Autonomic Neuroscience: Basic and Clinical 155 (2010) 109–114

Contents lists available at ScienceDirect

Autonomic Neuroscience: Basic and Clinical

journal homepage: www.elsevier.com/locate/autneu

Sweat production and the sympathetic skin response: Improving the clinical assessment of autonomic function

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ARTICLE INFO

Article history:
Received 14 October 2009
Received in revised form 4 January 2010
Accepted 11 January 2010

Keywords:
Sympathetic skin response
Sweat
Electrodermal potential
Spinal cord injury

ABSTRACT

The aim of this project was to establish the relationship between sweat production and the electrodermal events comprising the sympathetic skin response to arousal stimuli. A series of randomly timed magnetic stimuli were applied to the neck of healthy human volunteers. Sympathetic skin responses and the associated sweat responses were recorded from the palms of both hands. Sympathetic skin responses typically had a biphasic shape consisting of a negative initial potential (palm relative to dorsum of hand) followed by a positive deflection. Sweat production was positively correlated with amplitude of the second positive deflection of the sympathetic skin response and negatively correlated with the amplitude of the initial negative deflection. For subjects showing only an initial negative sympathetic skin response, sweat release was low or not detectable. During habituation, the negative initial wave increased relative to the second positive wave, and sweat production fell. The strong correlation between the positive wave of the sympathetic skin response and sweat production suggests that the former may provide a quantitative functional measure of sudomotor activity in situations when it is impractical to measure the amount of sweat produced in the startle response. Thus, the positive component of the biphasic sympathetic skin response may be employed in clinical assessment of the functional efficacy of the sympathetic sudomotor system.

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1. Introduction

The clinical assessment of sudomotor function, as a component of autonomic sympathetic function, can be achieved using a number of techniques, including recently refined developments such as the quantitative sudomotor axon reflex test (QSART) for sweat production (Sletten et al., 2009a,b). Employed in combination, certain methods allow distinction between central nervous and peripheral components of sudomotor function (see Illigens and Gibbons, 2009) and may be used to monitor deterioration or recovery from trauma or disease. Of the techniques available, the sympathetic skin response (SSR) is widely regarded as being indicative of the integrity of the combined central and peripheral components of the sympathetic cholinergic sudomotor system. However, the relationship between the electrodermal events of the SSR and sweat production remains unclear (Freedman et al., 1994; Krogstad et al., 2004). In order to accept the SSR as a valid tool for the assessment of sudomotor function it would be of value if this relationship could be firmly established.

The SSR is a slow change in electrical potential that can be recorded from the palmar and plantar surfaces when a human subject is presented with an unexpected stimulus, such as a loud noise or cutaneous electrical stimulus (Shahani et al., 1984). The presentation of an unexpected stimulus is thought to give rise to sympathetic activation through afferent input via hypothalamic, brain stem and other central connections (Isamat, 1961; Yokota et al., 1991; Critchley et al., 2000) leading to excitation of elements of the sympathetic chain and, finally, sweat gland activation (Magnifico et al., 1998). When two surface electrodes are placed one each on the palm and the dorsum of the hand, a biphasic SSR response associated with the sweat gland activation is most often recorded with the palm initially becoming negative with respect to the dorsum of the hand and then reversing. The waveform can however be simpler (monophasic) or more complex (Shahani et al., 1984; Baba et al., 1988; Andary et al., 1993) with variation in form within subjects (Hoeldtke et al., 1992; Levy et al., 1992; Toyokura and Murakami, 1996) and as a result of habituation (Toyokura, 1998; Cariga et al., 2001).

Mitani et al. (2003) made monopolar recordings from several sites on both the palm and the dorsum of the hand against a ground electrode at a remote site. The initial potential change during an SSR was negative on the palm and positive on the dorsum of the hand. In none of the above studies was the amount of sweat recorded at the time of an SSR, so the relationship between the various components of the SSR waveform and sweat release is unknown. Others have recorded the sweat produced in response to arousal stimuli that would presumably have elicited an SSR (Asahina et al., 2002; Kuwabara et al., 2008). In the absence of an SSR recording, the profile of sweat production was insufficient to predict any relationship to electrodermal events.

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1566-0702/$ – see front matter © 2010 Elsevier B.V. All rights reserved.
doi:10.1016/j.autneu.2010.01.008

The SSR is disrupted in a variety of central and peripheral nervous system disorders with sweat disturbances (Vetrugno et al., 2003). Although SSR has been used as a routine test in a number of neurological conditions there is, as yet, no standardised method of measuring the SSR waveform or any direct relation between the SSR and sweat production. The need for improved evaluation of autonomic function has been recognised, at least in spinal cord injury (Krassioukov et al., 2007; Alexander et al., 2009). In order to improve on the usefulness of the SSR as a predictor of functional outcome or as an objective assessment of recovery of cholinergic sympathetic pathways, the precise relationship between the amount of sweat produced and the different components of SSR needs to be understood. In this study we attempt to study the relationship between the different components of palmar SSR and the volume of sweat produced in the palm in healthy subjects.

The SSR has already been used (Curt and Dietz, 1999; Nicotra et al., 2005) to provide information about the extent and level of lesions of the spinal cord affecting the sympathetic nervous system. The SSR recordings were regarded as supplementary to the clinical examination (American Spinal Injuries Association — ASIA assessment) and would have the potential to provide additional guidance for the selection of appropriate therapy within a programme of rehabilitation. The present study aims to provide a functional element to the use of the SSR in assessing damage and disorders of the sympathetic sudomotor system particularly when access to direct recording of sweat production may be unavailable.

