Journal of Neurology, Neurosurgery, and Psychiatry, 1977, **40**, 611–615

Electrophysiological studies in familial spastic paraplegia

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SUMMARY Motor and sensory conduction studies have been performed in 10 patients from three families with uncomplicated familial spastic paraplegia whose ages ranged from 4 to 41 years. In all cases the values fell within the control range. The findings may be contrasted with those in Friedreich's ataxia and some other spinocerebellar degenerations in which peripheral nerve abnormalities are present.

Familial spastic paraplegia is characterised by progressive weakness and spasticity of the lower limbs which may be inherited as an autosomal or recessive gene (Bell, 1939). As first described by Strümpell (1880, 1886, 1904), the lesions were confined to the corticospinal tracts in the spinal cord, but since that time there have been a number of reports of the disease associated with extrapyramidal disorders (Dick and Stevenson, 1953), amyotrophy (Garland and Astley, 1950; Silver, 1966), and a variety of other conditions which have been reviewed recently by Behan and Maia (1974).

Greenfield (1954) classified familial spastic paraplegia with Friedreich's ataxia as a predominantly spinal form of the spinocerebellar degenerations. Characteristic electrophysiological abnormalities are found in the peripheral nerves of patients with Friedreich's ataxia; there is impaired sensory nerve conduction, and the motor nerve conduction velocities are normal or only mildly slowed (Dyck and Lambert, 1968; Preswick, 1968; McLeod, 1971; Oh and Halsey, 1973; Salisachs *et al.*, 1975). The impairment of sensory nerve conduction has been correlated pathologically with loss of large diameter fibres in the sural nerves (Dyck and Lambert, 1968; McLeod, 1971). In the other spinocerebellar degenerations the electrophysiological and pathological features are less well established although there have been reports of peripheral nerve abnormalities in some cases (Dyck, 1975; McLeod and Morgan, 1976).

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Accepted 23 December 1976

Since electrophysiological studies may be helpful in the differential diagnosis of the spinocerebellar degenerations, nerve conduction studies have been performed on patients with familial spastic paraplegia in order to establish whether or not abnormalities are present.

Subjects and methods

Ten subjects whose ages ranged from 5 to 41 years, from three families with familial spastic paraplegia, have been studied.

Electrophysiological studies were also performed on 20 control subjects whose ages ranged from 18 to 73 years. This is the same control group that was used in a similar study on patients with Friedreich's ataxia (McLeod, 1971).

ELECTROPHYSIOLOGICAL TECHNIQUES

Motor conduction velocities were determined in the median, ulnar, and lateral popliteal nerves. Action potentials were recorded through surface electrodes placed over the abductor pollicis brevis, abductor digiti minimi, and extensor digitorum brevis muscles respectively following supramaximal stimulation of the nerve through the skin at two places.

Sensory nerve action potentials were recorded through surface electrodes placed over the median and ulnar nerves at the wrist on stimulating the index and little fingers respectively with ring electrodes (Dawson, 1956). The mixed motor and sensory nerve action potential was recorded with surface electrodes from the ulnar nerve above the level of the elbow on stimulating at the wrist

(Gilliatt and Sears, 1958). The mixed nerve action potential was recorded from the lateral popliteal nerve with needle electrodes inserted at the neck of the fibula on stimulating the anterior tibial nerve at the ankle (Gilliatt *et al.*, 1961).

The electrical stimulus was a square wave of duration 0.2 ms derived from a Disa Ministim. The recording electrodes were connected to a Tektronix FM122 preamplifier, and the action potentials were displayed on the upper beam of a Tektronix 502A oscilloscope; a timescale derived from a Digitimer (Devices Ltd.) was displayed on the lower beam. Photographic records were made on 35 mm film. The skin temperature of the upper and lower extremities was measured with a thermistor and ranged from 31°C to 35°C.

Results

CLINICAL FEATURES

Family A Twelve members of the family (eight females, four males) are known to have been affected over four generations (Fig. 1). The history and physical findings are similar in all affected members. Walking began at the age of 15 to 18 months, but by the age of 2 years abnormality of gait with frequent falls was noted. Some deterioration tended to occur in the second decade, but there was little change thereafter. The oldest members of the family were able to perform manual and domestic work without aids or assistance. On examination, there were no abnormalities of speech or cranial nerves. There was no muscle wasting in upper and lower limbs and no pes cavus. Tone and deep tendon reflexes were markedly increased in the lower limbs, and plantar responses were extensor. The affected members walked on their toes with a spastic gait. Coordination was normal. There was no impairment of light touch, pain, temperature, position or vibration sense, or of two-point discrimination.

