

Short communication

Excitability recovery curve of the sympathetic skin response in healthy volunteers and patients with palmar hyperhidrosis

Davide Manca^{a,b}, Josep Valls-Solé^{a,*}, Marco Antonio Callejas^c

^aUnitat d'EMG, Servei de Neurologia, Departament de Medicina, IDIBAPS, Hospital Clínic, Facultat de Medicina, Universitat de Barcelona, Villarroel, 170, Barcelona, 08036, Spain

^bClinica Neurologica, Ospedale S. Giovanni di Dio, Cagliari, Italy

^cDepartament de Cirurgia Toràcica, Hospital Clínic, Facultat de Medicina, Universitat de Barcelona, Villarroel, 170, Barcelona, 08036, Spain

Accepted 7 July 2000

Abstract

Objectives: Patients with primary palmar hyperhidrosis (PPH) might exhibit hyperexcitability of the reflex circuits involved in sweating. We hypothesized that this hyperexcitability could become evident in the study of the excitability recovery curve of the sympathetic sudomotor skin response (SSR).

Methods: In 10 patients with PPH and 10 healthy volunteers used as control subjects, we recorded the SSR in the palm of the right hand to pairs of median nerve electrical shocks separated by inter-stimuli intervals (ISIs) ranging from 0.5 to 3.5 s. The amplitude of the SSR generated by the second stimulus (SSR2) was expressed as a percentage of that generated by the first (SSR1), and compared between control subjects and patients for each ISI.

Results: None of the control subjects showed a recovery of the SSR for ISIs of 1.5 s or less. On the contrary, patients showed a statistically significant enhancement of the SSR excitability recovery curve, with onset of recovery at 1.5 s in 5 patients. Two patients showed a double peak response to single electrical stimulation and were not considered in the calculation of the SSR recovery curve. Mean excitability recovery percentages were larger in patients than in control subjects at ISIs of 2, 2.5 and 3 s.

Conclusions: The enhancement of the SSR recovery curve in patients with PPH suggests hyperexcitability of the somatosympathetic polysynaptic pathway involved in sweating. This could partly underlie the pathophysiology of PPH. © 2000 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Sympathetic skin response; Primary palmar hyperhidrosis; Excitability recovery curve

1. Introduction

Palmar hyperhidrosis is a disorder consisting of excessive sweating of the palms, and other parts of the body, that can be socially and occupationally disabling. The disorder may occur in patients with malignancy, hypoglycemia, infections, and neurological diseases. However, it can also occur in patients with no other concurrent illnesses and, in these instances, it is labeled primary palmar hyperhidrosis (PPH). A positive family history can be found in about 30% of the cases (Adar et al., 1977). There may be a higher incidence in Orientals compared with subtropical areas (Adar et al., 1977; Edmondson et al., 1992).

The diagnosis of palmar hyperhidrosis is based on the patient's complaints and, on occasion, on the direct obser-

vation of hyperhidrosis. However, a neurophysiological technique demonstrating the eventual abnormal function of sudomotor pathways is still lacking. No consistent results have been reported from the assessment of the sympathetic sudomotor skin response (SSR), a change in the galvanic resistance of the skin related to activation of sweat glands (Shahani et al., 1984). Chen et al. (1995) found occasionally absent palmar SSR, while Lefaucheur et al. (1996) found enhanced amplitude and occasional double-peak responses to single median nerve stimuli. The pathophysiology of PPH is unknown. We thought that palmar hyperhidrosis may be the expression of an hyperexcitable sudomotor circuit, and that such abnormality may show in the assessment of the excitability recovery curve of the SSR to pairs of stimuli.

2. Patients and methods

The study was carried out in 10 patients, 6 men and 4

*Corresponding author. Tel.: +34 93-2275413; fax: +34 93-2275783.
E-mail address: valls@medicina.ub.es (J. Valls-Solé).

Table 1
Data on SSR to single electrical stimulus in control subjects and patients^a

	Latency (s)	Amplitude (μ V)	Duration (s)*
Control subjects	1.61 (0.2)	880 (330)	1.38 (0.23)
Patients	1.51 (0.3)	705 (324)	1.45 (0.32)

^a Figures are the mean and one standard deviation of the mean (in parenthesis). *In patients, duration was measured only in those with single peaked responses.

enhanced in patients compared to control subjects. Fig. 2 shows the responses obtained to paired stimuli in a representative patient. The SSR2 was present in two patients at the ISI of 1.0 s, in 5 patients at the ISI of 1.5 s, and in all 8 patients at the ISI of 2.0 s. The interval at which most patients showed onset of recovery of the SSR to the test stimulus was 1.5 s, compared to the ISI of 2.5 s observed in control subjects. Fig. 3 shows the excitability recovery curves of control subjects and patients, indicating the ISIs with statistically significant differences (ANOVA; $P < 0.05$).