2. Materials and methods

2.1. Subjects

With the approval of the local ethics committee 12 healthy and neurologically normal individuals (21–65 years, 6 females) gave informed consent to participate in the study.

2.2. Recordings

Subjects were seated comfortably in a chair with the room temperature maintained at 24 ± 1 °C. The SSR was recorded using surface electrodes placed on the hands. The volar and dorsal surfaces of both hands were cleaned using alcohol swabs. Two Ag–AgCl surface electrodes (2 × 3 cm Arbo neonatal ECG electrodes, Henley's medical) were deployed, one on the palm and the other on the dorsum of the hand. A reference electrode was placed at a remote site on the wrist. A differential isolated biological amplifier (IsoDam 7 — World Precision Instruments, USA) was used to record the potential difference between the palm and the dorsum of the hand. The signal was amplified 100 times and high and low pass filters were set at 0.1 Hz and 100 Hz respectively. Signals were sampled at 1 kHz using a data acquisition interface, host PC and software (Cambridge Electronic Design 1401+ and Signal version 3.1).

A sudorometer (Skinos Ltd., Japan) was used to record the sweat response from the palms. Each sudorometer probe consisted of an air chamber (1 cm^2 contact area) attached to the palm using adhesive stickers to make an air-tight seal. Two air hoses connected the chamber with the sudorometer, one that delivered dry air by pump action and the other that retrieved air moistened by any sweat. The difference in humidity between the air delivered and the air retrieved was measured by the sudorometer and the signal expressed in mg/cm^2/min. The humidity recording is a measure of the amount of sweat produced and, in response to an arousal stimulus, has been termed the sympathetic skin sweat response (SSwR) by Asahina et al. (2002). The SSwR was sampled at 1 kHz by the data acquisition interface (Cambridge Electronic Design 1401+ and Signal version 3.1) and stored on a computer, with the simultaneously recorded SSR signal, for offline analysis. SSR and SSwR were recorded from both palms. Following the application of SSR electrodes and sudorometer probes on the hands, the subjects were instructed to close their eyes and relax for approximately 10 min before the start of any recordings.

2.3. Magnetic stimulation

SSR and SSwR were elicited in subjects by applying an unexpected magnetic stimulus to the back of the neck. Magnetic stimuli have previously been shown to reliably evoke an SSR (Uozumi et al., 1993; Toyokura, 2003). Such magnetic stimuli are, in our experience, as consistent as other means of stimulation (electrical, acoustic, and inspiratory gasp) at evoking an SSR. A circular coil attached to a MagStim 200 magnetic stimulator (MagStim Co, Dyfed, Wales) was charged up to 65% maximum stimulator output and 15 to 20 stimuli were given at random intervals with the coil positioned over the back of the neck of a subject. To minimise habituation of the responses (Cariga et al., 2001), the stimuli were separated by at least a minute.

2.4. Analysis and statistics

Individual, stimulus-triggered SSR and SSwR traces were visually inspected and any anomalous records were discarded. Anomalous records were defined as shifts in the electrodermal signal with a

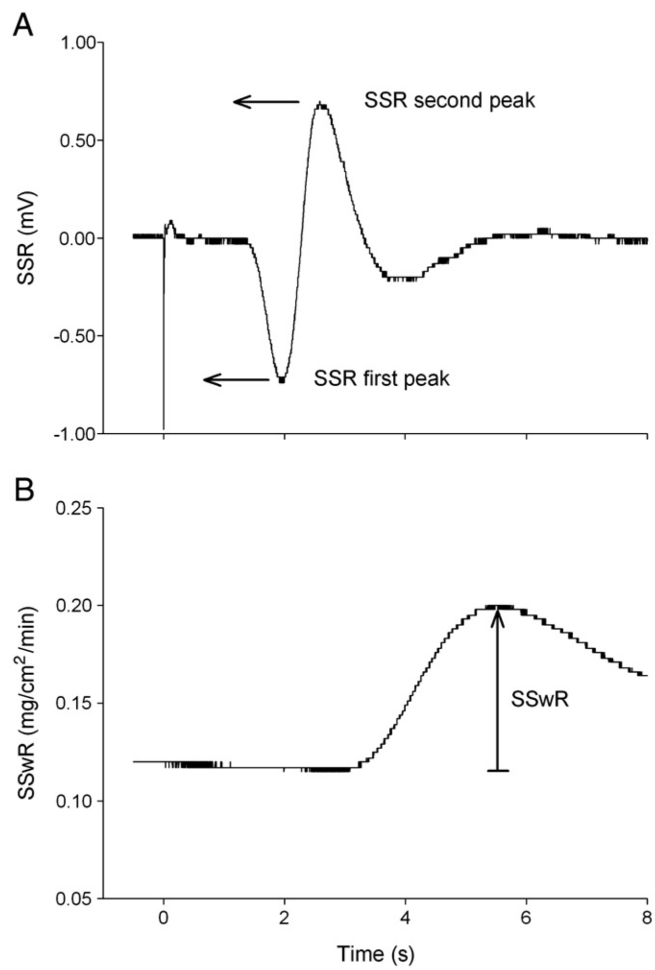

Fig. 1. The SSR (A) and SSwR (B) recorded from the palm. The responses were elicited by a magnetic stimulus to the neck of the subject at time zero. Polarity of the differential recording of the SSR refers to the voltage recorded from an electrode on the volar surface of the hand (palm) with respect to a second electrode on the back of the hand. A: Horizontal arrows represent measures made for analysis of SSR records. Absolute magnitudes of the first peak (typically negative) and of the second peak (typically positive going) are indicated. B. Vertical arrow represents magnitude of the maximum sweat production (from baseline) immediately following the SSR.

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