P100) and of the first and second negative peaks (N1 and N2) were determined. The N2–N1 latency difference was used as an index of temporal dispersion, and the amplitude was defined as the N1–N2 potential difference. The interocular P2 latency difference was also calculated. Normal ranges for these parameters were established in 32 healthy volunteers (aged 12–57 years) in the Newcastle study and 50 normal subjects (aged 17–65 years) in the Perth study by taking the means \pm 2.5 standard deviations. The upper limit for P2 latency was 131 ms in the Newcastle study and 113 ms in the Perth study,¹¹ and for the P2 interocular latency difference 6 ms in both series.

Results

All VER parameters were normal in 17 of the 20 cases, including all of the six Perth cases. In

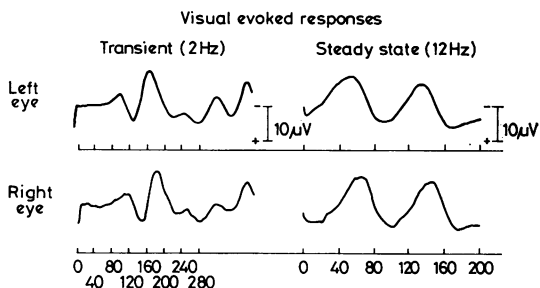


Figure VER tracing from case 11 showing a delayed response on the right with prolonged P2 latency of the transient response and delay in the waveform of the steady state response.

the remaining three cases (11, 12, 14) there were unilateral or bilateral latency changes. In case 11 the P2 latency for the left eye was normal (128 ms) while that for the right eye was prolonged (146 ms) (figure). In case 12 the P2 latencies for the two eyes fell within the normal range (R 120 ms; L 108 ms) but the interocular latency difference was increased (12 ms). Case 14 had bilaterally delayed responses, the right (156 ms) and the left (148 ms). The three patients with abnormal VERs were all sporadic cases. Each had previously had a normal myelographic study, and a CSF γ -globulin estimation performed in two cases was normal; the third case had a normal CSF protein level but a γ -globulin estimation was not done.

Discussion

The present findings of normal VERs in cases of dominant HSPP and abnormal responses in three of seven sporadic (presumably recessively inherited) cases contrast with those of Happell *et al.*⁷ In that study flash VERs were performed in six patients with recessive HSPP and five with dominant HSPP. Responses were abnormal in nine cases, with greatly increased latencies, and borderline in the other two. Although flash VERs were not recorded in the present study, it is unlikely that abnormalities would have been detected with the flash VER in cases with normal responses to pattern reversal. The most likely explanation for the discrepant findings in the two studies is that involvement of the visual pathway occurs in some families with dominant or recessive HSPP but not in others.

The finding of abnormal VERs in some sporadic cases of HSPP is open to two interpretations. Firstly, the visual pathway may be involved in these cases as part of a multisystem degeneration. Alternatively, they may have a chronic progressive form of spinal multiple sclerosis with asymptomatic involvement of the visual pathway rather than HSPP. The VER abnormality found in these cases, namely a unilateral or bilateral delay, is indistinguishable from that found in patients with demyelinating optic neuropathy.¹² Although there were no other features of MS in these cases, this possibility cannot be excluded as a proportion of such cases are found to have demyelinating disease at post-mortem.¹³

Further studies are required to determine the frequency of visual involvement and the extent of phenotypic variation in the different genetic forms of HSPP.

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