Clinical Neurophysiology 125 (2014) 1826–1833

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Influence of limb temperature on cutaneous silent periods

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ARTICLE INFO

Article history:
Accepted 26 January 2014
Available online 4 February 2014

Keywords:
A-delta fiber
Cutaneous silent period
Nerve conduction
Physiology
Spinal reflex
Temperature

HIGHLIGHTS

- The cutaneous silent period (CSP) is part of a spinal protective reflex mechanism, which may be affected by temperature.
- Changes in limb temperature result in disparate changes of conduction times in large- and small-diameter fibers.
- CSP latencies are disproportionately more affected by temperature than routine nerve conduction parameters, a fact which should be considered in clinical CSP testing.

ABSTRACT

Objective: The cutaneous silent period (CSP) is a spinal inhibitory reflex mediated by small-diameter afferents (A-delta fibers) and large-diameter efferents (alpha motoneurons). The effect of limb temperature on CSPs has so far not been assessed.
Methods: In 27 healthy volunteers (11 males; age 22–58 years) we recorded median nerve motor and sensory action potentials, median nerve F-wave and CSPs induced by noxious digit II stimulation in thenar muscles in a baseline condition at room temperature, and after randomly submersing the forearm in 42 °C warm or 15 °C cold water for 20 min each.
Results: In cold limbs, distal and proximal motor and sensory latencies as well as F-wave latencies were prolonged. Motor and sensory nerve conduction velocities were reduced. Compound motor and sensory nerve action potential amplitudes did not differ significantly from baseline. CSP onset and end latencies were more delayed than distal and proximal median nerve motor and sensory latencies, whereas CSP duration was not affected. In warm limbs, opposite but smaller changes were seen in nerve conduction studies and CSPs.
Conclusion: The observed CSP shift "en bloc" towards longer latencies without affecting CSP duration during limb cooling concurs with slower conduction velocity in both afferent and efferent fibers. Disparate conduction slowing in afferents and efferents, however, suggests that nociceptive EMG suppression is mediated by fibers of different size in the afferent than in the efferent arm, indirectly supporting the contribution of A-delta fibers as the main afferent input.
Significance: Limb temperature should be taken into account when testing CSPs in the clinical setting, as different limb temperatures affect CSP latencies more than large-diameter fiber conduction function.

1. Introduction

Noxious electrical stimulation of a cutaneous nerve produces transient suppression of electromyographic (EMG) activity in a voluntarily contracted muscle in the same limb, known as the cutaneous silent period (CSP) (Kofler and Poustka, 2005; Kofler, 2003; Leis et al., 1992; Shefner and Logigian, 1993; Uncini et al., 1991). The CSP is part of a complex spinal protective reflex mechanism (Floeter, 2003; Inghilleri et al., 1997; Leis et al., 2000), which

Abbreviations: APB, abductor pollicis brevis muscle; CMAP, compound muscle action potential; CSP, cutaneous silent period; DML, distal motor latency; DSL, distal sensory latency; EMG, electromyographic; D2, index finger; LLR, long-loop reflex; mNCS, motor nerve conduction study; mNCV, motor nerve conduction velocity; PML, proximal motor latency; PSL, proximal sensory latency; SNAP, sensory nerve action potential; sNCS, sensory nerve conduction study; sNCV, sensory nerve conduction velocity.

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http://dx.doi.org/10.1016/j.clinph.2014.01.018
1388-2457/

becomes evident as a sequence of inhibitory and excitatory events in the EMG trace of a volitionally activated muscle (Floeter, 2003). This EMG activity can be attributed to concomitant activation of various fiber types as well as spinal and supraspinal reflex pathways. In more detail, high-threshold slowly conducting small-diameter fibers of the A-delta group (Erlanger and Gasser, 1937; Lloyd, 1943) have been identified as the most important afferent inhibitory input to the spinal cord for evoking the CSP (Kofler, 2003; Kofler et al., 2001; Leis et al., 1992; Romaniello et al., 2004; Shefner and Logigian, 1993). Evidence is based on (1) the requirement of stimuli at or above pain threshold in order to induce reproducible and profound EMG suppression (Kofler, 2003; Leis et al., 2000; Rodi and Springer, 2011); (2) calculation of conduction velocities of the respective afferents by stimulating two points along a cutaneous nerve, yielding estimates of 9–18 m/s, consistent with A-delta fibers (Inghilleri et al., 1997; Kranz et al., 1973; Leis et al., 1991); (3) preservation of normal CSPs in the presence of ischemia-induced blocking of large-diameter fibers (Serrao et al., 2001); (4) presence of normal CSPs in patients with profound large-diameter fiber sensory neuropathies with absent SNAPs or somatosensory evoked potentials (Inghilleri et al., 1995; Leis et al., 1992; Uncini et al., 1991), (5) induction of CSPs by laser stimulation exclusively activating A-delta fibers (Romaniello et al., 2004). Low-threshold, fast-conducting, large-diameter Inhibitory afferent fibers have been suggested to produce cortical inhibition (Chen and Ashby, 1993; De Noordhout et al., 1992). A contribution to CSP generation of large-diameter inhibitory afferents, which are known to evoke cutaneomuscular reflexes, has also been suggested (Serrao et al., 2001, 2002). Their inhibitory effect, however, was detectable only in thenar muscles following index finger stimulation, but not in other finger-muscle-combinations (Kofler, 2003; Kofler et al., 2001). Different spinal circuitry is activated by high- and low-threshold afferents (Floeter, 2003; Serrao et al., 2001, 2002). Concomitant excitatory reflex activity of variable magnitude which may occur during and after the CSP can be attributed to activation of large-diameter excitatory fibers. CSPs are often interrupted by burst-like EMG activity occurring at latencies around 60–70 ms, i.e. during the first part of EMG suppression, consistent with an excitatory transcortical long-loop reflex (LLR) (Leis, 1994). LLR probability and magnitude varies with stimulus intensity, combination of muscle recorded and digit stimulated, and applied muscle force (Kofler, 2003; Kofler et al., 2007). TMS studies revealed presence of spinal nociceptive EMG suppression even during "superimposed" transcortical LLRs (Kofler et al., 2008). Large LLRs which may divide the CSP as well as small-amplitude LLRs do not interfere with accurate CSP onset measurements, yielding so called "early-onset" CSPs. Large LLRs, however, may also overly the initial CSP segment, resulting in a seemingly delayed CSP onset (so-called "late-onset" CSP) (Kofler, 2003, 2004; Kofler and Poustka, 2004; Kofler et al., 2007; Leis et al., 1992; Rodi and Springer, 2011). Excitatory EMG activity following the CSP is due to both post-inhibitory resynchronization of motoneuron discharge (Kranz et al., 1973) and a superimposed somatosensory startle reaction (Kumru et al., 2009).

