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THERMOREGULATORY AND RHYTHM-GENERATING MECHANISMS GOVERNING THE SUDOMOTOR AND VASOCONSTRICTOR OUTFLOW IN HUMAN CUTANEOUS NERVES

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SUMMARY

1. Recordings of multiunit sympathetic activity were made from human nerve fascicles supplying hairy and glabrous skin of the extremities in healthy subjects exposed to different ambient temperatures. Sudomotor and vasomotor events accompanying the neural activity were monitored by simultaneous recordings of electrodermal and pulse plethysmographic events (Pleth) in the neural innervation zones.

2. By exposing the subject to warm (43 °C) or cold (15 °C) environments, it was possible to obtain a selective activation of either the sudomotor or the vasoconstrictor neural system, respectively, with suppression of spontaneous activity in the other system.

3. Bursts of both vasoconstrictor and sudomotor nerve activity were found to occur at certain preferred intervals which were integer multiples of a period of about 0·6 sec (100 cycles/min). With high sudomotor or vasoconstrictor tone the 100 cycles/min rhythm was prominent but with decreasing tone slower subharmonic rhythms prevailed. Respiratory rhythms were also discerned as well as slower rhythms attributable to oscillatory tendencies in thermoregulatory servos.

4. Vasoconstrictor bursts had longer mean duration than sudomotor bursts, a finding attributed to a slower conduction velocity of vasoconstrictor as compared to sudomotor impulses.

5. With increasing incidence of bursts transient electrodermal or plethysmographic responses following individual bursts merged, and thus the fast neural rhythms were not discernible in either the electrodermal or Pleth traces. Given increments in firing rate of nerves produced less additional vasoconstriction at high than at low firing rates. The rhythm generating mechanisms may help to restrict firing rates of individual fibres to the low range which provides high gain in the neuroeffector transfer functions.

INTRODUCTION

As previously shown (for reference see Vallbo, Hagbarth, Torebjörk & Wallin, 1979) vasomotor and sudomotor neural impulses in post-ganglionic C fibres can be led off with tungsten micro-electrodes in peripheral nerves of awake human subjects.

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Single unit recordings are rare (Hallin & Torebjörk, 1974); the resting activity usually consists of more or less rhythmically occurring, multi-unit bursts of C fibre action potentials. The spike density in the bursts and the burst incidence vary in response to different manoeuvres known to produce changes in the vasoconstrictor or sudomotor tone (Delius, Hagbarth, Hongell & Wallin, 1972*a*, *b*, *c*; Hagbarth, Hallin, Hongell, Torebjörk & Wallin 1972). Several studies deal with the baroreflex control of the sympathetic neural activity in human muscle nerves (m.s.a.) (for reference see Wallin, 1978). Less attention has been devoted to sympathetic neural activity that can be recorded from human skin nerves (s.s.a.). Most of these recordings have been made from nerves supplying hands and feet where sympathetic activity consists of a mixture of sudomotor and vasoconstrictor impulses, appearing in bursts which vary in strength and incidence with the attentive state of the subject and with the environmental temperature (Delius *et al.* 1972*c*). No entrainment of s.s.a. impulses by the baroreflex (as is so typical for m.s.a.) has been observed, but s.s.a. bursts can easily be triggered by a variety of suddenly applied external stimuli (auditory, visual, tactile etc.). As judged by simultaneous recordings of electrodermal responses and plethysmographic events, skin nerve sympathetic bursts evoked by arousal stimuli are usually made up of both sudomotor and vasoconstrictor impulses, whereas the strong sympathetic skin nerve activity induced by cooling seems to consist of vasoconstrictor impulses exclusively. Moderate warming reduces the vasoconstrictor outflow but more intense warming increases the s.s.a., an effect attributed to an enhancement of sudomotor impulse activity (Normell & Wallin, 1974). In the present study sympathetic activity has been recorded from different skin nerves in healthy adults exposed to changes in environmental temperature from 15 to 45 °C. Simultaneous electrodermal and plethysmographic recordings were also made to see whether observed neural events were followed by sudomotor and, or vasomotor changes in the skin. Since thermoregulatory mechanisms could be used to activate either sudomotor or vasoconstrictor fibres, it became possible to perform separate analyses of these two sympathetic systems with respect to the quantitative relationships between neural events and succeeding effector organ responses, the rhythms entraining the neural impulses and the temporal dispersion of the sympathetic bursts.

