Evoked potentials in a man with a complete large myelinated fibre sensory neuropathy below the neck

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Summary Cortical somatosensory evoked potentials (SEPs) were recorded from a man with a severe neuropathy without touch and proprioception below the neck. Peripheral neurophysiological tests showed a complete large myelinated fibre sensory neuropathy. Sensory threshold to electrical stimulation of the median nerve was 15 mA (normal 2–4 mA). With a stimulus of 39 mA, duration 400 μsec, applied at the wrist a cortical SEP was recorded with a latency of 84 μsec, giving a propagation velocity of 11.9 m/sec. At stimulation rates of above 3.3 Hz the SEP was absent. It is concluded that the SEPs recorded were conducted along Aδ peripheral fibres.

Key words: Sensory neuropathy; Aδ SEPs; Electrical stimuli

Cortical SEPs have conventionally been recorded following stimulation of low threshold large myelinated fibres. Recently, however, techniques for activating selectively nociceptive afferents had been developed using a low power long wave length CO₂ laser (Mor and Carmon 1975; Chudler and Dong 1983). The fibre type responsible for the conduction of this SEP peripherally has been considered to be Aδ (Bromm and Treede 1984; Bjerring and Arendt-Nielsen 1988; Treede et al. 1988; Kakigi et al. 1989).

Attempts to stimulate Aδ fibres electrically have proved difficult in man, both because of the painful quality of the sensation and because of contamination from activity in low threshold afferents. This paper reports results from such electrical stimulation of peripheral nerves in a man with a complete large myelinated fibre sensory neuropathy.

Case history

Fourteen years before the experiments AN (a pseudonym) suffered an acute sensory neuropathy. After this he had no perception of light or deep touch nor joint position sense below the neck. This absence was complete and uniform over the body surface (at the junction between normally and abnormally sentient skin around the collar there was a small area of reduced sensation). Pressure was present — if he pressed with a finger as hard as possible on the hand or forearm then he just felt it but this sensation faded in a couple of seconds. Joint position sense was absent although sometimes difficult to test. For instance if his shoulder was moved then he had some sensation of change because of coolness in the axilla and pulling of skin in the sentient cervical area. However, in any meaningful way there was no joint position sense below the neck.

Two-point discrimination was 2.7 cm on the index finger pulp (normal 0.2 mm), and 17 cm on the forearm (normal 2 cm), to very firm pressure. Directional sensitivity was just present on the finger and forearm.

Pain and temperature sensation remained. Pin-prick pain sensation was felt similarly on the unaffected head and on the body. However, in everyday life he reported an altered pain if say he hit his shin. Then the pain was more diffuse, unpleasant and longerlasting, possibly reflecting nociceptive functioning in the absence of large myelinated fibre activity. Temperature discrimination was within the normal range (< 1.0°C in both the cold and warm ranges, 16 and 33°C).

At the time of his acute illness motor power on formal clinical testing was normal but he was completely unable to move, since peripheral movement-related feedback was abolished. Clinical tests were positive for infectious mononucleosis (Paul Bunnell and monospot). CSF examination showed a protein of 600 mg/l (normal < 550 mg/l), and 17 white cells/mm³ (normal < 4–6 cells). Peripheral neurophysiology showed normal motor conduction and EMG with no sensory potentials. A diagnosis of polyneuropathy due to a cross-reaction between cells involved in the host
response to glandular fever and peripheral nerve was made. A nerve biopsy was not performed then and it was considered unethical on re-presentation.

AN was unable to perform any useful movement for several weeks. After 2 months he could feed himself. Within 1 year he was upright and after 15 months he was walking. He spent in all nearly 2 years as an in-patient in neurological and rehabilitation wards. He has subsequently worked as an able bodied man as a clerk, living independently.

He was lost to neurological follow-up for a decade. When he represented, because of increasing tiredness, there had been no recovery of peripheral nerve function. He still had no light touch nor proprioception below the neck and used visual feedback for all movement. Power, tested clinically, was within normal limits and there was no wasting. All his recovery had been using visual feedback and conscious control of movement.

Methods

(a) Nerve conduction studies

Conventional nerve conduction studies of the median, radial, ulnar and tibial nerves were made. Sensory nerve activation was attempted by averaging 16 responses on at least 2 occasions at 1 Hz. Intensities used were up to 100 mA, 200 μsec. Filters used were 20 Hz–20 kHz for motor recording and 20 Hz–5 kHz for sensory. Near-nerve needle electrodes were used to record from the median nerve at the elbow following similar stimulation at the wrist. Concentric needle electrode examination of muscle activity was also made.

(b) Evoked potential studies

All results were duplicated on 2 different days as well as during each experiment. A Nicolet Pathfinder II was used throughout.

