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Short communication

Sympathetic skin response. Glabella stimulation may be more useful than peripheral nerve stimulation in clinical practise ☆

Mauro Mondelli [a,*], Alessandro Aretini [a], Michele Ballerini [b], Benito Vecchiarelli [b], Alessandro Rossi [b]

[a] EMG Service, Local Health Unit 7, Siena, Italy
[b] Dept. Neurological, Neurosurgical and Behavioural Sciences, Siena University, Italy

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ABSTRACT

The aim is to verify whether glabella electrical stimulation evokes sympathetic skin responses (SSR) without inter-side differences in latency and area of the responses and is more useful in mononeuropathies than peripheral nerve stimulation. SSRs were recorded in 25 healthy subjects from right palm, third (M3SSR) and fifth fingers and contralateral third finger. The inter-side differences of grand mean area and mean of largest area of M3SSR were significant only by ulnar nerve and not by glabella stimulation. Therefore glabella stimulation may be used in mononeuropathies comparing SSR area recorded from affected side with respect to contralateral healthy side.

1. Introduction

Sympathetic skin response (SSR) is the result of a complex polysynaptic reflex arc and represents a change of skin potential as a result of sudomotor activity. The deep inspiration, coughing, binaural click, burst, flash, electrical stimulation of a peripheral or cranial nerve, and magnetic stimulation at the level of C7 spinous process or of a peripheral nerve or brain are able to evoke the SSR. The most common method is to record the SSR by electrical stimulation of a peripheral nerve in the distal part of a limb.

The SSR has many limitations in the clinical routine because of inter- and intra-individual variability of latency and amplitude of the single responses and of the phenomenon of habituation that makes difficult to calculate the normative values of SSR parameters. Therefore, in common clinical practise, the SSR is considered impaired with certainty only if absent. Some reviews on the pathophysiology and clinical applications of SSR were recently published (Vetrugno et al., 2003; Kucera et al., 2004; Chroni et al., 2006).

If the stimulation of a common peripheral nerve is used, the responses recorded from the contralateral side to the stimulated nerve show amplitude lower than those recorded by the side of stimulation, probably due to a greater dispersion of excitation afferent arc (Montagna et al., 1985; Caccia et al., 1993; Vetrugno et al., 2003). To demonstrate the involvement of the sympathetic fibres in mononeuropathies, the comparison of parameters between the two sides could eliminate the problem of obtaining the absolute reference values because the unaffected side may be used as an internal control, and then the ratio between the values of the two sides could be calculated. Thus a stimulus that does not produce significant differences in response parameters between the two sides should be used.

The aim of this study was to verify whether the electrical stimulation of the skin of the glabella can be used to obtain responses with similar parameters between the two sides of registration, compared to responses obtained with electrical stimulation of a common peripheral nerve of an upper limb.

2. Methods

Twenty-eight healthy volunteers with no history of systemic, neurological and endocrine diseases were recruited in the territorial electromyographic service of Local Health Unit no. 7 of Siena and at the Department of Neuroscience of the University of Siena, Italy. Three subjects (11%) did not complete the trial for the glabella stimulation because the electrical current applied to the glabella skin was considered painful even at low intensity (<20 mA). Therefore the results of this study relate to 25 subjects (15 women and 10 men, mean age 42.7 ± 14.1, range 19–65 years).

The study of SSR was performed some days after the execution of standard neurography (nerve conduction velocity of the median, ulnar and radial nerves and of palmar branches) according to methods reported elsewhere (Mondelli et al., 2009). All subjects gave written informed consent.

SSR was recorded with the subjects lying in a bed in a quiet and warm room, asking to keep their eyes open to stay awake, not sighing, laughing, coughing or breathing deeply as possible. Their level of

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* Corresponding author at: Servizio di EMG, ASL 7, Via Pian d'Ovile, 9, 53100 Siena, Italy. Tel.: +39 0577 535904; fax: +39 0577 535983.
E-mail address: m.mondelli@usl7.toscana.it (M. Mondelli).

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vigilance was also visually monitored. Skin temperature was kept constant >32 °C in both hands with an infrared lamp, the same used for the neurographic study.

