

A study of posterior column function in familial spastic paraplegia

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SUMMARY A family is described in which affected members have clinical features consistent with the late onset form of Strümpell's Familial Spastic Paraplegia which is of dominant inheritance. Abnormalities in cortical somatosensory responses to peroneal nerve stimulation were found in all affected members of the family and in several who were clinically unaffected. In some cases responses were better defined at slow rates of stimulation. Peripheral nerve conduction velocity was normal. These changes are consistent with previous findings of degeneration in the posterior columns at necropsy and with a dying back process in the first sensory neuron. Clinically unaffected members of the family with abnormalities in the somatosensory response may represent asymptomatic heterozygotes.

An early description of familial spastic paraplegia was given by Strümpell¹⁻³ but the four families described by Seeligmüller⁴ may have represented the same condition. In reviewing the literature Ozvath⁵ found less than 145 cases with findings consistent with Strümpell's original description. These included a spastic gait with increase in muscle tone and hyperactive stretch reflexes but a few patients also showed other features such as optic atrophy. When the diagnostic criteria were restricted to hereditary progressive weakness and spasticity of the lower extremities Holmes and Shaywitz⁶ could only identify 104 cases. However a number of cases have been described in which there was also clinical evidence of posterior column involvement.^{7,8} Neuropathological studies have only been carried out in a small number of cases but in the two described by Behan and Maia⁹ there was degeneration of the posterior columns particularly at high levels in addition to severe involvement of corticospinal pathways.

In several studies measurements have been made

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of nerve conduction velocity,¹⁰ visual evoked responses to flash stimulation,¹¹ to pattern stimulation,¹² and spinal¹³ and cerebral¹⁴ evoked responses following median nerve stimulation. In the present study a family is described in which the clinical presentation is consistent with Strümpell's familial spastic paraplegia. In addition to clinical evaluation, and in order to assess the integrity of the posterior column along the whole length of the spinal cord, cerebral somatosensory responses following stimulation of the common peroneal nerve have been studied.

Methods

We have studied 16 members of the family including the patient originally referred for assessment. Evaluation of the patients included full neurological examination together with the recording of somatosensory evoked responses.

Somatosensory evoked responses were recorded through surface stick-on silver-silver chloride electrodes at a point 1.50 cm behind the Cz position with reference electrode at Fz according to the 10-20 system. Recordings were made with Elema Schonander EEG equipment (high frequency cut-off 700 Hz, time constant 0.15 seconds) together with a Hewlett Packard 5480A signal analyser which was used to average 128 sweeps. A Disa Ministim provided stimulation that was in the form of a rectangular pulse of 500 microseconds duration and an

amplitude that produced a minimal motor response when delivered to the common peroneal nerve at the knee. Stimuli were delivered at a frequency of 0.5 and 1.2 or 2 Hz in order to determine how far the characterisation of the response was dependent on frequency of stimulation. Control values for the somatosensory responses were taken from 10 healthy members of staff who volunteered for the examination.

Motor nerve conduction velocity was studied in the median and common peroneal nerves in the proposita and three other members of the family and in the proposita sensory conduction was also studied in the median and ulnar nerves.

Results

CLINICAL PRESENTATION

The proposita, a female patient was born in 1913 and in about 1950 began to drag her right leg while walking, subsequently developing progressive difficulty in gait with cold feelings in the extremities, difficulty in balance and, since about 1959, urgency of micturition. Examination showed no abnormality in the cranial nerves or in the upper limbs but in both lower limbs power was diminished with lively tendon reflexes and clonus at the left knee but a depressed left ankle jerk. Plantar responses were extensor and abdominal reflexes absent. Touch and pin prick sensation were intact over the limbs and trunk and vibration and joint sense over the toes on either side. Using the extended sensory examination described by Wall and Noordnobs¹⁶ errors

made in the goggle localisation procedure ranged from 3 mm in the right calf to 54 mm in the left calf. Other sensory tests described in this protocol showed no abnormality.