The distribution of the scalp recorded evoked potential was investigated with a cortical montage of 11 electrodes using the international 10–20 system. The electrodes (Ag-AgCl and with impedances of less than 3 kΩ) were Fpz, Fz, F4, a coronal line of 6 electrodes at C3', Cz', C4', with electrodes midway between C3 and Cz', Cz and C4' and C4' and T4', all 2 cm behind the measured 10–20 location, and at Pz and P4, linked ear reference (see Fig. 2). A 6-channel averager was used and each run was recorded from the 6 coronal and then the 6 sagittal electrodes, with the C4' channel used in both to check consistency. The bandwidth of the amplifiers was 5–1000 Hz. There was an artefact rejection which excluded EOG.

Stimulation was applied via saline-soaked felt electrodes. The intensity of stimulation was 39 mA, pulse duration 400 μsec and the rate 0.3–3.3 Hz. Analysis time was 200 msec. Between 40 and 150 stimuli were averaged in each run and each run was repeated.

The stimulus repetition rate was altered between 0.3 and 3.3 Hz. The stimulation site was changed from the wrist to the elbow to observe the change in latency of the cortical wave and hence calculate the peripheral conduction velocity. Recordings were also made with a long time base to observe the late components of the wave, with sampling up to 800 msec. The effect of the intensity of stimulus was observed by increasing from 10 mA to 39 mA, with duration of 200 μsec, and finally to 39 mA and 400 μsec.

The montage for recording SEPs after stimulation of the posterior tibial nerve was of 7 channels; Fpz and 2 coronal lines 3 cm in front and 2 cm behind C3, C2 and C4 with a linked ear reference. Analysis time ranged from 250 msec to 3 sec and stimuli up to 39 mA and 500 μsec were used.

Results

(a) Peripheral conduction studies

He was arreflexic clinically. He had no sensory nerve action potentials from stimulation of sural, radial, median and ulnar nerves including their digital branches.

Threshold for twitch on stimulation of the median nerve at the wrist was 6 mA (duration 200 μsec), with sensory threshold just above twice that. A near-nerve recording from the median nerve at the elbow following stimulation of the nerve at the wrist was made. Two waves were recorded (see Fig. 1). The first had a latency of 3.8 msec with an amplitude of 1.2 μV. This gave a conduction velocity of 63 m/sec and is considered to represent an antidiromically activated motor response. The second wave was 0.6 μV in amplitude with a latency of 14.3 msec giving a velocity of 16.7 m/sec.

Median nerve motor terminal latency was 3.8 msec, with a forearm conduction velocity of 59.4 m/sec and a normal amplitude of motor response. Terminal latency of the posterior tibial nerve was 3.5 msec, with a conduction velocity of 43.1 m/sec, all these being within normal limits. F waves in the median and posterior tibial nerves were normal in latency for height (32 msec and 62 msec, respectively, subject's height 1.88 m). H

![Fig. 1. Near-nerve recording from the left median nerve at the elbow in response to stimulation of the median nerve at the wrist. Stimulus intensity 100 μA, duration 200 μsec, rate 1 Hz. Filters 20 Hz–5 kHz, 16 stimuli ×2. Note 2 components, one at 3.8 msec with an amplitude of 1.2 μV and the other at 14.3 msec with an amplitude of 0.6 μV.](image-url)
reflexes to soleus were absent. No reflexes could be elicited by supramaximal cutaneous stimulation of a digit when recording with intramuscular electrodes from the first dorsal interosseous nerve (Baker et al. 1987). This was performed with a peripheral stimulus of 100 mA, 200 μsec duration at 1 Hz. The aim was to exclude reflexes dependent on large myelinated afferents. Repetitive stimulation to investigate nociceptive reflexes was not performed.

Concentric needle EMG of muscles in both the arm and leg showed no spontaneous activity, normal amplitude motor units, normal interference patterns and no increase in polyphasic potentials.

(b) Evoked potentials

(i) Median nerve. The sensory threshold in control subjects for stimulation is 3–4 mA (duration 200 μsec), and for twitch around 6 mA. In AN, threshold for twitch was 6 mA and for sensation 15–16 mA (duration of 200 μsec). No SEP was recorded until a stimulus of 6.5 times motor threshold was used. A reliable wave was not recorded until the pulse duration was increased to 400 μsec, a stimulation intensity not reported to be painful. The effect of stimulus intensity and duration on the evoked potential is shown in Fig. 2. The SEP had a negative peak with an onset latency of 84.4 msec and an amplitude of 5 μV from stimulation at the wrist. The first wave's latency corresponded with a propagation velocity of 11.9 m/sec. On stimulation of the median nerve at the elbow the onset latency of the wave was 64.4 msec, corresponding to an elbow to cortex propagation velocity of 11.3 m/sec. This gives a peripheral conduction velocity of 14.0 m/sec, by deduction, although there can be no proof that identical afferents were activated from the wrist as from the elbow.