For each subject two experimental trials were performed, one for the nerve stimulation and the other for stimulation of the glabella region. To avoid constraints and bias linked to the first site of stimulation, the trial with nerve stimulation was firstly performed in 13 subjects and that with glabella region in the remaining 12. For each subject the two trials of stimulation were performed after 2–5 days of each other. SSRs were recorded simultaneously from third finger (M3SSR), fifth finger (U5SSR) and palm (PSSR) on right side (contralateral to the stimulated nerve side) and from third finger ipsilateral to the stimulated nerve side (M3iSSR). Recording ring electrodes were placed around the proximal (negative = active site) and distal (positive site) interphalangeal joints of the fingers; for PSSR, surface Ag/AgCl disc electrodes 9 mm in diameter were applied to the palm (negative) and dorsum (positive) of the hand. The ground electrode (a metallic band 2 cm wide) was placed around the wrist. Skin impedance was reduced to <5 kΩ by abrasion and application of conductive gel. A band pass of 0.5 Hz–2 kHz, a base time of 500 ms/division and an amplification of 100–200 μV/division (or sometimes 500 for palmar recording only) were used.

The SSR was obtained using an electrical shock consisting of a single square-wave pulse of 0.3 ms duration and 20–45 mA intensity, just sufficient to produce a slightly painful sensation. Similar intensity was used in the same subject regardless of the stimulation site. The electric stimulation was applied to the wrist at the left ulnar nerve with the cathode orientated proximally and to the glabella with the cathode positioned on the glabella and the anode 2 cm proximally. Thirteen stimuli were administered at random intervals of more than 30 s. SSR latencies were measured from the origin of the trace to the first deflection of the trace from baseline. SSR areas were calculated between the first deflection of the response and the return of the trace to baseline (i.e. the full area of the response, including the first negative and subsequent positive components, was measured). When onset potential was shallow, the recorded trace (x2–x8) was further amplified to pinpoint the exact onset of SSR.

For each recording site the following parameters were measured: 1) mean latency and area of 12 consecutive responses, excluding the first (Toyokura and Murakami, 1996; Toyokura and Murakami, 1997); automatic average was avoided because latency and morphology vary from one recording to the next and phase cancellation is possible (Vetrugno et al., 2003); 2) latency of the shortest response; 3) area of the largest response (i.e. the response with maximum area); 4) grand means (mean of means) of 1) and means of 2) and 3); 5) the form of responses: P type (the greatest positive component is larger than the highest negative component, regardless of the initial polarity and number of phases) or N type (characterised by a predominant negative deflection) (Toyokura, 1998).

Habituation was quantified in each subject as the mean area of the last four SSRs (10th to 13th responses) divided by the mean area of the first four SSRs excluding the first (2nd to 5th responses) and as the mean latency of the last four SSRs divided by the mean latency of the first four SSRs excluding the first. These ratios were named "habituation ratio (HR)". No habituation was indicated by ratios ≥1. Mean HRs were also measured.

The SSR methods are similar to those used in our previous studies (Mondelli et al., 2001; Mondelli et al., 2009).

As the distribution of SSR values was not normal (Kolmogorov–Smirnoff test with Lilliefors correction) a nonparametric test was employed. Differences in the following parameters between the responses obtained by nerve stimulation and those by glabella stimulation were analysed using Wilcoxon test for paired data: grand mean latency, grand mean area, mean latency of shortest response, mean area of largest response and mean HR latency and area of M3SSR, U5SSR, PSSR and M3iSSR. The differences between the values of M3SSR and M3iSSR were also calculated in both samples of stimulation (in that with nerve and in that with glabella stimulation).

3. Results

Neurographic findings were normal in all subjects. SSR results, including HR, (means ± SD) and differences between the all responses obtained by nerve stimulation and those by stimulation of glabella are reported in Table 1. It was possible to evoke SSRs in all subjects. The area of the responses varied widely between subjects and tended to decrease with subsequent stimulations in single subjects. Responses generally showed P type (20 subjects) and less often N type waveform (5 subjects). Constant shape was generally observed in both trials of stimulation from all recording sites of the same subject.

