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Laser evoked potentials in Carpal Tunnel Syndrome

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ABSTRACT

Objectives: The aim of this study was to evaluate the function of Aδ fibers at the hand level in patients with clinical symptoms of Carpal Tunnel Syndrome (CTS) using CO_2 laser evoked potentials (LEPs), in light of the intensity and distribution of sensory symptoms and pain.
Methods: Thirty-four CTS outpatients (62 hands) were compared to 23 sex- and age-matched control subjects (46 hands). The periungueal skin of the first, second, third and fifth fingers, and the dorsum of the hands were stimulated in random order. The latency and amplitude of the N2, P2 and N1 components were evaluated with respect to the Nerve Conduction Study (NCS) data, clinical scales, pain intensity and glove-like symptoms distribution.
Results: The amplitude of the N2–P2 complex was significantly reduced in CTS hands compared to normal hands after stimulation of the second and third fingers, even in patients with mild nerve conduction impairment. No significant fifth finger LEP abnormalities were found in patients with glove-like distribution symptoms. The N2–P2 amplitude at the second and third fingers was positively correlated with the severity of sensory symptoms.
Conclusions: The involvement of median nerve Aδ fibers in CTS seems to be an early phenomenon, which concurs with the impairment of large motor and sensory afferents and is linked to the severity of the disease.
Significance: The finding of reduced sensory symptoms in patients with severe thin afferents damage, may suggest a slight expression of central sensitisation phenomena in the advanced stage of CTS syndrome.

1. Introduction

Carpal Tunnel Syndrome (CTS), a clinical disorder resulting from compression of the median nerve at the wrist (Phalen, 1966), is the most common entrapment neuropathy. A consensus conference identified a combination of symptoms (numbness, tingling, burning and pain in combination with nocturnal symptoms) together with abnormal median nerve function based on a Nerve Conduction Study (NCS) as the best "gold standard" for diagnosis of CTS (Rempel et al., 1998). The quantification of CTS clinical impairment has been evaluated by several validated scales including the Boston Carpal Tunnel Questionnaire (BCTQ) (Levine et al., 1993), hand diagram (Katz and Stirrat, 1990) and clinical historical-objective (Hi-Ob) scale (Giannini et al., 2002; Padua et al., 1999). The neurophysiological aspects of CTS have been widely studied (AAEM et al., 1993, 2002) and some neurophysiological classifications have been developed (Padua et al., 1997). Different approaches have been introduced, assessed and critiqued, all of which are based on motor and large sensory fiber conduction studies (Jablecki et al., 2002a,b; Rosenbaum and Ochoa, 2002).

Pain is an early and invalidating symptom of CTS, and is caused by the involvement of thin nociceptive fibers that suffer from an intraneural ischaemia secondary to a chronic low-force compression (Dahlin et al., 1989). Although common sensory NCSs are not a valid tool to examine the function of small fibers in CTS patients, a few studies have examined the neurophysiology of the function of thin myelinated afferents (Arendt-Nielsen et al., 1991; Lang et al., 1995). Brief radiant heat pulses, generated by a laser (infrared CO_2, argon or thulium-YAG laser), can be used to elicit an evoked potential. The potentials can be recorded from the vertex ("late components") and temporal ("early components") regions of the skull by selective activation of Aδ (laser evoked potentials (LEPs)) and C (ultra-late LEPs) mechano-thermal nociceptors in the superficial layers of the skin (Bromm and Treede, 1984, 1987). In the last two decades, LEPs have been found to be a useful tool for selective evaluation of nociceptive pathways in experimental pain models as well as in central and peripheral neurological

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diseases (Treede et al., 2003). Furthermore, LEPs have recently been proposed to be a reliable neurophysiological assay for the clinical assessment of neuropathic pain (Cruccu et al., 2004). Using an argon laser together with a NCS, Arendt-Nielsen et al. demonstrated that the pain threshold in CTS patients was elevated in the third finger compared to the fifth finger (Arendt-Nielsen et al., 1991). Moreover, in CTS patients, the amplitude of the LEPs was reduced by stimulation of the third, but not the fifth finger (Arendt-Nielsen et al., 1991).

The present study, aimed to further add knowledge to the state of δ fibers in CTS syndrome, described in previous studies (Arendt-Nielsen et al., 1991; Lang et al., 1995), in light of NCS classification and clinical features, including the intensity and distribution of sensory symptoms and pain.

2. Materials and methods

2.1. Patients and clinical evaluation

A series of 34 idiopathic CTS outpatients (62 hands) aged 46.11 ± 13.39 years, consisting of 15 males and 19 females, with a mean duration of symptoms for 31.04 ± 25 months were enrolled in this study. Twenty-three sex- and age-matched control subjects (aged 45.85 ± 12.67 years; 22 males and 24 females) were also enrolled providing a total of 46 normal hands. The presence of diabetes mellitus, renal or hepatic failure, pregnancy, alcohol abuse, drug or toxin exposure or any central or peripheral nervous system disease was excluded after careful consideration of the patient's clinical history and a neurological examination. Patients were also asked to avoid analgesics in the 48 h preceding the neurophysiological examination.