Family B A woman aged 30 years and her only child, a girl aged 5 years, were affected. No other relatives were known to be abnormal. Difficulty in walking in the mother's case began at the age of 5 years and in the case of her daughter at the age of 14 months. The physical findings were similar in both patients. There was no impairment of intellect or of speech. Cranial nerves were intact. There was pes cavus, with equinovarus deformity. There was no muscle wasting. Tone and deep tendon reflexes were markedly increased in the lower limbs, and plantar responses were extensor. Coordination was normal. Light touch, pain, temperature, position and vibration sense, and two-point discrimination were normal. Gait was spastic with a tendency to walk on the toes.

Family C Two brothers aged 18 and 12 years were affected, and three other siblings and parents were all normal. In both cases, difficulty in standing and walking was first noticed during the second year of life. The physical findings were similar in the two patients. There were no abnormalities of intellect, speech, or of cranial nerves. There were

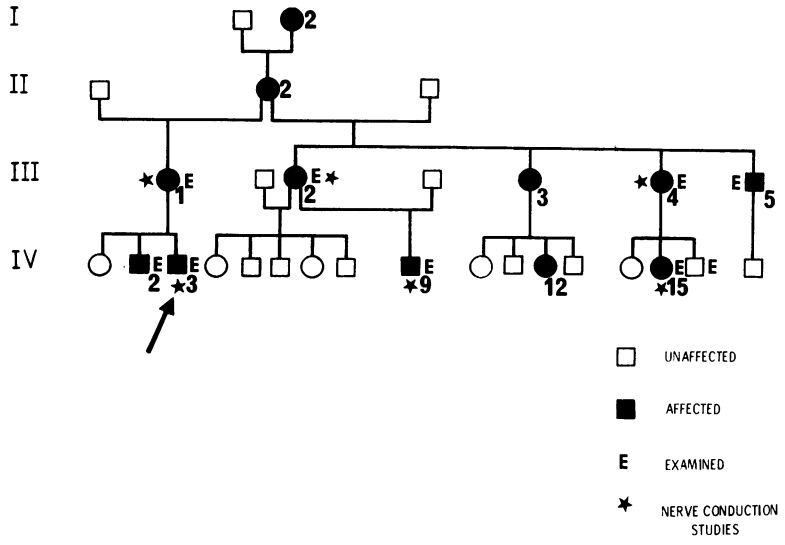

Fig. 1 *Family A with familial spastic paraplegia.*

no foot or skeletal deformities, and there was no muscle wasting. Tone and deep tendon reflexes were markedly increased in the lower limbs; there was ankle clonus, and plantar responses were extensor. Coordination was normal. All modalities of sensation were intact. Gait was spastic with a tendency to walk on the toes.

ELECTROPHYSIOLOGICAL STUDIES

In all the patients with familial spastic paraplegia, motor conduction velocities in median, ulnar, and lateral popliteal nerves, amplitudes and latencies of sensory nerve action potentials in the median and ulnar nerves, and of the mixed nerve action potentials in ulnar and lateral popliteal nerves fell within the normal range. These results are summarised in the Table and in Fig. 2.

Discussion

All the patients included in the present study suffered from the relatively rare uncomplicated form of Strümpell's familial spastic paraplegia (Bell, 1939; Behan and Maia, 1974). They all had a family history of the disease and presented in the first decade with spastic paraparesis. There was no clinical evidence of cerebellar ataxia, muscle wasting, extrapyramidal involvement, mental deterioration, or sensory impairment. The inheritance was autosomal dominant in two of the families (A and B) and probably recessive in the third (C). The pathological features of the uncomplicated cases are degeneration of the corticospinal tracts and posterior column degeneration which may be associated with clinical impairment of deep sensation in later life (Strümpell, 1880, 1886, 1904; Schwarz, 1952; Schwarz and Liu, 1956; Behan and Maia, 1974).

The normal nerve conduction studies are consistent with the absence of fibre loss in the posterior and anterior roots and the normal appearance of anterior horn cells and peripheral nerves in the cases reported by Behan and Maia (1974). Dyck (1975), however, has reported that there may be a reduction in the amplitude of the sural nerve action potential, and that in older patients there may be a mild reduction in the density of myelinated fibres in the sural nerve. It seems possible, therefore, that some degeneration may occur in the peripheral nerves in later life. By contrast, in Friedreich's ataxia, unequivocal abnormalities of sensory nerve conduction and in the sural nerve biopsy may be detected early in the first decade (Dunn, 1973; McLeod and Morgan, 1976).

The present finding of normal motor and sensory conduction in the uncomplicated form of familial spastic paraplegia, at least up to the age of 40 years, may be helpful in the differential diagnosis of patients with spinocerebellar degenerations.