METHODS

With the understanding and consent of each subject investigations were performed on twenty-one healthy adults ranging in age from 22 to 52 years. Micro-electrode recordings were made from cutaneous nerve fascicles in the median nerve at elbow level with receptive fields on the volar side of the hand (fifteen experiments); the posterior cutaneous antebrachial nerve with receptive fields on the dorsal side of the forearm (nineteen experiments); the peroneal nerve at knee level with receptive fields on the dorso-lateral side of the foot (nine experiments) and the supraorbital nerve with receptive fields on the forehead (six experiments).

Nerve electrodes and display systems were the same as used in many previous studies (Sundlöf & Wallin, 1977). The micro-electrode was an insulated tungsten needle with a shaft diameter of 0·2 mm and a tip diameter of 1–5 μm. The reference electrode, similar but with a larger uninsulated tip, was inserted subcutaneously 1–2 cm from the intraneural micro-electrode. The signal-to-noise ratio was improved by the use of a 700–2000 Hz bandpass filter and an amplitude discriminator. A RC integrating network with a time constant of 0·1 sec was used to obtain a mean voltage display of the multiunit neural activity.

Skin resistance changes (electrodermal responses) were recorded by a Van Gogh GSReflec Module, type IGSR – 7A (a.c. coupled), with Ag/AgCl electrodes (Beckman) applied within the receptive skin area of the fascicle impaled by the microelectrode. *The pulse plethysmogram* was recorded by a Van Gogh light plethysmograph module, tpe ILP – 7A with the probe kept firmly in contact with the receptive skin area by tape or a band placed around a finger or a toe. *Respiratory movements and e.c.g.* were also recorded.

Unfiltered nerve records, integrated neurograms, e.c.g. signals and inputs from the different transducers mentioned above were stored on an eight-channel FM tape recorder (Sangamo 4) and displayed on an inkjet recorder (Mingograph 800, Siemens Elema Ltd). Histograms of burst intervals, plots of burst durations against burst amplitudes and plots of neural activity against plethysmographic events were obtained as described below.

General procedure. The subject sat or lay in a comfortable position, fully alert in a relaxed resting state. The micro-electrode was inserted manually and its position adjusted until a skin nerve fascicle was impaled, as judged by (1) the appearance of an insertion shower of impulses accompanied by skin paraesthesias and (2) mechanoreceptive afferent impulses arising in response to touch stimuli within the fascicular receptive field. Further minute electrode adjustments were made until an intrafascicular recording position was reached from which (besides the evoked afferent responses) spontaneous and, or, evoked sympathetic activity could be recorded. This activity was recognized by its highly characteristic temporal pattern with bursts of multiunit impulses which appeared in a more or less rhythmical fashion and also could be triggered or potentiated by arousal and emotional stimuli. As previously shown, such impulse bursts are conducted distally at a speed consistent with efferent C fibres and in contrast to mechanoreceptive afferent impulse volleys, they are not succeeded by any sensory experience but rather by vaso- or sudomotor skin responses (Hagbarth *et al.* 1972, Delius *et al.* 1972*c*; Hallin & Torebjörk 1974).

Intrafascicular sympathetic recording sites could often be kept for several hours and while testing the effects of various manoeuvres described below, care was taken that no external stimulus was applied to the receptive skin field of the impaled fascicle.

Changes in environmental temperature. In five experiments involving recordings from the median or antebrachial nerves the subject, clad in shorts, lay inside a box used for hypothermic surgery (auto hypoderm mod. superautomatic neural surgery XM. M. T. I. Heljestrand). The arm on which the recordings were performed passed through an opening and was (from the axillary region) exposed to a constant room temperature of 22–24 °C. After having recorded activity at a box temperature of 22–24 °C, the temperature in the box was increased gradually to 45 °C and was then kept at this level for 5–20 min until the subject started to sweat profusely. After having tested the effects of various stimuli, the temperature was lowered to 15 °C and kept there for 5 min while the tests were repeated. In six other experiments environmental temperature changes between 18 and 30 °C were achieved simply by exposing the subject to chilly air from a fan, to cool air coming from an open window or by warming the room with electrical heating elements.

Arousal stimuli were elicited by sudden noises, taps or electrical skin stimuli applied on a free extremity. *Mental stress* was induced by asking the suject to solve mental arithmetic problems. *Muscle work* was performed as strong Jendrassik-like isometric contractions of muscles in the free arm and hand for 30–45 sec.

