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Short communication

Reappearance of sympathetic skin response below a thoracic level-9 complete spinal cord injury

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ABSTRACT

Reappearance of sympathetic skin response (SSR) below lesion is reported in a patient with a complete thoracic-9 spinal cord injury 6 months following injury. SSR was elicited by electrical stimulation of supraorbital nerve (SON) and pudendal nerve (PN). SON stimulation induced SSRs only in the hand. SSRs were initially absent below the level of SCI but reappeared only with PN stimulation.
This case suggests that 6 months following a complete lesion, the isolated spinal cord can generate a SSR. Possible underlying mechanisms and implications for autonomic plasticity below spinal lesion are discussed in view of the literature.

1. Introduction

Sympathetic skin response (SSR) is a simple, non-invasive electrophysiological test that examines the common efferent pathways of the sympathetic nervous system (Veciana et al., 2007; Vetrugno et al., 2003). Centers of the cerebral cortex and the brainstem have been proposed as sites where sensory signals generate the SSR (Korpelainen et al., 1993; Vetrugno et al., 2003).

The recording of SSR allows an independent and objective assessment of disconnection of the sympathetic spinal centers from supraspinal control, which has been related with autonomic dysfunction in lesion levels above T6 (Curt et al., 1997). Except in one study where reproducible SSRs had been shown below a complete SCI elicited by pudendal nerve stimulation (Reitz et al., 2002) in seven subjects, no further evidence was found to support the hypothesis that the spinal cord isolated from the brain stem could generate a SSR (Cariga et al., 2002; Kumru et al., 2009; Nicotra et al., 2005a,b; Previnaire et al., 2012). Here, we describe the reappearance and reproducibility of SSR below the spinal lesion level at different time points of neurophysiological evaluations, following SCI from subacute until chronic phase and its relation with detrusor overactivity. The case reported here was observed within a clinical trial: 'Effectiveness of a treatment of neurogenic detrusor overactivity by application of early external pudendal nerve stimulation' performed within the European multi-center study about SCI (see www.emsci.org). SSR was repeatedly assessed to evaluate effects on autonomic neuroplasticity.

2. Methods

A twenty-four-year-old male patient suffered a complete SCI, with a spinal cord transection, due to a traffic accident three days prior to admission at our institution. On admission, initial neurological examination revealed sensory and motor complete SCI at the thoracic (T) 9.

2.1. Neurophysiological studies

We performed electrophysiological studies with the patient supine (with ambient temperature: 22–24°). Patient underwent a neurophysiological evaluation (see www.emsci.org) for motor evoked potentials (MEPs), somatosensory evoked potential (SSEP) recordings and SSR. A Medelec synergy electromyograph (Oxford Instruments, England) was used for all the tests.

MEPs were elicited by single transcranial magnetic stimulus using a Magstim Super Rapid (Magstim Company, Whitland, UK) through a double-cone coil over the vertex. MEPs were recorded by surface electrodes over tibialis anterior and adductor hallucis muscles bilaterally. Single sweeps of 100 ms were recorded, filtered at 10–2000 Hz and amplified with a gain of 0.1 mV/div.

For somato-sensory evoked potentials (SSEPs), the tibial nerve and the pudendal nerve (PN) were stimulated. For PN SSEPs, the stimulation was applied with ring electrode over penis (cathode on penis, anode

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2–3 cm further distal) (with 100 mA intensity and 0.5 ms duration). Two sets of responses were averaged with sweeps of 100 ms, filters set at 10 and 2000 Hz, and amplified at a gain of 2 μV/div.

MEPs and SSEPs were recorded after 15 days and after 1 year following SCI to verify completeness of injury of somatosensory afferents and efferents.

SSRs were recorded on the right hand, the right and left feet, and the perineum. For the hand, the active electrode was attached to the palm and the reference electrode to the dorsum. For the foot, the active electrode was attached to the sole and the reference to the dorsum. For perineum recordings, the active electrode was attached to the perineum (below the scrotum) and the reference electrode to the iliac crest with the ground on the right leg. For all SSR recordings, we used a band-pass of 0.1 to 100 Hz and a sensitivity of 0.5 mV per division. Sweep duration was 10 s.

For stimulation above SCI lesion level, electrical stimulus was applied to the right supraorbital nerve (SON), and below SCI lesion level the pudendal nerve (PN) was stimulated. Duration of electrical stimulus of SON was 0.5 ms and the intensity was set at 15 mA to induce a clear SSR. For PN stimulation, we used a ring electrode over the penis (cathode proximal, anode 2–3 cm distal) (with 100 mA intensity and 0.5ms duration). Each stimulus was repeated at least 3 times at each point with an interstimulus interval at least 30 s to reduce habituation (Chroni et al., 2006; Kumru et al., 2009).

Urodynamic testing: Cystomanometry (CMG) and ice water test (IWT) were performed subsequently (Abrams et al., 2003). SSR and urodynamic recordings were obtained in independent sessions around 15 days (just SSRs) and 1, 3, 6 and 10 months following SCI.