The work was supported by grants from the National Health and Medical Research Council of Australia and the Postgraduate Medical Foundation, University of Sydney.

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Table *Nerve conduction studies in familial spastic paraplegia*

		Motor nerve conduction velocity			*Sensory nerve action potentials*				*Nerve action potentials*			
		Median nerve	*Ulnar nerve*	*Lateral popliteal nerve*	*Median nerve*		*Ulnar nerve*		*Ulnar nerve*		*Lateral popliteal nerve*	
		m/s	*m/s*	*m/s*	*latency (ms)*	*amplitude (μV)*	*latency (ms)*	*amplitude (μV)*	*latency (ms)*	*amplitude (μV)*	*latency (ms)*	*amplitude (μV)*
Control subjects (20)	Range	50–66	47–69	41–56	2.4–3.2	11–40	2.1–3.1	7–36	4.1–6.7	28–88	5.1–8.1	3–15
Age: 18–73 yr	Mean ± SD	58.7 ± 4.4	56.2 ± 4.9	48.7 ± 4.4	2.8 ± 0.3	20.9 ± 7.6	2.4 ± 0.3	15.9 ± 6.6	5.1 ± 0.6	53.6 ± 17.4	6.3 ± 0.8	6.7 ± 3.7
Familial spastic paraplegia (10)	Range	55–70	50–66	41–60	2.2–4.0	12–33	1.9–3.7	10–25	3.7–5.8	23–80	4.0–6.3	3–10
Age: 5–41 yr	Mean ± SD	62.0 ± 5.4	59.8 ± 6.0	50.0 ± 5.9	3.0 ± 0.6	22.0 ± 7.9	2.6 ± 0.6	15.7 ± 4.8	4.7 ± 0.8	47.9 ± 23.9	5.5 ± 0.9	6.8 ± 2.9
Significance of difference (Student's *t* test)		Not significant ($P > 0.05$)										

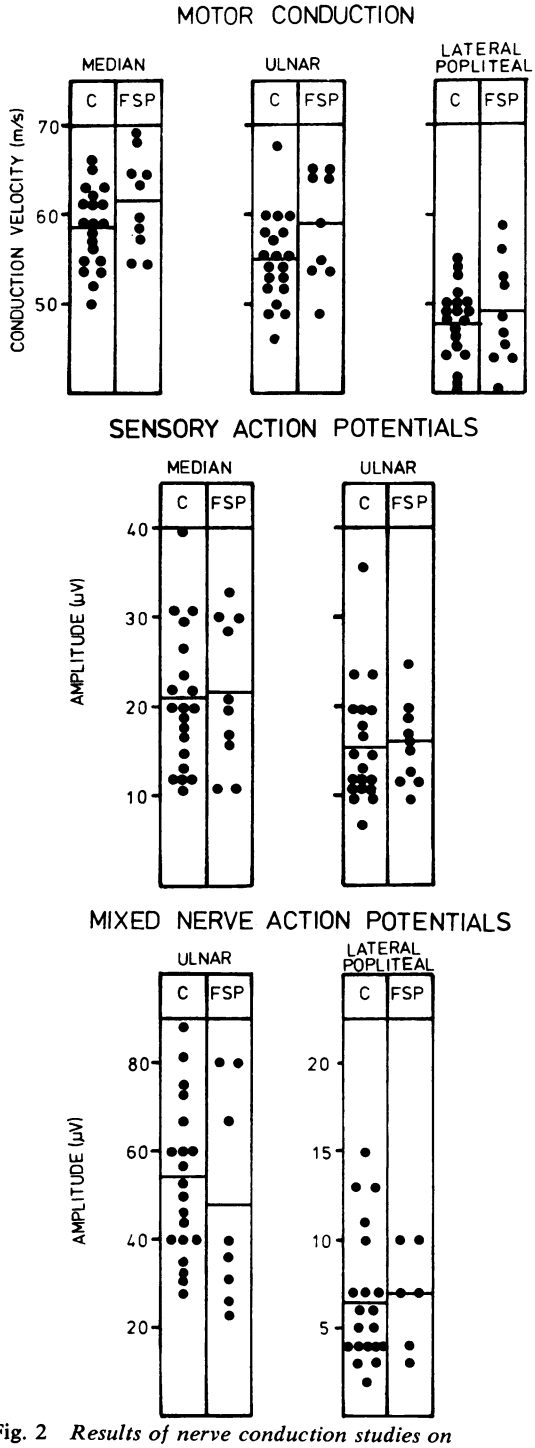

Fig. 2 *Results of nerve conduction studies on patients with familial spastic paraplegia (FSP) and control subjects (C).*

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