INTRODUCTION

The sympathetic skin response (SSR) is a slow wave resulting from the activation of sudomotor sympathetic efferent fibres, due to a transient voltage change in the palm of the hand or in the sole of the foot, related to a change in skin resistance induced by various stimuli. This reflex comprises three phases: i) somatosensory myelinated afferent, ii) central coupling, and iii) efferent sympathetic cholinergic controlled output (1). The SSR is closely correlated with other autonomic function tests and its abnormalities are documented in a variety of neurological disorders (2-6). When strict experimental paradigms are respected,

The aim of this study was to establish a simple method for estimating the conduction velocity (CV) of postganglionic sympathetic sudomotor C fibres (SSFCV) in the upper and lower limbs by simultaneously measuring the sympathetic skin reflex (SSR) in two distant sites. Fifty healthy volunteers were studied. SSRs were recorded with standard surface electrodes applied to both proximal (axilla and crural line) and distal sites for each limb (hand and foot). The CV of the efferent branch of the SSR was calculated by dividing the difference in the latencies of the response from two recording sites by the distance between the sites (axilla-hand for upper limb; crural line-foot for lower limb). Day-to-day reproducibility and intra-individual variability of the SSFCV were calculated. For the upper limbs, the SSFCV in the axilla-hand tract was 2.0±0.3 m/sec (range 1.6-2.4 m/sec). For the lower limb, the SSFCV in the crural line-foot tract was 1.4 ±0.4 m/sec (range 1.2-1.6 m/sec). Mean intra-individual variability of the SSFCV for the upper and lower limbs was 0.11 and 0.09, respectively. The coefficient of variation of the SSFCV for the upper and lower limbs was 5.1% and 5.4%, respectively. Our data show that this simple and non-invasive method can reliably be used to measure the CV of the sympathetic sudomotor fibres, in suitable temperature conditions, and may be useful when investigating the physiological functions of peripheral nerves in patients with peripheral neuropathies.

KEY WORDS: Conduction velocity, SSR, sudomotor C fibres.
SSR is a simple, useful and reproducible electrophysiological technique for the investigation of sympathetic sudomotor outflow in central and peripheral nervous system disorders (7,8). In peripheral disorders, the evaluation of the latency and amplitude of the SSR may help in the monitoring of post-ganglionic sympathetic cholinergic fibres. However, as the amplitude and latency of the response can vary greatly on consecutive stimulations and as there is a marked tendency to habituation, there is actually no simple way of quantifying the expression of sympathetic activity. One of the most important laboratory examinations for patients with peripheral neuropathies is the measurement of conduction velocities (CVs) of the peripheral nerves. Microneurographic measurement (9) of the CV of efferent sympathetic fibres is too complex for routine diagnostic work. Although the CV of post-ganglionic sympathetic sudomotor fibres (SSFCV) has been obtained by measuring the SSR in two different sites (10,11), reports on this method are anecdotal, were based on few subjects and were performed either in the upper or lower limbs, or not both together.

The aim of this study was to establish a simple method for estimating the CV of post-ganglionic sympathetic sudomotor C fibres (SSFCV) in the upper and lower limbs by simultaneously measuring the SSR in two distant sites.

MATERIALS AND METHODS

Subjects

Fifty healthy right-handed volunteers (30 F, 20 M; age range 20-60 years; mean age 40.5 years) participated in our study.

No subjects had symptoms or signs of central or peripheral nervous system diseases, showed autonomic nervous disturbances (e.g., postural hypotension or abnormal perspiration) or were on medication affecting autonomic function.

All participants gave their informed consent after a full explanation of the protocol.

Techniques

Fifteen minutes before the start of the experiment, the subjects were placed in supine position in a quiet air conditioned room with a mean temperature of 26°C. As suggested by Deltombe et al. (12), during the study skin temperature was monitored on the skin surface by using a digital infrared thermometer (First Temp Genius Thermometer, Model 3000 A) immediately prior to and after each series of electrical stimulations. The skin temperature was measured on the electrode sites. Owing to the correlation between skin temperature and the SSR (12,13), a constant skin temperature of 36±0.5°C at the proximal sites, and 34±0.5°C at the distal sites was maintained, if necessary, by using an infrared thermistor lamp.

SSRs were recorded with standard electromyographic disk AgCl electrodes, covered with conducting paste, applied to both proximal and distal sites for each limb. For the proximal site, in the upper limb the active electrode was attached to the axilla, and the reference electrode to the shoulder (8-10 cm apart); in the lower limb, the active electrode was attached to the crural line, and the reference electrode to the sacro-iliac anterior-superior spinae (8-10 cm to one side of the active electrode). For the distal site, the electrodes were attached to the palm (active electrode) and dorsum (reference electrode) of the hands and on the soles (active electrode) and dorsum (reference electrode) of the foot. SSRs were obtained by means of simultaneous recordings in the proximal and distal sites (Fig. 1).