RESULTS

Thermoregulatory influences on skin nerve sympathetic activity; discrimination between vasoconstrictor and sudomotor neural signals

Human skin nerve sympathetic activity at normal room temperature. At room temperature (22–24 °C) spontaneous and reflexly induced bursts of sympathetic activity were regularly found in skin nerve fascicles of the median and peroneal nerves at elbow or knee level (with innervation zones in the hand or foot). On the other hand, in fascicles of the posterior antebrachial nerve (with innervation zones on the dorsal side of the forearm) spontaneous sympathetic activity was encountered only once

in one of the subjects, and in none of seven experiments (on four subjects) was any sympathetic activity (spontaneous or evoked) detected in the supraorbital nerve.

Under these temperature conditions most of the spontaneous and reflexly induced s.s.a. bursts in the *median* and *peroneal* nerves were followed by transient plethysmographic signs of vasoconstriction in the fingers and toes (Fig. 1*A*, *B*, *C*). Some bursts, in particular those evoked by arousal or emotional stimuli, were also followed by hand and foot electrodermal responses (Fig. 1*A*, *B*), whereas others were not accompanied by such signs of sudomotor activity (Fig. 1*C*). Bursts followed only by electrodermal responses without signs of significant vasoconstriction were exceptional (Fig. 1*D*). These relationships between sympathetic bursts and subsequent plethysmographic and electrodermal responses did not change appreciably when the electrode was moved from one sympathetic recording site to another within the fascicle.

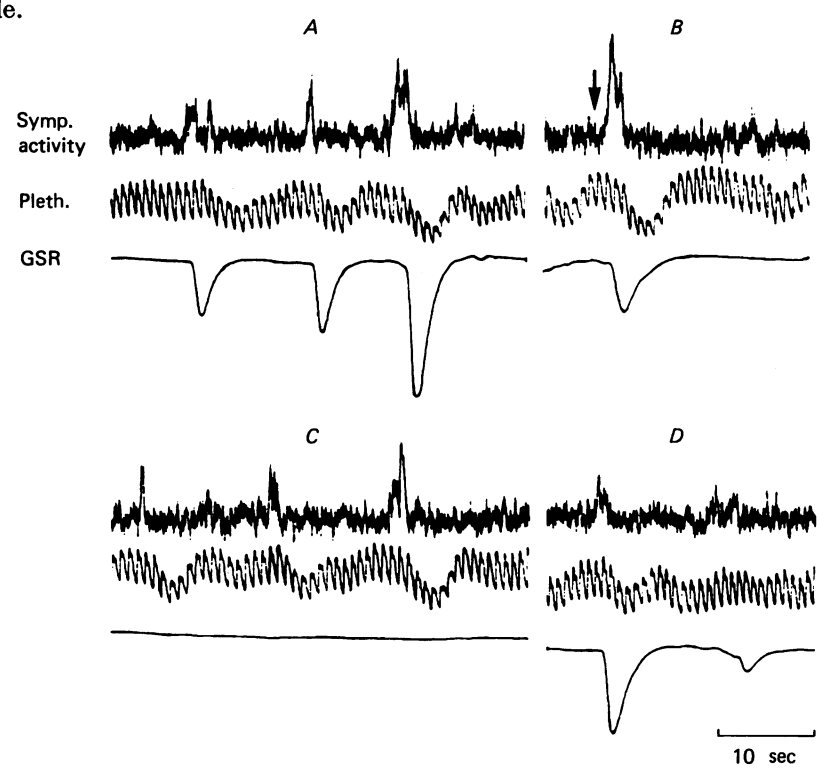

Fig. 1. Spontaneous (*A*, *C*, *D*) and evoked (*B*) bursts of skin sympathetic activity in median nerve with accompanying finger plethysmographic and palmar electrodermal responses. Normal room temperature (22–24 °C). Traces are from above: integrated neural activity, pulse plethysmogram, skin resistance. Arrow in *B*; electrical skin stimulus on contralateral arm.