2.2. Data analysis

MEPs and SSEPs were evaluated visually at highest resolution, and latency and amplitude were calculated if there was any response.

We calculated the onset latency of SSR in the hand, the feet and in the perineum. SSR was considered present if the amplitude of SSR was ≥50μV and amplitudes were determined peak to peak. If there was no identifiable SSR, response amplitude was considered "0" and no value was entered for response latency. The SSR probability (%) to the total number of stimuli ($n = 3$) was calculated for each stimulated nerve. We used one-way ANOVA to compare latencies of SSR in feet and perineum.

3. Results

The patient completed neurophysiological studies without any complaints at all time points. He did not present any symptoms of autonomic dysreflexia such as sweating, change of skin color, or blood pressure, spontaneously or during any of the neurophysiological examinations. During PN stimulation, he did not report any sensation (complete SCI). The clinical diagnosis of complete SCI at T9 was confirmed one year following SCI, clinically and by neurophysiological evaluation. After 15 days and 1 year following SCI, MEPs were absent in the studied muscles on both sides and SSEPs also were absent with TN stimulation from both sides and with PN stimulation. Popliteal fossa potentials with TN stimulation were always normal.

The SON stimulation induced SSRs only in the hand without any SSRs in the feet, or in the perineum, at any time of evaluation following SCI (Fig. 1A, Tables 1–2).

PN stimulation did not induce SSRs in any of the recorded areas (right hand, feet and perineum) after 15 days, 1 and 3 months following SCI (Fig. 1B, Table 1). However, after 6 and 10 months following SCI, SSRs reappeared with PN stimulation in the feet and perineum, but not in the right hand (Table 1, Fig. 1B). The latencies of SSR in the feet and the perineum were not significantly different ($p > 0.2$).

The SON stimulation induced SSRs in the hand with 100% persistency, without any SSRs in the feet, or in the perineum, at any time of evaluation following SCI (Fig. 1A). The PN stimulation induced SSRs in the feet and perineum with 100% of persistency after 6 months following SCI, but not in the hand (0% persistency) at any time of evaluation following SCI (Fig. 1B).

Urodynamic testing at 1 month showed a contractile bladder with low compliance and negative IWT. After 3 months, it was hypocontractile with normal bladder compliance and positive IWT. After 6 and 10 months, the bladder showed neurogenic detrusor overactivity with detrusor sphincter dyssynergia.

4. Discussion

This is the first case report of a reappearance of SSR below lesion with pudendal nerve stimulation (i.e. stimulation below the lesion level) after 6 and 10 months following SCI, despite clinically- and electrophysiologically-proven sensory and motor complete SCI lesion.

4.1. SSR elicited by supraorbital nerve stimulation

Appearance of the SSRs in SCI following supraorbital stimulation (SON) depends on the level of lesion. Our patient confirms previous observations in complete SCI patients with a neurological lesion level at T9, and showed that stimulation above the level of lesion evoked normal palmar SSRs, without any plantar SSRs, suggesting preserved sympathetic pathway function to the arm, but not to the leg.

4.2. SSR elicited by pudendal nerve stimulation below the lesion

To our knowledge, this study showed for the first time reappearance and reproducibility of SSRs in humans below a complete SCI, elicited by pudendal nerve stimulation 6 and 10 months following a complete SCI, as was ascertained with clinical- and neurophysiological-examination (Fig. 1). When testing with SON stimulation the existence of palmar SSRs in combination with a lack of plantar SSRs indicates the complete lesion of efferent sympathetic pathways while testing with PN stimulation the existence of a plantar SSRs without palmar SSR suggests that spinal sympathetic pathways below the lesion were reactivated and after a latency of 6 months became excitable without supra-spinal sympathetic input.

Reitz et al. (2002) have reported plantar SSRs with PN stimulation in seven complete SCI patients, while in other more recent studies, no more evidence was found to support their hypothesis that the spinal cord isolated from the brainstem could generate a SSR. The differences between earlier studies searching below level SSR (Cariga et al., 2002; Fuhrer, 1971; Prévinaire et al., 1993; Reitz et al., 2002), and our study, pertain 1. to methods of stimulation (stimulation parameters or site of stimulation), and 2. to observation of reproducibility during the time course following SCI. In earlier studies showing SSR below lesion level, unusually strong electrical stimulations were used (trains of ten 50 Hz-stimuli up to 80 mA; Reitz et al., 2002, or Fuhrer, 1971 used electrical stimuli with intensity "deemed the maximum permissible to avoid visible damage of the skin"). Similarly, bladder distension with a rise in intravesical pressure associated with bladder hyperreflexia induced SSR below the level of spinal lesion (Prévinaire et al., 1993). We report evaluation at different time points following SCI, from the very early through chronic phases, when strong electrical PN stimulation elicited perineal and plantar SSR, while the stimulus remained unnoticed by the subject, thus proving completeness of spinal lesion. With respect to the above discussion of differences in methods, we assume that stimulus characteristics are responsible for the presence of below level SSR, because these responses may be difficult to obtain, requiring strong stimuli as was suggested earlier (Reitz et al., 2002).