The exact neural mechanism of exteroceptive inhibition has as yet to be elucidated, as the CSP could be evoked either by postsynaptic inhibition of the motoneuron itself or through presynaptic inhibition of excitatory inputs to those motoneurons which sustain the voluntary contraction due to corticomotoneuronal activation (Inghilleri et al., 1997; Leis et al., 1995; Shefner and Logigian, 1993). Several characteristics of the CSP depend on physiological parameters, e.g. the combination of nerve stimulated and muscle recorded from (Kofler, 2003). Most CSP studies so far have focused on the upper limbs and thenar or hypothenar muscles. Other physiological determinants comprise gender (de Leonni Stanonik et al., 2010; Kofler and Poustka, 2004), body height (Kofler and Poustka, 2004; Koo et al., 2010) or age (de Leonni Stanonik et al., 2010; Koo et al., 2010). To our knowledge, the influence of limb temperature on the CSP has so far not been assessed.

Nerve conduction in large-diameter fibers is known to be affected by temperature (Abramson et al., 1966, 1969; Lucas, 1908; Maxwell, 1907; von Helmholtz, 1850). It is less clear, however, whether temperature affects nerve conduction in thinly myelinated nerve fibers (de Jesus et al., 1973; Douglas and Malcolm, 1955; Paintal, 1965a,b). We reasoned that analysis of the influence of temperature on various CSP parameters could possibly shed light on the fiber types contributing to CSP production We hypothesized that changes in limb temperature will affect CSP parameters in a predictable manner in the efferent arm (large-diameter motor axons originating from alpha-motoneurons), whereas any additional effect would be attributable to a temperature-associated influence on afferent fibers. If the effect of temperature on various fiber sizes is linear, changes seen in the CSP would indirectly provide information about the type of afferent fibers participating in the generation of the CSP.

We therefore studied routine median motor and sensory nerve conduction, F-wave latency, and CSP in thenar muscles following index finger stimulation at three different limb temperatures in a group of healthy volunteers, and correlated the observed temperature-associated changes of routine nerve conduction studies to temperature-associated changes in CSP parameters.

2. Subjects and methods

Twenty-seven healthy volunteers (11 males; age 22–58 years) without evident neurological history were investigated; 11 subjects (4 males) were studied in Prague, Czech Republic; 16 subjects (7 males) were tested in Zirl, Austria. Subjects underwent serial CSP testing after granting written informed consent. Routine electrodiagnostic equipment was used in all experiments: Nicolet Viking IV, Viasys, Madison, Wisconsin, USA (in Zirl, Austria); Dantec Keypoint, Dantec-Medtronic, Skovlunde, Denmark (in Prague, Czech Republic). The study was approved by both institutional review boards.

Subjects were seated on a height-adjustable chair with their arms resting relaxed on adjustable tables on each side. The non-dominant hand was tested in a slightly pronated position with the fingers extended; 25 subjects were right-handed, two left-handed. Each experimental block consisted of:

(1) Median motor nerve conduction study (mNCS), applying supramaximal square wave stimuli of 0.2 ms duration to the median nerve at the wrist and at the elbow using a bar electrode with 3 cm interelectrode distance. Surface stainless steel recording electrodes were attached in belly-tendon arrangement over abductor pollicis brevis muscle (APB). Filters were set at 10 and 10 000 Hz. Median mNCS yielded distal motor latency, DML (wrist to APB), proximal motor latency, PML (elbow to APB), motor nerve conduction velocity, mNCV (elbow to wrist), compound muscle action potential (CMAP) peak-to-peak amplitude (following wrist stimulation), and minimum F-wave latency (following antidromic wrist stimulation);

(2) Median sensory nerve conduction study (sNCS), applying supramaximal square wave stimuli of 0.5 ms duration to the median nerve at the wrist and elbow. Stainless steel adjustable ring electrodes were attached to the distal and middle phalanx of the non-dominant index finger (D2). Filters were set at 5 and 2000 Hz. Median sNCS yielded distal sensory latency, DSL (wrist to D2), proximal sensory latency, PSL (elbow to D2), distal sensory nerve conduction velocity, sNCV (wrist to D2), proximal sNCV (elbow to wrist), and sensory nerve action potential (SNAP) peak-to-peak amplitudes (following wrist stimulation);