Changes in skin nerve sympathetic activity with accompanying effector responses during variations in ambient temperature. In all subjects, moderate warming (35–40 °C) caused a reduction of frequency and amplitude of sympathetic bursts in the median nerve. There were accompanying plethysmographic signs of finger vasodilatation while skin resistance remained relatively stable, indicating little or no change in

sudomotor activity (Fig. 2*B*, *C*). With a further rise in temperature the period of relative sympathetic silence was in all subjects followed by a reappearance of sympathetic bursts which gradually increased in frequency and amplitude at about the same time as the subject started to sweat and rhythmical fluctuations appeared in skin resistance (Fig. 2*D*). At 45 °C there were still plethysmographic signs of finger vasodilatation but in most subjects there was also hyperpnea and tachycardia which caused respiratory fluctuations and a small reduction of the mean pulse amplitude in the plethysmogram (cf. Fig. 2*C*, *D*).

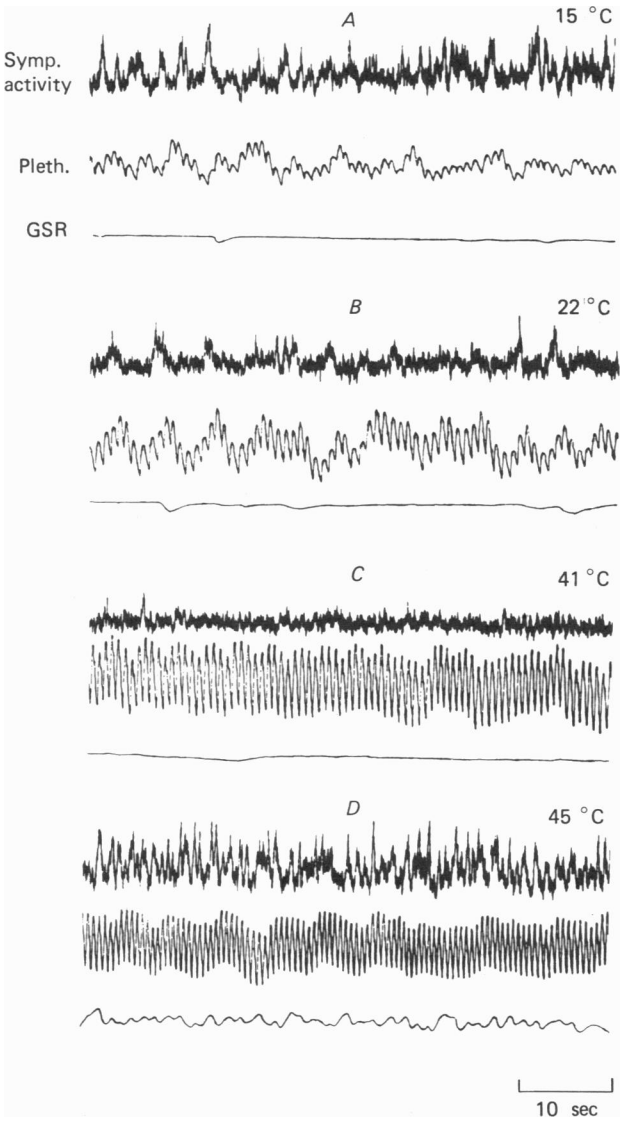

Fig. 2. Thermoregulatory changes in median nerve activity with accompanying vasomotor and sudomotor effects. Traces as in Fig. 1. *A–C*; decreasing vasoconstrictor activity with rising temperature (from 15 to 41 °C), *D*, strong sudomotor activity at 45 °C.

Both the neural and electrodermal signs of sudomotor activity vanished soon after the ambient temperature started to fall below 45° C. In two subjects, the intense neural activity stopped within a few seconds after the cooling fan was turned on, before any change was noted on the thermometer. Relative neural silence then remained until the temperature approached or fell below room temperature, when sympathetic bursts reappeared, now accompanied by obvious plethysmographic