4. Discussion

The SSR recorded in the palm of the hand to median nerve stimulation is a slow resolving action potential, with a long time course, attributable to the depolarization of epidermal eccrine sweat glands, innervated by cholinergic sympathetic fibers (Edelberg, 1967). In spite of its variability, the SSR has been used by many authors in the assess-

ment of dysfunctions of the somatosensory and autonomic pathways (Shahani et al., 1984; Fagius and Wallin, 1980; Valls-Solé et al., 1991; Hoeldtke et al., 1992; Obach et al., 1997). The parameters that have been measured in the SSR are latency, peak amplitude, and duration, although most authors consider the lack of the SSR as the only convincing abnormal result (Claus and Schondorf, 1999). In our patients, we were not able to find abnormalities in the latency, amplitude and duration of the SSR, except for the observation of double peak responses to single stimuli in two patients, suggesting a form of hyperexcitability in the pathway of the SSR (Lefaucheur et al., 1996).

In this article, we obtained further evidence of the disturbed excitability of sudomotor circuits in patients with PPH by examining the SSR excitability recovery curve. In our healthy volunteers, the mean interval of initial recovery of the SSR to the test stimulus was 2.5 s. Response inhibition before that interval could be due to refractoriness of the sudomotor pathway, after activation in response to the conditioning stimulus. However, the physiology underlying these changes is unknown. We found that the period of inexcitability after a conditioning stimulus is longer in the SSR than in other reflex responses investigated so far. Duration of the SSR inhibition in normal subjects was longer than the duration of the response itself. Although there may be a long refractory period in the sweat gland secretion (Shaver et al., 1962), activation of the sweat gland membrane should not prevent the sympathetic neurons to be activated at the sympathetic ganglia, and generation of a new action potential should be possible at the end of, and even partly superimposed to, the action potential induced by the previous stimulus. Therefore, the fact that onset of excitability recovery takes longer than the time required for resolution of the action potential, of a mean duration of 1.5 s, suggests that an active process of inhibition is probably taking place at the integrative structures of the central nervous system in which the SSR is generated. Inhibitory fibers, together with

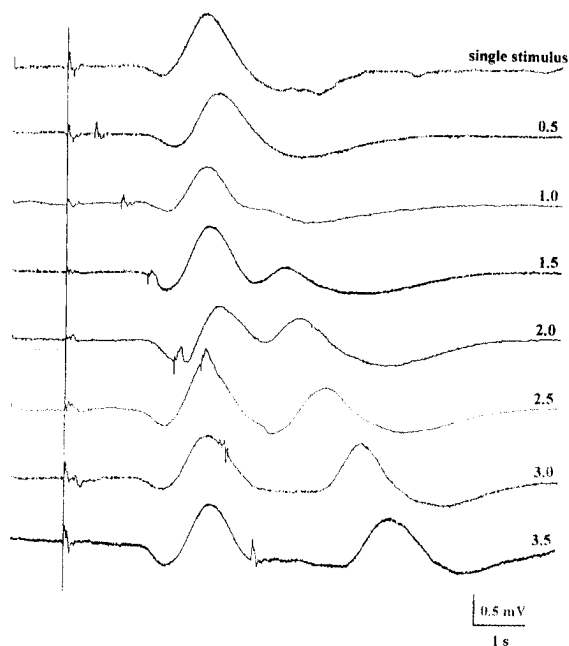


Fig. 2. Recording of the SSR to paired stimuli in a patient with palmar hyperhidrosis. Interstimuli intervals are marked at the right side of each graph. Onset of recovery in this patient occurred at 1.0 s.

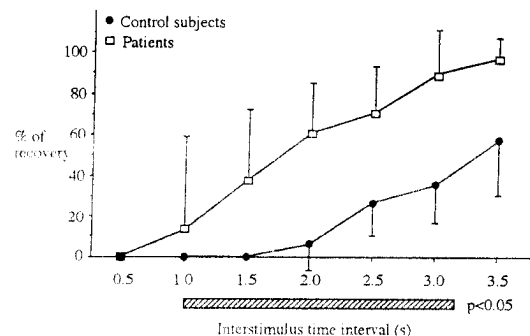


Fig. 3. The SSR excitability recovery curve in control subjects and patients with palmar hyperhidrosis. Vertical bars are one standard deviation. The bar at the bottom of the figure underlines the intervals in which the percentage of the SSR2 recovery was significantly different in control subjects and patients.

excitatory ones, project from the hypothalamus to the sympathetic preganglionic neurons involved in sweating (Labar et al., 1988). The conditioning stimulus may activate the whole circuit of the SSR, inducing an initial excitation followed by a period of active inhibition.