There were no significant differences with regard to grand mean of latencies, mean of the shortest latencies and HR of latencies and areas obtained from all 4 recording sites between nerve stimulation and glabella stimulation.

On the contrary, grand mean area and mean of largest responses obtained from all 4 recording sites were significantly lower by glabella stimulation than by nerve stimulation.

Furthermore, grand mean area and mean of the largest responses obtained with nerve stimulation were higher for M3iSSR than for M3SSR ($Z = 3.81$, $p = 0.0001$; $Z = 3.45$, $p = 0.005$, respectively). These differences were not noticed if glabella stimulation was used ($Z = 1$, $p = 0.31$; $Z = 0.12$, $p = 0.9$, respectively). Differences in M3iSSR vs. M3SSR latencies apart from the site of stimulation were not found. Therefore glabella stimulation evoked M3SSR with similar areas in the two sides of registration; on the contrary nerve stimulation evoked M3SSR of major areas in the side ipsilateral to stimulated nerve. The

Table 1
The *Z* values were calculated using Wilcoxon test for paired data.

SSR parameters	Nerve stimulation	Glabella stimulation	Differences in nerve vs. glabella stimulation	
	Mean ± SD	Mean ± SD	*Z* values[a]	*p* Values
P mean latency (s)	1.38 ± 0.19	1.35 ± 0.16	1.71	0.09
P shortest latency (s)	1.3 ± 0.16	1.27 ± 0.14	1.96	0.051
P HR latency	0.93 ± 0.04	0.94 ± 0.02	−0.96	0.34
M3 mean latency (s)	1.58 ± 0.18	1.56 ± 0.17	0.92	0.35
M3 shortest latency (s)	1.48 ± 0.16	1.46 ± 0.16	0.65	0.51
M3 HR latency	0.94 ± 0.04	0.94 ± 0.02	−1.84	0.07
U5 mean latency (s)	1.53 ± 0.17	1.51 ± 0.19	0.69	0.49
U5 shortest latency (s)	1.4 ± 0.15	1.41 ± 0.17	0.31	0.75
U5 HR latency	0.92 ± 0.05	0.95 ± 0.03	−1.37	0.09
M3i mean latency (s)	1.56 ± 0.2	1.54 ± 0.2	0.33	0.77
M3i shortest latency (s)	1.46 ± 0.18	1.45 ± 0.19	0.33	0.77
M3i HR latency	0.95 ± 0.04	0.96 ± 0.03	−0.78	0.44
P mean area (μV/s)	446.4 ± 216.2	369.3 ± 214.2	2.6	0.009
P largest area (μV/s)	556.3 ± 251.2	467.8 ± 270.2	2.76	0.006
P HR area	0.7 ± 0.1	0.66 ± 0.13	1.53	0.13
M3 mean area (μV/s)	266.3 ± 174.5	206.6 ± 192	2.65	0.008
M3 largest area (μV/s)	405.7 ± 258	301.4 ± 231.3	3.4	0.0007
M3 HR area	0.59 ± 0.13	0.61 ± 0.16	−0.37	0.71
U5 mean area (μV/s)	184 ± 116	137.9 ± 125	2.97	0.003
U5 largest area (μV/s)	277 ± 159.1	209.4 ± 171.6	2.97	0.003
U5 HR area	0.62 ± 0.07	0.56 ± 0.12	1.89	0.07
M3i mean area (μV/s)	335.2 ± 189.9	210.8 ± 186.6	4.26	<0.0001
M3i largest area (μV/s)	474.5 ± 253.3	302.3 ± 233.3	4.34	<0.0001
M3i HR area	0.62 ± 0.11	0.57 ± 0.13	1.68	0.09

Table of SSR results.
Mean and standard deviation (SD) of sympathetic skin response (SSR) findings and differences between values obtained by ulnar nerve and those by glabella stimulation. P: palmar, M3: 3rd finger, U5: 5th finger recordings contralateral to the side of stimulated nerve, M3i: 3rd finger ipsilateral to side of stimulated nerve, HR: habituation ratio (mean latency or area of the last four SSRs – i.e. 10th to 13th responses – divided by the mean latency or area of the first four SSRs excluding the first—i.e. 2nd to 5th responses).
[a] Wilcoxon test.