



# Paradoxical shortening of sympathetic skin response latency at distal recording sites

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## ABSTRACT

**Objective:** The purpose of this study was to investigate and to discuss the neurophysiological mechanism of paradoxical shortening of the sympathetic skin response (SSR) latency at distal recording sites.

**Methods:** The latency and peak-to-peak amplitude of SSRs evoked by magnetic stimuli were analyzed. Eight active electrodes were placed on the palmar (anterior) and dorsal (posterior) sides of the hand (forearm) proximal to the distal arrangement.

**Results:** SSRs from two palm sites had significantly shorter latencies and larger amplitudes than the SSRs at the other six sites, including the proximal sites of the forearm.

**Conclusions:** This finding indicated that the SSR latency at different sites was not linearly prolonged as the distance of the recording sites from the proximal to distal areas increased. The paradoxical shortening of the latency and the large amplitude of the SSR from the palm can be explained by a recent model of the equivalent current dipole caused by the Na<sup>+</sup> concentration gradient. The high density of sweat glands in the palm possibly produced the present findings.

**Significance:** We should carefully interpret the sudomotor conduction velocity derived from latency difference between two sites, especially for thermal and emotional sweating.

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## 1. Introduction

The sympathetic skin response (SSR) (Shahani et al., 1984) is a transient change in the electrical potential of the skin induced by various kinds of stimulation. Earlier studies have focused on the clinical significance of SSR in various pathological conditions (Gutrecht, 1994; Arunodaya and Taly, 1995; Marchello et al., 1996; Ravits, 1997; Vetrugno et al., 2006). Latency and amplitude are commonly measured for quantitative analysis of SSR. The actual significance of these parameters will not be completely understood until the neurophysiological mechanism of SSR forming is clearly established. The electrophysiological attributes of the latency and amplitude in SSR differ from those observed in conventional motor and sensory nerve conduction study.

The SSR from the sole always appears later than that from the palm after stimulation. Investigators have yet to establish whether the SSR latencies at different sites are linearly prolonged with the increasing distance of the recording sites from proximal to distal areas. One study reported a shortening of SSR latency at more distal site (Kanzato et al., 1997). Another study found no difference between the SSR latency at the mid-palm and at the forearm (Matsunaga et al., 1998). The mechanisms underlying these findings have not been fully investigated. Based on the principal of

conventional nerve conduction study, sudomotor conduction velocity (CV) is sometimes measured by calculating the difference in latency between two recording sites (Shahani et al., 1984; Knezovic and Bajada, 1985; Uncini et al., 1988; Elie and Guiheneuc, 1990; Parisi et al., 2001). The issues and findings mentioned above merit a reassessment of the validity of this method for calculating the CV.

The present study was conducted to analyze SSRs obtained from several sites on the hand and forearm. Magnetic stimulation of a rather high intensity was used to elicit SSRs at the forearm. The author also discussed the neurophysiological mechanism responsible for the paradoxical shortening of the latency at the distal site.

## 2. Methods and materials

The subjects were 10 healthy male volunteers (aged 20–40, average 28 years), all of whom gave their informed consent to be studied.

### 2.1. SSR record

The SSRs were elicited between 5 and 7 p.m. in a quiet, brightly lit room, maintained at an almost constant temperature and humidity year round by air-conditioning. The subjects were instructed not to fall asleep, cough, or breathe deeply while the SSRs were being recorded.

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The magnetic stimulator was a Magstim 200 (The Magstim Company) with a maximum magnetic field of 2 T. A Neupack 8 (NIHON KODEN) was used to record and analyze the SSRs. Eight active electrodes were, respectively, placed on the palmar (p-A and p-B) and dorsal (d-A and d-B) sides of the hand and the anterior (p-C and p-D) and posterior (d-C and d-D) sides of the forearm (see Fig. 1) in a proximal-to-distal arrangement. One reference electrode was set on the nail of the index finger. In the present work, the author did not aim to investigate the influence of stimulation modality on the paradoxical shortening of SSR. Magnetic stimulation was selected for the stimulation modality because it can elicit reproducible responses (Matsunaga et al., 1995; Toyokura, 2003).

Magnetic stimulus was applied to the subject's neck (C7 or C8 spinous process) using a round coil with inner and outer diameters of 66 and 123 mm. The current direction was counter-clockwise, according to the method of Matsunaga et al. (1995). The subject was exposed to four consecutive sets of three stimuli of different strengths (10%, 35%, and 70% of the maximum output in that order). The reproducibility of the response to this stimulation method is easily confirmed, and habituation to stimulation by this method is infrequent (Toyokura, 2003, 2006). The stimuli were delivered at an irregular interval of 40–60s.

The filter bandpass was set between 0.5 and 3000 Hz, and the analysis time was 10 s. The skin temperature was monitored with a thermometer's probe placed on the skin surface throughout the experiment.