The period of SSR inexcitability was significantly reduced in our patients with PPH. This can be the consequence of hyperactivity in the excitatory fibers or hypoactivity in the inhibitory fibers. The enhancement of sweating in PPH occurs predominantly in the palm of the hands. This can be explained, at least in part, by the fact that the density of eccrine sweat glands in this region is the largest in the body (Low, 1993). The eccrine glands receive innervation from structures controlling both emotional and thermoregulatory sweating (Linden and Berlit, 1995). Emotional stimuli are more effective in causing hyperhidrosis than thermal or gustatory stimuli in patients with PPH (Adar et al., 1977). The hypothalamus, which probably modulates the excitability of the SSR, receives inputs from structures related to emotional stimuli, such as the piriform cortex, hippocampus, amygdala and frontal lobes. We think that a change in the modulatory influence of the hypothalamus over the preganglionic neurons could account for an enhancement of sweating, and of the SSR excitability recovery curve, in patients with PPH.

Our conclusion is that patients with PPH have an abnormal excitability enhancement of the multisynaptic somato-sympathetic circuits involved with sweating. The findings of enhanced SSR amplitude reported by Lefaucheur et al. (1996), and the double peak responses to single stimuli found in two of our patients, are also consistent with enhanced sudomotor pathways excitability. The assessment of the excitability recovery curve of the SSR could be added to the electrophysiological tools used in studying patients with PPH.

References

- Adar R, Kurchin A, Zweig A, Mozes M. Palmar hyperhidrosis and its surgical treatment. *Ann Surg* 1977;186:34–31.
- Chen HL, Cheng MH, Lin TH, Chee ECY. Recordings of pre- and post-operative sympathetic skin response in patients with palmar hyperhidrosis. *Stereotact Funct Neurosurg* 1995;64:214–220.
- Claus D, Schondorf R. Sympathetic skin response. *Electroenceph clin Neurophysiol, Suppl* 1999;52:277–282.
- Edelberg R. Electrical properties of the skin. In: Brown CC, editor. *Methods in psychophysiology*. Baltimore, MD: Williams and Wilkins, 1967. pp. 1–52.
- Edmondson RA, Banerjee AK, Rennie JA. Endoscopic transthoracic sympathectomy in the treatment of hyperhidrosis. *Br Med J* 1992;215:289–293.
- Fagius J, Wallin BG. Sympathetic reflex latencies and conduction velocities in normal man. *J Neurol Sci* 1980;47:433–438.
- Hoeldtke RD, Davis KM, Hsieh PB, Gaspar SR, Dworkin GE. Autonomic surface potential analysis: assessment of reproducibility and sensitivity. *Muscle Nerve* 1992;15:926–931.
- Labar DR, Mohr JP, Nichols III FT, Tatemichi TK. Unilateral hyperhidrosis after cerebral infarction. *Neurology* 1988;38:1679–1682.
- Lefaucheur JP, Fitoussi M, Becquemin JP. Abolition of sympathetic skin responses following endoscopic thoracic sympathectomy. *Muscle Nerve* 1996;19:581–586.
- Linden D, Berlit P. Sympathetic skin response (SSR) in monofocal brain lesions: topographical aspects of central sympathetic pathways. *Acta Neurol Scand* 1995;91:372–376.
- Low PA. Peripheral neuropathy. In: Dyck PJ, Thomas PK, Griffin JW, Low PA, Poduslo JF, editors. 3rd edition. Philadelphia, PA: Saunders WB, 1993. pp. 729–745.
- Obach V, Valls-Solé J, Vila N, Gonzales LE, Chamorro A. Sympathetic skin response in patients with lateral medullary syndrome. *J Neurol Sci* 1997;155:55–59.
- Shahani BT, Halperin JJ, Bould P, Cohen J. Sympathetic skin response-A method of assessing unmyelinated axon dysfunction in peripheral neuropathies. *J Neurol Neurosurg Psychiatry* 1984;47:536–542.
- Shaver BA, Brusilow SW, Cook RF. Origin of the galvanic skin response. *Proc Soc Exp Biol* 1962;110:559.
- Valls-Solé J, Monforte R, Estruch R. Abnormal sympathetic skin response in alcoholic subjects. *J Neurol Sci* 1991;102:233–237.