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SHORT REPORT

Ultralate cerebral potentials in a patient with hereditary motor and sensory neuropathy type I indicate preserved C-fibre function

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Abstract

Late and ultralate cerebral potentials in response to cutaneous heat (CO_2 laser pulses) and electrical nerve stimuli were studied in a patient with hereditary motor and sensory neuropathy type I who showed severe impairment of myelinated nerve fibre function. Cerebral potentials in response to electrical stimuli were absent (tibial nerve) or small (median nerve). With the laser pulses applied to the foot only ultralate, but no late potentials were observed, indicating intact C-fibres, but disturbed Aδ-fibres. Laser stimulation of the hand resulted in both late and ultralate components, indicating at least partly preserved Aδ-fibre function. The results document the usefulness of laser stimuli in the assessment of small nerve fibre function.

Carbon dioxide laser radiation (10·6 μm wavelength) is absorbed at the surface of the skin, thus activating only the most superficial nerve fibres, which are Aδ- and C-fibres.[1] As a correlate of Aδ-fibre mediated first pain, late cerebral potentials with latencies from 200 to 400 ms have been demonstrated.[2] If A-fibres were blocked experimentally by pressure, ultralate cerebral potentials with latencies of more than 1000 ms were recorded as correlates of C-fibre mediated second pain.[3 4] The differentiation of Aδ- and C-fibres by cold pain stimuli are described elsewhere.[5]

In patients with hereditary motor and sensory neuropathy type I (HMSN I, hypertrophic form of Charcot-Marie-Tooth), especially thick myelinated nerve fibres are affected with signs of de- and remyelination as well as of axonal atrophy.[6] The consequences are gait difficulties, muscle weakness, diminished stretch reflexes, disturbances of vibratory and position sense and drastically decreased nerve conduction velocities.[7 8] Disturbances of pain and temperature sense due to destruction of thin myelinated fibres are characteristically less prominent.[6 7] This article describes the suitability of CO_2 laser heat pulses to assess disturbances of small nerve fibres by evoked cerebral potentials.

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Methods

Case report

Like his mother this 25 year old male had had slowly progressive gait disturbance from early childhood. He showed a bilateral pes cavus deformity, atrophy of the small foot muscles, muscular weakness and areflexia. Clinical sensory disturbance was limited to the lower extremities with distal accentuation. Vibration and position sense were missing in both feet. There was a strong impairment of touch and pressure sense. Cold, warm and pain sensation, tested with water-filled test tubes and pinprick, hair pulling and sharp/blunt discrimination, respectively, were less disturbed. Upper limbs were only mildly affected with areflexia and a light dystaxia of the hands. Motor nerve conduction velocities were heavily reduced (left peroneal nerve 10·0 m/s, normal 45 to 60 m/s; left median nerve 14·6 m/s, normal 52 to 65 m/s).

Stimulus and recording technique

Conventional electrical nerve stimuli (0·2 ms, constant current, 15 mA) were used as well as brief radiant heat pulses elicited by the CO_2 laser (20 ms, 15 and 20 W, 20 mm^2;[1]. Two stimulus blocks were given to the upper and lower left limb to prove reliability. Each block consisted of 60 stimuli: 20 laser stimuli with 15 W, 20 laser stimuli with 20 W and 20 electrical nerve stimuli, delivered in random order and with random interstimulus intervals between 10 and 30 s.

EEG was recorded from Cz versus linked earlobes (bandpass 0·1–70·0 Hz, sampling rate 200 Hz, eyes closed). Only late somatosensory evoked potentials (SEP) were analysed, because in the case of laser stimuli early components have not yet been detected.[9] The cerebral potentials were obtained by averaging the 20 poststimulus EEG segments of 3000 ms in response to each kind of stimulus. Ocular artefacts were rejected.

Reaction times were measured with another 20 laser stimuli (20 W). The patient had to