The genealogy of the family is shown in the figure. The mother of the proposita had developed difficulty in walking in her early thirties and in the last eighteen years of her life had been confined to a wheelchair and for the last eight had worn a Foley catheter. She died at the age of 79 years. The older sister of the proposita had no history of any neurological disorder but on examination showed a slight deficit of postural control in the upper arm; power in the lower limbs was intact but vibration sense was depressed at the toes. Abdominal reflexes were absent and knee and ankle jerks were lively with extensor plantar responses. The younger sister had had an episode of virus labyrinthitis 10 years previously but prior to that had developed an abnormality in her gait. On examination there was a mild degree of unsteadiness on walking heel to toe. There was also some decrease in muscle power in the lower limbs with impairment of vibration sense, lively tendon reflexes, brisk abdominals and extensor plantar responses. In the subsequent generation, no one gave a history of impairment of gait but one daughter of the proposita and the daughter of her oldest sister each had symmetrically lively reflexes but with flexor plantar responses. In the fifth generation, none of the individuals examined showed any neurological abnormality on clinical examination.

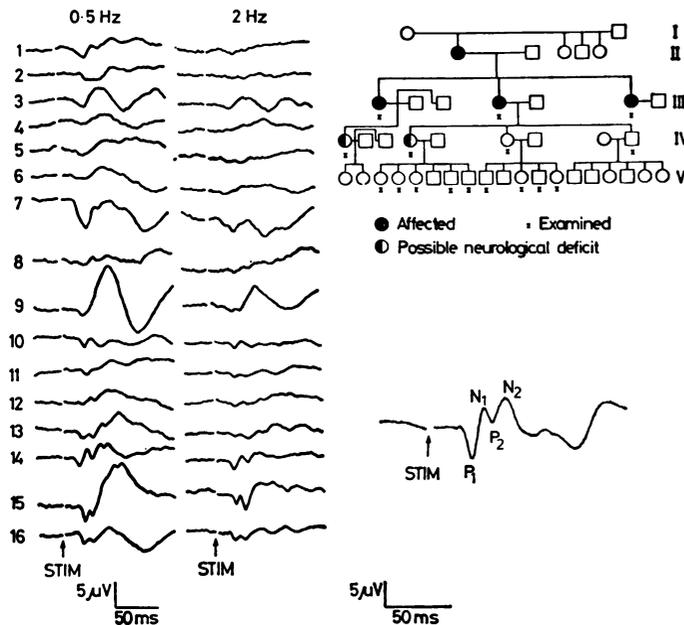


Fig Examples of cerebral somatosensory responses following common peroneal nerve stimulation at different frequencies for the 16 members of the family who were studied. The family tree is also illustrated together with a somatosensory response from a control subject. The nomenclature of the deflections on this illustration is based on that described by Tsumoto et al.¹⁸ Positive deflection downwards at every instance.

NEUROPHYSIOLOGICAL STUDIES

Somatosensory potentials evoked by stimulation of the common peroneal nerve at the knee in the 16 patients studied together with the averaged response in our control population are illustrated in the fig and the table. Responses were considered to be

Table SEP latency values (ms): control and patient data

SEP peak*		P1	N1	P2	N2
Controls					
Mean and standard deviation		33.4 ±1.89	45.6 ±2.97	55.4 ±2.73	74.9 ±4.39
Patients	Age (yr)				
1.	65	42	50	63	84
2.	59	44	58	64	82
3.	34	38	62	96	
4.	45	42	72	116	
5.	20	36	66	84	100
6.	14	44	66	140	
7.	11	39	50	58	72
8.	66	38	52	60	74
9.	12	34	70	110	
10.	43	32	42	55	72
11.	39	32	42	48	68
12.	26	31	42	48	66
13.	24	32	40	48	60
14.	22	30	38	48	61
15.	20	32	38	42	74
16.	16	33	40	48	68

*To electrical stimulation of common peroneal nerve at the knee.

