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Habituation of sympathetic sudomotor and vasomotor skin responses: neural and non-neural components in healthy subjects

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Abstract

Objective: Sympathetic skin response (SSR) and skin vasomotor response (SVR) habituation was thought to be induced by neural mechanisms. Here, we investigate the hypothesis that non-neural mechanisms could also be involved.

Methods: We recorded sympathetic skin nerve activity (SSNA) from median nerve by microneurography and the corresponding SSR and SVR in 16 healthy subjects. Superficial electrical stimulation of the opposite median nerve was used to induce arousal responses.

Results: Throughout stimulation, SSNA, SSR and SVR amplitude showed a significant reduction. During the first ten stimuli, SSNA showed a marked decrease highly correlated to SSR and SVR changes. During the subsequent 20 stimuli SSNA did not change whereas SSR and SVR significantly decreased. SVR was significantly influenced by skin temperature changes.

Conclusions: Both neural and non-neural mechanisms are involved in SSR and SVR habituation. The neural mechanisms were predominant during the first part of stimulation whereas non-neural mechanisms prevailed during the last part of stimulation.

Significance: During repeated arousal stimuli SSR and SVR amplitude changes did not reflect the strength of the corresponding sympathetic nerve traffic and must be interpreted with caution.

Keywords: Sympathetic skin nerve activity; Sympathetic skin response; Skin vasomotor response

1. Introduction

The skin is important for thermoregulation and sympathetic activity directed to the skin is sensitive to thermal stimuli but arousal or emotional stimuli may also increase sympathetic skin activity (Wallin, 1992). Direct recording of sympathetic activity to skin was made possible when the microneurography technique was developed (Vallbo and Hagbarth, 1967). Multiunit sympathetic activity in human skin nerves (SSNA) contains a mixture of impulses to blood vessels and sweat glands and provides a useful method for studying the corresponding sympathetic skin neuroeffector mechanisms (Bini et al., 1980a; b; Blumberg and Wallin, 1987; Hagbarth et al., 1972). A burst of SSNA can be easily triggered by a variety of arousal stimuli (auditory, sensory, visual, etc.) which usually contain, at thermoneutral ambient temperature, both sudomotor and vasomotor components, as indicated by changes in electrodermal responses (sympathetic skin response, SSR) and plethysmographic signs of vasoconstriction (skin vasomotor response, SVR) (Wallin, 1992).

Habituation is a common mechanism described independently for SSNA (Satchell and Seers, 1987) and skin sympathetic effectors (SSR and SVR) (Cariga et al., 2001; Kolev et al., 1995) when repeated arousal stimuli are applied and is characterised by a progressive loss of amplitude while the intensity of the stimulus remains constant. The exact nature of habituation is uncertain but the variable time course of adaptation between subjects in relation to attention confirms a commonly accepted

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hypothesis that the main mechanism of sympathetic skin habituation results from cognitive (neural) adaptation to the stimuli by reducing the levels of selective attention after several minutes of stimulation (Bloch, 1965; Elie and Guiheneuc, 1990). Changes in sympathetic skin effectors, especially SSR, in response to arousal stimuli have been reported as an indirect measure of SSNA strength useful to monitor autonomic changes related to cognitive processes and sympathetic dysfunctions (Aramaki et al., 1997; Eisenstein et al., 1995; Fusina et al., 1999; Hugdahl, 1996). However, besides neural adaptation, non-neural mechanisms at skin or sweat gland level have been suggested to cause a loss of SSR amplitude during repeated arousal stimuli (Bini et al., 1980a; Cariga et al., 2001; Kunimoto et al., 1991; 1992) but direct evidence is lacking.

The present study was undertaken to investigate the hypothesis that non-neural mechanisms were involved in SSR and SVR habituation. Using repeated electrical stimuli of constant intensity and short intervals to induce habituation, we compared SSNA loss of amplitude, recorded by microneurography technique, with amplitude decrease of SSR and SVR, recorded in the corresponding impaled skin fascicle.

2. Methods

2.1. Subjects

We studied 16 healthy individuals aged 28 ± 2 (range 24–32) years, 7 females and 9 males; subjects were not on medication and tobacco and caffeine were not allowed for 12 h before the examination. The recordings were always performed in the afternoon between 3 and 5 p.m., 1–3 h after a light meal.

The experimental procedures were approved by the Human Ethics Committee at Bologna University and all subjects gave their written informed consent to the study.

2.2. Measurements

Subjects were reclining in a comfortable bed in a semi-dark sound-proof room. The room temperature was maintained at 25 ± 0.2 °C and the humidity was $27 \pm 2\%$.

Respiratory movements were monitored by a strain gauge belt around the lower part of the chest.

Multiunit efferent post-ganglionic skin sympathetic nerve activity (SSNA) was recorded with an insulated tungsten microelectrode with a tip diameter of a few microns inserted into the left median nerve, at the wrist. A low-impedance reference electrode was inserted subcutaneously a few centimetres away. The nerve signal was amplified ($\times 50{,}000$), filtered (bandpass 700–2000 Hz) and fed through a discriminator for further noise reduction and audio-monitoring (Wallin, 1994). A mean voltage (integrated) display was obtained by passing the original signal through a resistance–capacitance circuit (time constant 0.1 s). When a skin nerve fascicle had been identified, small electrode adjustments were made until a site was found in which sympathetic impulses with a good signal-to-noise ratio could be recorded. A burst of SSNA was considered if it showed the following characteristics: (1) irregular occurrence varying in strength and duration unrelated to the heart pulses; (2) evoked by various arousal stimuli; (3) at rest followed by changes in skin blood flow and/or skin electrical potential (Hagbarth et al., 1972).

Changes in skin blood flow (skin vasomotor response—SVR) were monitored by an infrared photoelectric transducer (model PPS, Grass Instruments; filter setting 0.2–200 Hz) and changes in skin potential (sympathetic skin response—SSR) were measured by Ag–AgCl surface electrodes (filter setting 0.2–200 Hz). SVR and SSR were recorded from the innervation zone of the impaled skin nerve fascicle, usually on a finger supplied from the median nerve where the photoelectric transducer was applied distally and the active surface electrode proximally whereas the reference surface electrode was placed on the dorsal side of the same hand (Fig. 1). The electrode gel under the surface electrodes contained 0.1 M KCl. Skin temperature was monitored continuously using a thermistor probe (model 43TF; Yellow Springs, Ohio) placed on the tip of the 5th finger or on the hypothenar side of the recorded hand. The filtered and integrated nerve signals were sampled and stored together with other signals in a personal computer through an analogue/digital interface and using a locally produced data acquisition system. The signals were sampled at a rate of 200 Hz. In addition, all signals were stored on analogue tape. During the experiment, neural activity and effecter responses were monitored on a storage oscilloscope.

2.3. Stimulation

To study the habituation of SSNA, SSR and SVR, repeated constant current square wave stimuli (0.2 ms duration, 18–50 mA amplitude) were delivered via surface electrodes applied to the median nerve at the wrist of the arm opposite to the microneurography recording (Fig. 1). In each subject the strength of the stimulus was adjusted to be as high as possible without causing pain. Electrical stimuli were delivered randomly at short intervals (between 30 and 60 s), as commonly applied in a clinical setting (Elie and Guiheneuc, 1990; Fusina et al., 1999; Herbaut et al., 1990).

2.4. Procedure

After acquiring a stable recording site, resting SSNA was recorded for 10 min. After that, the subject was informed that the stimulation was about to start at the predetermined intensity. During stimulation periods the loudspeaker was turned off but the experimenter monitored the integrated neurogram on an oscilloscope screen to detect artefacts