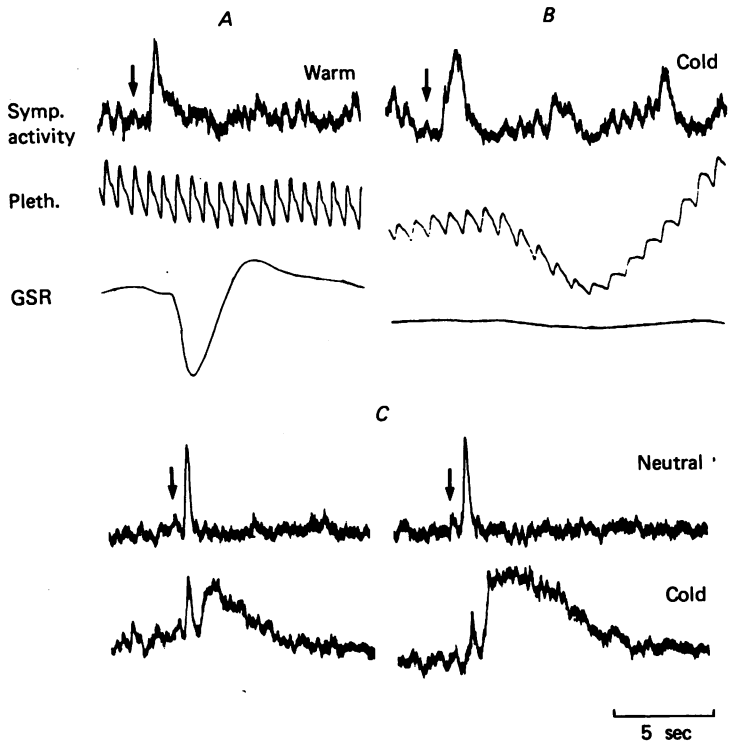

Fig. 3. Sympathetic responses to arousal stimuli at different ambient temperatures. *A*, 25–30 °C, auditory stimulus (arrow) eliciting a sympathetic reflex volley in peroneal nerve skin fascicle (upper trace). Note succeeding electrodermal response in foot innervation zone (bottom trace). *B*, 15–20 °C. Auditory stimulus (arrow) eliciting a sympathetic reflex volley in median nerve skin fascicle (upper trace) without signs of electrodermal response in palmar innervation zone (bottom trace). *C*, electrical skin stimuli (arrows) eliciting sympathetic impulse volleys in posterior cutaneous antebrachial nerve at 22–24 °C (upper) and at 15–20 °C (lower). Note that in the cold environment the sympathetic volleys are succeeded by sighs of piloerection seen in the neurograms as afferent discharges from hair follicle mechanoreceptors.

signs of finger vasoconstriction. At 15 °C most subjects exhibited sympathetic activity of similar strength as during intense warming, but the effector organ responses at low temperature were the reverse: strong vasoconstriction and no electrodermal signs of sudomotor activity (Fig. 2*A*). Similar thermoregulatory neural changes were also observed in a series of *peroneal nerve* recordings.

Findings from the *posterior cutaneous antebrachial nerve* were somewhat different from those illustrated in Fig. 2. In most subjects no spontaneous sympathetic activity

was seen in this nerve at normal room temperature or during moderate cooling, but sympathetic bursts accompanied by transient changes in skin resistance appeared in response to warming. These regional differences in thermoregulatory functions will be dealt with separately (Bini, Hagbarth, Hynninen & Wallin, 1980).