The cortical localization of the evoked potential was studied with an array of 10 scalp electrodes linked to an ear reference. Following a left median nerve stimulus the early negative components of the SEP were found maximally in the right central area, with some spread parietally but with no component seen in the frontal electrodes (see Fig. 3). Later positive components had a more symmetrical distribution.

The shorter latency components of the evoked potential were followed by a complex comprising several

Fig. 2. Cortical evoked potentials following stimulation of the left median nerve at the wrist to show the effect of stimulus intensity. Each run is the average of 50 stimuli. Recordings with a linked ear reference. Repetition rate 0.5–1.3 Hz. Stimulus intensity given in mA and duration (Dur) in μsec. Filters 5–1000 Hz.

Fig. 3. Scalp distribution of the cortical somatosensory evoked potential to stimulation of the left median nerve. Stimulus 39 mA, 400 μsec duration, repetition rate 0.5–1.3 Hz, each run the average of 150 stimuli. Filters 5–1000 Hz. For recording method see text.
components, from stimulation at the elbow namely N64, P83, N123, P163, N209, and P332. These potentials showed a marked fall-off with increased stimulation rate and were not present at rates above 3.3 Hz.

(ii) Tibial nerve. In AN, the earliest cortical evoked potential was a post-central negativity at around 117 msec, giving a propagation velocity of 15 m/sec. Stimuli below 39 mA and a duration of 500 μsec were reported as tingling or jabbing which became uncomfortable. At 39 mA and 500 μsec it was described as a painful thumping. Evoked potentials under this circumstance showed an increase in the post-central positivity beginning at around 200 msec, although on subtraction of SEPs no any additional wave was seen.

Discussion

A most important aspect of this case is to establish the selectivity of the neuropathy. The clinical history and examination suggested a selective large fibre sensory neuropathy. His arreflexia, both clinically and electrically, supported this, as did the peripheral clinical neurophysiological tests. His illness conforms to the acute sensory neuropathy syndrome described by Sterman et al. (1979). Their original cases and those of Albin et al. (1987) were associated with vitamin overdose. A similar case investigated by Caramia et al. (1987) was thought to be triggered by mal-reacttion to rubella virus, and so is closer to AN in origin.

Peripheral conduction velocities of low threshold Aδ fibres have been estimated to be 19.2 +/− 7.2 m/sec (Buchthal 1973; Adriaensen et al. 1983). The fastest propagation velocity of fibres activated by cutaneous heat has been 10–14 m/sec (Bromm and Treede 1984), similar to the latencies found in AN. Aδ fibres are excited with stimuli of 3–10 times the perceptual threshold although in some situations 5–7 times motor threshold is enough (Burke et al. 1975). In AN, SEPs were observed at 6.5 times motor threshold.

Previously Aδ SEPs have been described following selective blocking of large A fibres in the cat by Handwerker and Zimmermann (1972) and by Alspán (1981). Colon et al. (1978) investigated 4 subjects with Friedrich’s ataxia, considered to be a selective large sensory fibre degenerative condition. They recorded SEPs to stimulation of the sural and median nerves and correlated these with sural nerve biopsies. SEPs with propagation velocities of around 23 m/sec were found. However, the biopsies showed some fibres in the range of group II cutaneous afferents of Boyd and Davey (1968). The stimulus intensity used was “perceptible” at 180% of that used in controls, which may not be sufficient to excite all Aδ fibres. Subject AN had no sensory perception until 2.5 times motor threshold and no SEP was evident until 6 times that threshold or higher.

In AN, the SEP fell off sharply above 2 Hz whereas in control subjects SEPs are visible up to 25–30 Hz after median nerve stimulation (Cole et al. 1984). Torebjörk and Hallin (1974) found that Aδ fibres could follow a 50 Hz stimulus peripherally but that the perceptual correlate of Aδ activation fatigued between 0.5 Hz and 5 Hz due to central effects. A similar central fatiguing effect of the Aδ SEP would seem likely in AN.

In AN, the early negative components of the SEP were maximal in the contralateral central and parietal areas, a similar distribution to that found for cutaneous heat evoked SEPs by Treede et al. (1988) and not incompatible with a cortical origin. The later components of the SEP in AN were distributed more symmetrically, as in Treede et al.’s sample. These later components have some similarities with vertex potentials (Davis et al. 1972).

Treede et al. (1988) considered whether the first negative wave they recorded to cutaneous heat stimulation was equivalent to the N70 found after electrical nerve activation. In AN’s case SEPs were observed unlike those found in control subjects and so they may have no homologue in SEPs following stimulation of low threshold afferents.

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References

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