## 2.2. Analysis

All the SSRs selected for the analysis were responses evoked by the stimulation of maximum strength. The latency and peak-to-peak amplitude of each response were measured. When measuring the onset latency, the sensitivity to a level around 0.2 mV/div was changed to make clear the point for the beginning of the response. In a previous study, the author had already confirmed the reproducibility of the latency values (Toyokura and Murakami, 1996).

The differences in the measurements (latency and amplitude) between the recording sites were examined. Responses from palmar (anterior) and dorsal (posterior) recording sites were analyzed using one-way repeated-measure-ANOVA followed by a Fisher PLSD test for multiple comparison. Significance was accepted at  $p < 0.05$ .

## 3. Results

The skin temperature ranged from 32.2 to 35.8 with a mean of 33.9 °C. Every maximum stimulus evoked an SSR in every subject. Examples of the responses are shown in Fig. 1. A total of 320 responses (8 recording sites  $\times$  4 trials  $\times$  10 subjects) were analyzed.

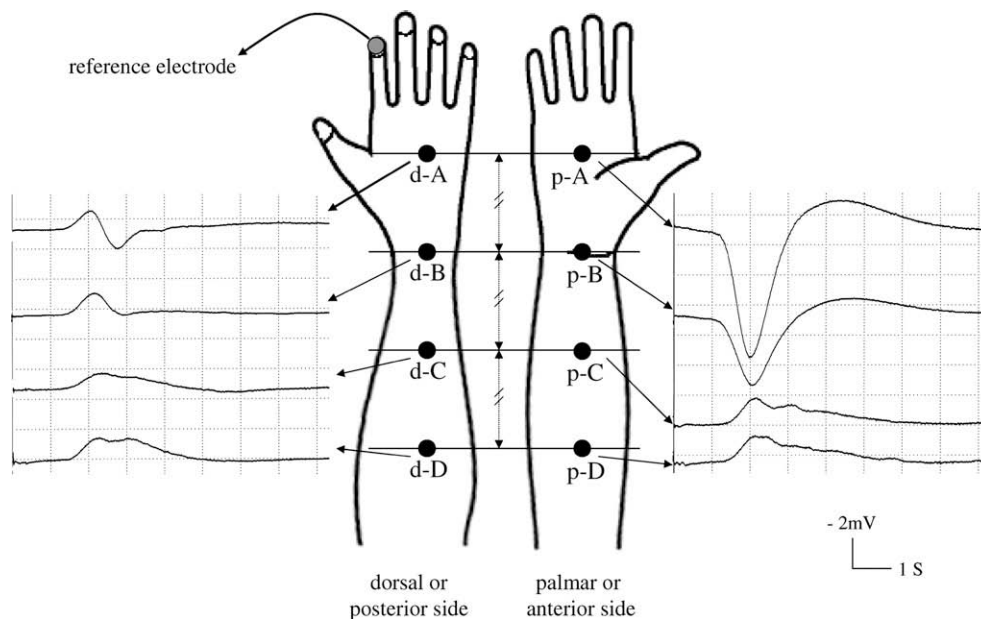
### 3.1. Habituation

The amplitude of SSRs obtained from each recording site usually remained stable over the four trials. Only a few of the responses declined in the later trials. The amplitudes of the four serial SSRs were statistically unchanged in all but one recording site. The exception was a significant decrease at p-D ( $F = 3.36$ ,  $p < 0.05$ ). The mean (SD) values (mV) of the four trials were 1.98 (1.17), 1.36 (0.73), 1.49 (1.04), and 1.35 (0.67). Habituation appeared at the second trial.

The latency, however, showed no significant change across time in any of the recording sites.

### 3.2. Comparison of latency among the eight different sites (Fig. 2)

The latencies of the eight responses significantly varied in every trial ( $F = 4.48$ , 4.48, 3.70, and 5.64 for the first to fourth trials, respectively,  $p < 0.001$  for all). On palmar side of the hand and anterior side of the forearm, the latency values of two SSRs from p-A and B were significantly shorter than the values of the other two SSRs (p-C and D). In other words, the SSRs from the distal sites paradoxically appeared earlier than the SSRs from the proximal sites. In contrast, the SSRs on the dorsal side of the hand and pos-



**Fig. 1.** Examples of SSRs evoked from eight different sites. Four sites (d-A, d-B, d-C, and d-D) are on the dorsal or posterior side (left) and the corresponding four sites (p-A, p-B, p-C, and p-D) are on the palmar or anterior side (right). The p-B site is on the distal wrist crease. The p-A site is located at a palmar midpoint between the p-B and metacarpophalangeal joint. The p-C (p-D) is set at a point proximal to p-B (p-C) by the same distance between p-A and p-B. Therefore, each distance between neighboring sites is identical. The pair of corresponding sites in the palmar and dorsal sides (i.e. d- and p-A) is positioned at about the same distance from the site of stimulation. Note that the SSRs from p-A and p-B have shorter latencies and larger amplitudes than those from the other six sites. A reference electrode is placed on the nail of the index finger.

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