abnormal if the individual components were poorly differentiated, of prolonged latency or unduly dispersed. In subjects 1 to 9 the responses were considered to be abnormal. In the proposita and her two sisters (subjects 1, 2, and 8) there was an ill-defined response at a stimulation frequency of 0.5 Hz and a barely observable response to common peroneal nerve stimulation at a stimulation frequency of 2 Hz. The two subjects (3 and 4) who showed exaggerated reflexes without any clinical history had a dispersed response with prolonged latencies of later peaks at a stimulation frequency of 0.5 Hz (table) and subject 4 also had an ill-defined response at 2 Hz frequency. Latencies of the abnormal responses were markedly prolonged (table). Subjects 1 to 8 showed longer peak latencies for the P1 deflection (following peroneal nerve stimulation) and subjects 3, 4 and 9 had a dispersed response with longer latencies at N1 and P2 deflections. Subjects 5, 6 and 7 in the fifth generation who showed abnormal responses were the grandchildren of the proposita but their mother (subject 10) was clinically and electrophysiologically normal. The remaining fifth generation subject who showed abnormal responses (subject 9) was the child of subject 4 who showed clinical abnormality as well as abnormal evoked responses. Nerve conduction velocity was normal in all the subjects studied.

Discussion

Families of Strümpell's familial spastic paraplegia which have been reported in the literature have been found to fall into two major groups; in the first, the onset tends to be in childhood and the inheritance appears to be autosomal recessive. In the second group, the onset is generally over the age of twenty years and transmission may be as autosomal dominant.^{6,9} In the present family, the onsets were relatively late and affected cases appear in several generations so that dominant transmission is probable.

Although in the majority of the recorded cases the clinical features have been largely confined to signs of descending tract involvement, pathological changes in described cases have affected the posterior columns in addition to the corticospinal tracts.⁹ In the present family the subjects who showed neurological changes all had signs consistent with descending tract involvement but only minor sensory abnormalities were found. Nevertheless, two patients in the fourth generation and four in the fifth generation showed abnormalities in the evoked responses following peroneal nerve stimulation. Moreover, abnormalities in the somatosensory responses were present in all three patients who were clinically affected and also in the two patients without evidence of disability who showed abnormalities in descending tract function on neurological examination. Somatosensory responses are dependent on the integrity of the dorsal column in the spinal cord¹⁷ so that the findings in this family are consistent with the known pathological abnormality in this condition. Although responses showed delay in the peak of the P1 deflection the most conspicuous finding in a number of responses was poor definition of the components. This is likely to be indicative of impaired conduction in the ascending pathway giving rise to increased temporal dispersion. The different components of the response in healthy subjects however show significant degrees of unresponsiveness to repetitive stimuli which in the case of the late components may last for as long as 800 ms.¹⁸ The finding that responses in some cases were better defined at a slow frequency of stimulation suggests that prolonged unresponsiveness to repetitive stimuli may also contribute to the impaired capacity of the sensory pathways to mediate evoked responses.

The finding of normal nerve conduction velocity in the patients in which this function was evaluated is consistent with the report of McLeod *et al*¹⁰ and with the conclusion that abnormalities in the somatosensory response are due to impairment of function in spinal afferent pathways and not to involvement of peripheral nerves. Different families

studied have not always shown the same findings. Thus of seven patients with hereditary spastic paraplegia reported by Mastaglia *et al*,¹⁴ two had abnormalities in cortical somatosensory responses evoked by median nerve stimulation. In the unusual family described by Stewart *et al*¹⁹ in which features of familial spastic paraplegia were accompanied by peroneal neuropathy and crural hypopigmentation, somatosensory responses were normal but pattern reversal visual evoked responses were delayed. In the present family abnormal cortical somatosensory responses were present in all affected members who were available for study.

Thomas *et al*¹³ conclude from their finding of abnormal cervical spinal evoked responses in hereditary spastic paraplegia that the change in the dorsal columns represents a dying back process in the dorsal sensory neurons and our finding of small delays in the somatosensory pathway is consistent with this interpretation. A defect in myelination in the visual pathways, on the other hand, is supported by the reported finding of delayed visual evoked responses in a proportion of affected patients.^{11 12 15}

It is of interest that the electrophysiological evidence of impairment of dorsal column function has now been recorded in several different studies in patients with a predominantly motor disorder some of whom have no clinical evidence of sensory impairment. The present finding of abnormal somatosensory responses in several subjects who are neurologically intact may in addition represent evidence of impaired dorsal column function in clinically normal heterozygotes.

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