A bandpass of 0.16 to 3200 Hz and a sensitivity value of 0.5 to 2 mV per division were used, while the sweep speed was 1.0 second.
per division. Single electrical stimuli were delivered to the wrist contralaterally to the recording side. The stimuli were given at irregular long intervals to avoid habituation with an interval of >30 s between two stimuli. The response was considered absent if no consistent voltage change was seen when using a sensitivity of 50 µV per division after six or more trials. Measurements were performed 10 times for each subject. The SSR latencies were measured from the start of the stimulus to the first deflection of the signal from baseline (Fig. 1). Baseline-to-peak, and peak-to-peak amplitudes were not measured because these parameters were irrelevant to the purposes of our study. The CV of the efferent branch of the SSR was calculated by dividing the difference in the latencies of the response from two recording sites by the distance between the sites (axillary-hand for upper limb; crural line-foot for lower limb). Right and left sides were evaluated separately.

In order to render the method as accurate as possible, we calculated individual responses offline. Only traces in which the onset latency was clearly detectable from the baseline were used for the calculation of the SSFCV. Individual SSFCVs were calculated as the mean of 10 traces. Intra-individual variability of the SSFCV was measured by calculating the SD/mean ratio of the values obtained in 10 traces.

All the subjects underwent conventional motor and sensory nerve conduction studies with F responses.

Sensory nerve action potential amplitudes were used to estimate the functional integrity of large diameter somatic afferent fibres. Testing was performed with an electromyographic machine (Mystro System, Medelec MS20, Vickers Healthcare Company).

Day-to-day reproducibility was assessed by calculating the coefficient of variation (SD of the within-subject variance divided by the mean percentage) between two repeated measurements in 20 subjects within seven days.

RESULTS

Conduction velocity

The SSR was measured in all subjects at the hand and foot sites.

In 5% of the subjects, we were not able to measure any SSR at the axilla and/or the crural line sites. Table I shows SSR latencies and SSFCV for the upper and lower limbs.

For the upper limbs, the SSFCV in the axilla-hand tract was 2.0 ± 0.3 m/sec (range 1.6-2.4 m/sec). For the lower limbs, the SSFCV in the crural line-foot tract was 1.4 ± 0.4 m/sec (range 1.2-1.6 m/sec). No significant difference was found between the right and left SSR recordings (p>0.05).

There was no significant correlation between the CV values and the age of the subjects for either the upper or lower limbs (p>0.05).

Mean intra-individual variability of the...
SSFCV for the upper and lower limbs was 0.11 and 0.09, respectively. The coefficient of variation of the SSFCV for the upper and lower limbs was 5.1% and 5.4%, respectively.

**DISCUSSION**

Sympathetic C fibres are difficult to evaluate in man. Although microneurographic techniques allow a more direct assessment of sympathetic neural outflow, this method is too complex, invasive and time-consuming for a routine diagnostic examination.

The SSR is usually recorded only at distal sites of the upper and lower limbs (the palmar and plantar surfaces) at ambient temperature. It has been shown that by increasing ambient temperature, the SSR appears on other parts of the body surface (13). As the aim of this study was to measure the SSR at a more proximal site, the room temperature was kept at 26°C and skin temperature was kept >34°C, thus providing optimal experimental conditions for recording the SSR at the axilla and crural line in a high percentage of healthy subjects (95%). Repeated measurements showed a degree of reproducibility of the SSR which was good enough to allow the measurement of the CV of the sudomotor C fibres.

Considering the difficulties in investigating peripheral fibres with slow conduction velocities (C-fibres) in humans, the method used in the present study may be useful in both experimental and clinical studies.

Data from the literature indicate that the SSR recorded from the palm of the hand and the sole of the foot is a method that can reliably be used to describe a small section of the autonomic nervous system (sympathetic sudomotor function) and to calculate group differences.

Owing to habituation and the great variability in the amplitude and morphology of the SSR, it is generally accepted that amplitude

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Table I - Sympathetic skin reflex (SSR) latencies and sympathetic sudomotor C fibre conduction velocity (SSFCV) values in healthy subjects.