Our study was approved by the local Ethics Committee of the Neurological and Psychiatric Department of Bari University (Italy). The study was performed in accordance with the ethical standards of a responsible committee, the Helsinki Declaration and IASPs guidelines for pain research in humans (Pain, 1995;63:277–78). Written informed consent was obtained in all cases. CTS was clinically diagnosed on the basis of the American Academy of Neurology clinical diagnostic criteria (AAN et al., 1993), which included paresthesia, pain, swelling, weakness or clumsiness of the hand provoked or worsened by sleep, sustained hand or arm position, repetitive action of the hand or wrist that is mitigated by changing posture or by shaking the hand, sensory deficits in the median innervated region of the hand, and motor hypotrophy of the median innervated thenar muscles. The diagnosis was often supported by positive Tinel's or Phalen's signs, the absence of which did not exclude patients from the study. The minimum duration of symptoms was two months for a patient to be included (Padua et al., 1999). We studied a total of 62 CTS hands. We choose not to include the normal not symptomatic hands of CTS patients, to avoid minimal LEPs abnormalities, eventually preceding the clinical onset of symptoms.

Before the neurophysiological examination, all patients completed the BCTQ by Levine et al. (1993), which was translated into Italian and validated by Padua et al. (1998). This patients-oriented validated measurement evaluates two domains of CTS: "symptoms" (SYMPT), assessed using an 11-item scale, and "functional status" (FUNCT), assessed using an 8-item scale (each item has five possible responses). Clinical assessment of the severity of the syndrome was made using a 1–5 points clinical Hi-Ob scale, where the presence or absence of pain was separately evaluated (Giannini et al., 2002). In addition, the glove distribution of the symptoms was assessed by asking subjects to locate as accurately as possible the areas associated with sensory symptoms and pain, according to a self-administered hand symptoms diagram (Katz et al., 1990; Zanette et al., 2006).

In addition, referred pain from these subjects was evaluated using a visual analogue scale (VAS), in which 0 indicated no pain and 10 represented the most severe pain imaginable.

2.2. Electrophysiological evaluation: motor and sensory nerve conduction study

After clinical evaluation, all subjects were submitted to electrodiagnostic studies based on the protocol inspired by the American Association of Electrodiagnostic Medicine recommendations (AAEM et al., 1993, 2002; Padua et al., 1997). The tests were performed by the same neurophysiologist using MICROMED apparatus (MICROMED System Plus; MICROMED, Mogliano Veneto, Italy, http://www.micromed-it.com), with the skin temperature of the extremity maintained at or above 31 °C.

Sensory NCSs were performed using an antidromic technique with sensory electrodes stimulating the wrist over the median and ulnar nerves. Stimulation of the sensory nerve was characterized by a duration of 100 μs, an intensity of 10–30 mA, with the filter setting at 20 Hz–2 kHz. Sensory NCSs were recorded by surface electrodes placed over the proximal phalanx of the first, second, third and fifth fingers. The sensory conduction velocity (SCV) and peak-to-peak action potential amplitude (SAP) were measured.

Motor NCSs was performed, stimulating the median nerve proximal to the carpal tunnel at the wrist and elbow, and the ulnar nerve at the wrist. Stimulation of the motor nerve was characterized by a duration of 100 μs, an intensity of 30–90 mA, with a band pass filter settled at 20 Hz–50 kHz. The motor response of the median nerve was recorded by surface electrodes placed over the abductor pollicis brevis muscle, whereas the motor response of the ulnar nerve was recorded over the abductor digiti minimi muscle. The distal motor latency (DML) was measured at the onset of the compound muscle action motor potential (cMAP). The motor conduction velocity (CMV) and peak-to-peak amplitude of the cMAP were calculated. When the standard tests yielded normal results, a comparative median/ulnar sensory study was performed.

The severity of neurophysiological CTS impairment was assessed according to Padua et al. (1997). Six classes were considered on the basis of neurophysiological findings: negative (normal findings on all tests), minimal (abnormal segmental or comparative tests only), mild (abnormal digit/wrist SCV and normal DML), moderate (abnormal digit/wrist SCV and DML), severe (absence of sensory response and abnormal DML) and extreme (absence of sensory motor responses) (see Supplementary Table S1).

2.3. CO_2 laser evoked potentials: recording

Each subject was seated in a comfortable chair positioned in a quiet room with an ambient temperature of 21–23 °C, in an awake and relaxed state with their eyes closed. Subjects and observers wore protective goggles during data acquisition. All subjects underwent a recording session with scalp electrodes placed over the Fz, Cz and Pz positions of the 10–20 International System (impedance below 5000 Ω), referring to the nasion with the ground at Fpz, and by T3 and T4 derivation, referred to the Fz position. Another electrode was placed above the right eye to record the electroculogram. Signals were amplified, filtered (0.5–80 Hz) and stored on a biopotential analyzer (MICROMED System Plus).

2.4. Stimulation

The stimulation site was visualized by a He–Ne laser beam. After each stimulation, the laser beam was slightly shifted to a nearby spot to avoid nociceptor sensitization and skin damage. A preliminary observation of possible skin damage was done in