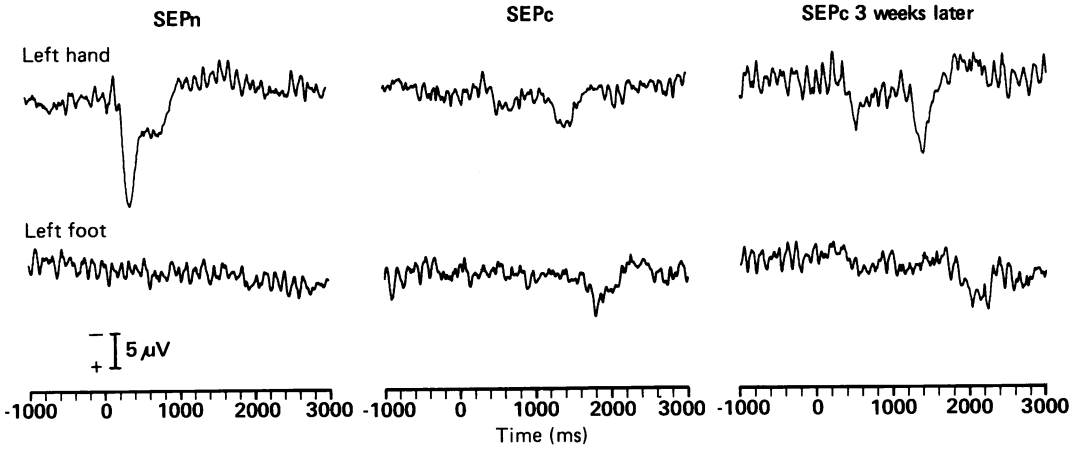

Figure Evoked cerebral potentials due to electrical (15 mA, left, SEPn) and laser stimuli (20 W, middle, SEPc). Measurements with laser stimulation were repeated with a three week interval. Late SEPn after stimulation of the median nerve showed a well defined response, but after stimulation of the tibial nerve there was no potential at all. After laser stimulation of the hand late and ultralate components were observed. After foot stimulation only ultralate potentials were measured. Averages over 40 stimuli, vertex (Cz) versus linked earlobes, negativity upward.

press a button immediately after perceiving the stimulus. Results are presented for two experimental sessions with a three weeks interval.

Results

The figure illustrates the results of the evoked potential measurements. In agreement with the clinical picture strongest alterations were seen with lower limb stimulation (lower row). Late cerebral potentials in response to conventional electrical nerve stimuli (SEPn) of the tibial nerve were completely missing. The same was found for the late cerebral potentials in response to cutaneous laser stimuli (SEPc). Instead, ultralate cerebral potentials could be detected with a latency of 1800 ms according to the low conduction velocity of C-fibres. The reaction time in response to laser stimulation of the foot was 1900 ms, mean (SD) 850 ms. With intact A-fibres we normally observe reaction times with foot stimulation of 370 ms (SD) 65 ms.

In contrast, the upper part of the figure demonstrates well defined SEPn with median nerve stimulation, indicating that A-fibres were partly intact. In fact, the amplitude of the SEPn was only half as large as in normal subjects.[9] Accordingly, a clear stimulus locked Aδ-fibre mediated SEPc could be detected, consisting of a small negativity with a peak at 340 ms and a positivity at 520 ms. The amplitudes again were rather small. Interestingly we also observed an ultralate C-fibre response, consisting of a large positivity with a peak maximum at 1400 ms. In agreement with the appearance of these two cerebral potential complexes we found a biomodal distribution of motor reaction times in response to laser stimulation of the hand with peaks at 500 and 1100 ms, mean (SD) in normal subjects: 340 (55) ms.

The results of the laser investigation were reproduced three weeks later.

Discussion

In healthy volunteers laser stimuli usually evoke late SEPc due to Aδ-fibre mediation. Ultralate potentials appear only, if for example A-fibres are blocked experimentally by pressure,[3 4] or if a pathological process has disturbed A-fibre function in patients.[10] Obviously the brain focuses attention mainly on the first appearing event, within certain time limits.[11]

The complete absence of SEPn found in this patient agrees with the loss of thick myelinated fibre function in the lower limb observed in the clinical examination: electrical stimuli always activate the largest and fastest conducting fibres.[12] The lack of late SEPc revealed especially disturbances of Aδ-fibres, which are predominantly activated by the laser stimulus.[2 4] However, ultralate SEPc in response to C-fibre mediation were observed. The assumption of Aδ-fibre impairment with preserved C-fibre function was supported by the increase of reaction time to 1900 ms. These findings were very close to those in healthy volunteers after A-fibre block.[3 4 13]

With hand stimulation the findings are especially interesting because of the appearance of both, Aδ- and C-fibre mediated SEPc. Obviously there were some functionally normal Aδ-fibres, which evoked the typical late potentials. The Aδ-fibre input to the brain, however, seemed to be heavily reduced, so that the Aδ-fibre correlated potentials were diminished and the patient was able to recognise C-fibre-input. We had previously observed a combined appearance of Aδ- and C-fibre mediated potentials only in experiments with volunteers who were trained to ignore first pain and to focus attention selectively upon second pain.[11] In the investigated patient second pain might have been unmasked by a subclinical disturbance of Aδ-fibres, and consequently we find its electrical correlate in ultralate SEPc.

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