<table>
<thead>
<tr>
<th></th>
<th>Mean ± SD (no. = 50)</th>
<th>Range (no. = 50)</th>
<th>Intra-individual variability^ (mean; no. = 50)</th>
<th>Day-to-day reproducibility^ (mean %; no. = 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SSR onset latency (msec)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wrist</td>
<td>1.76 ± 0.52</td>
<td>1.4-2.4</td>
<td>0.29</td>
<td>13.6%</td>
</tr>
<tr>
<td>Axilla</td>
<td>1.4 ± 0.42</td>
<td>0.96-1.9</td>
<td>0.32</td>
<td>13.8%</td>
</tr>
<tr>
<td><strong>SSFCV (m/sec)</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Axilla-wrist</td>
<td>2.0 ± 0.4</td>
<td>1.7-2.2</td>
<td>0.11</td>
<td>5.1%</td>
</tr>
<tr>
<td><strong>SSR onset latency (msec)</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Foot</td>
<td>2.1 ± 0.66</td>
<td>1.4-2.8</td>
<td>0.32</td>
<td>14.7%</td>
</tr>
<tr>
<td>Crural line</td>
<td>1.5 ± 0.5</td>
<td>0.98-2.1</td>
<td>0.3</td>
<td>14.1%</td>
</tr>
<tr>
<td><strong>SSFCV (m/sec)</strong></td>
<td></td>
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</tr>
<tr>
<td>Crural line-foot</td>
<td>1.4 ± 0.4</td>
<td>1.2-1.6</td>
<td>0.09</td>
<td>5.4%</td>
</tr>
</tbody>
</table>

^ Intra-individual variability was calculated as SD/mean of the values obtained in 10 EMG traces.

° Day-to-day reproducibility was assessed by calculating the coefficient of variation (SD of the within-subject variance divided by the mean percentage) between two repeat measurements in 20 subjects within seven days.
values are not suitable for the assessment of sympathetic sudomotor fibre function, and that only the absence of the SSR should be regarded as an abnormal parameter (14-17).

Prolongation of the latency has recently been advanced as a further criterion for abnormality (18). Thus, for clinical purposes, both the abnormalities in the latency and the absence of SSR should be taken into account for the evaluation of sympathetic sudomotor C fibres.

However, SSR latency values include the afferent component, central coupling processing and the efferent branch of the sympathetic system. As the efferent component includes the lateral column of the spinal cord, pre- and post-ganglionic fibres and nervous-gland junctions, the onset latency of the SSR provides only indirect information on the post-ganglionic sudomotor C fibres. Furthermore, Fagius (9) showed that the reflex latencies of sympathetic skin activity recorded using microneurography varied considerably from trial to trial. Thus, a more accurate and reproducible parameter is required for the quantitative assessment of sudomotor C fibres. An estimation of the CV of sympathetic fibres may be obtained indirectly by the simultaneous recording of the SSR latency in two distant sites.

In this study, we applied this method to estimate the CV of the SSF in the axilla-wrist and crural line-ankle tracts. The values obtained for the upper and lower limbs (2.0 and 1.4 m/sec respectively), are within the range of C-fibre CV reported in both animal and human models (19-23).

With regard to the CV recorded on the lower limb, our data are in agreement with those reported by Elie (11) and Uncini (10) in a small group of healthy subjects. Elie et al. (11) calculated a mean CV of 1.40 ± 0.14 m/sec (crural line-foot). Uncini (10) reported a CV of 1.2 m/sec for the cavus popliteus-ankle tract.

As for the upper limbs, the CV of SSF has previously been calculated only in the short wrist-digits tract (24). Kanzato et al. (24) calculated a mean CV of 0.8 m/sec in the wrist-middle phalanx tract, and a CV of 2.3 m/sec in the wrist-distal phalanx tract, postulating that such a marked difference was due to a facilitation of the sudomotor nerve impulse to the distal phalanx. Our results (2.0 m/sec in the axilla-hand tract) are in contrast with the CV of the wrist-middle phalanx tract, while closely resembling that of the wrist-distant phalanx tract. The much shorter distances used by Kanzato et al. (24), when compared with the ones we used to calculate the CV, make it difficult to measure accurately the difference between the onset latencies at distal and proximal sites. Moreover, SSRs recorded on the wrist and phalanxes do not provide a correct measurement of the onset latency because of their morphology and low amplitudes (personal observation).

We suggest that our method allows an easier and more accurate estimation of the CV of the SSF and explores a longer tract of the peripheral sudomotor fibres.

The conduction times given in this report are tentative because we measured responses innervated by different sympathetic axons. However, the CV calculated from the mean conduction time is compatible with the velocities of unmyelinated C fibres directly measured in vivo and in vitro (19-21). Moreover, the SSFCVs showed a good reproducibility and a low intra-individual variability, and the inter-electrode distance permitted an easy measurement of the conduction times.

Our data show that this simple and non-invasive method can, in suitable temperature conditions, be used reliably to measure the CV of the SSF and may be useful when investigating the physiological functions of peripheral nerves in patients with peripheral neuropathies.

We suggest that the “absence” of SSR combined with an abnormal SSFCV may in-
crease the sensitivity of the SSR method, thus allowing the sudomotor C fibres in many types of neuropathies to be assessed.

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