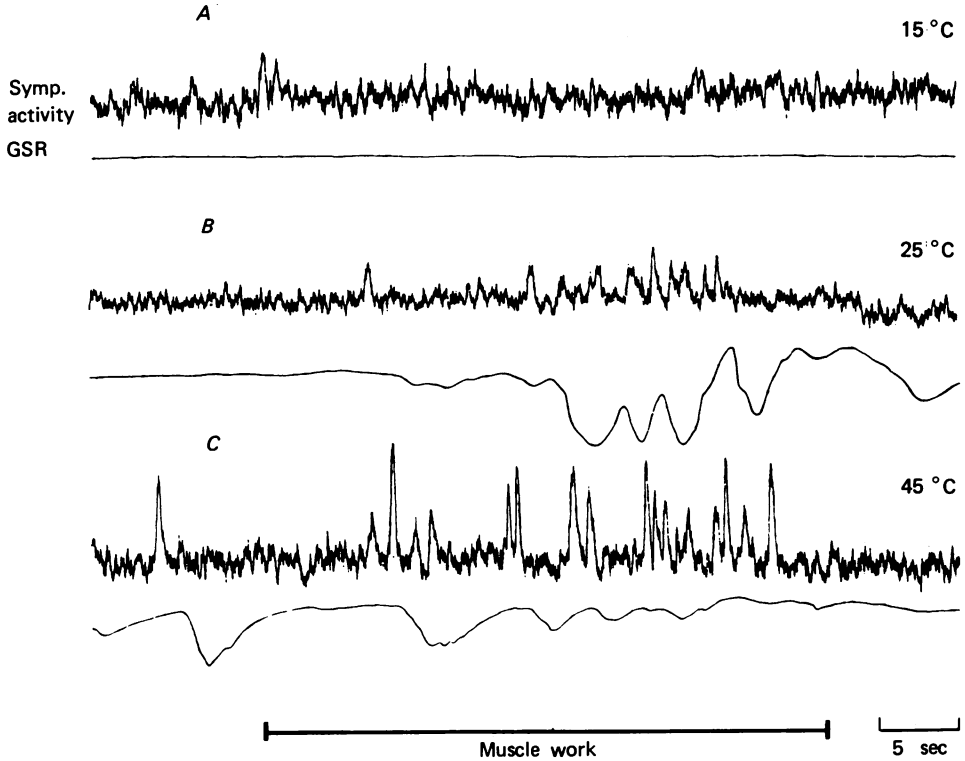

Fig. 4. Forearm sudomotor responses to muscle work at increasing environmental temperature (from *A* to *C*). Neural sympathetic responses recorded from posterior cutaneous antebrachial nerve (upper traces) with accompanying electrodermal responses (lower traces). The lack of quantitative relationship between neural sudomotor activity and succeeding electrodermal responses is due to the saturation of the GSR unit when working out of range (as in *C*).

Effects of arousal at different ambient temperatures. Sympathetic bursts in the *median and peroneal* nerves were in all subjects easily triggered by sudden unexpected stimuli, not only at normal room temperature but also during warming and cooling. As evidenced by succeeding plethysmographic and electrodermal responses, the reflex sympathetic bursts obtained at room temperature, were regularly composed of both vasoconstrictor and sudomotor impulses (cf. Fig. 1*B*). However, when the vasoconstrictor tone was reduced by moderate warming, many of the bursts triggered by weak arousal stimuli seemed to be composed exclusively of sudomotor impulses (Fig. 3*A*), and shifts towards pure vasoconstrictor arousal responses occurred when the sudomotor tone was reduced by cooling (Fig. 3*B*). Arousal stimuli also evoked sympathetic bursts in the *posterior cutaneous antebrachial* nerve, and at normal room temperature these bursts were succeeded by electrodermal responses in the

hairy skin of the forearm. Arousal bursts accompanied by such responses were not as easily elicited in the cold environment. Transient vasoconstrictor arousal responses such as those seen in the finger and toe plethysmograms, were not encountered in the forearm plethysmograms. In two experiments when the subjects were exposed to the chilly draught of the fan, arousal stimuli gave rise to transient piloerector responses in the forearm skin, and then each reflex sympathetic burst was followed by a strong barrage of neural impulses, apparently an afferent response arising from hair follicle receptors responding to the piloerection (Fig. 3*C*).

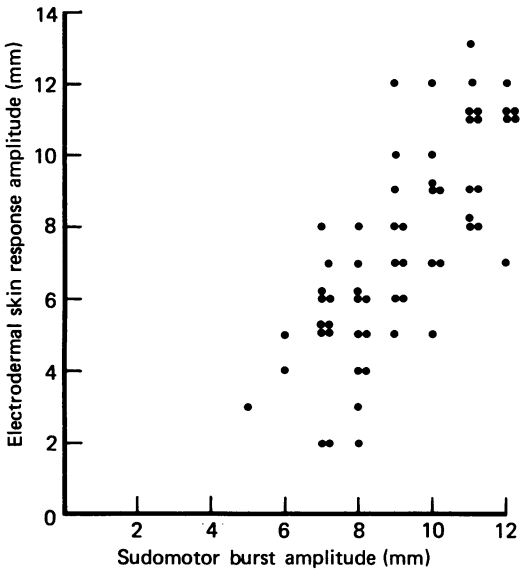

Fig. 5. Quantitative relationship between sudomotor bursts and accompanying electrodermal events. Correlation coefficient for linear regression $r = 0{\cdot}76$. Slope of line significantly different from zero, $P < 0{\cdot}01$. Record obtained from median nerve at an ambient temperature of about 28 °C. Abscissa: amplitude of single sudomotor bursts. Ordinate, amplitude of corresponding electrodermal responses.

Effects of muscle work at different ambient temperatures. Muscle work carried out at normal room temperature gave similar responses as a moderate rise in ambient temperature. For subjects exposed to an environmental temperature of 40–45 °C muscle work caused a strong sensation of increasing warmth and produced or increased sweating. Fig. 4*C* illustrates the rapid increase in sudomotor bursts from the *posterior antebrachial nerve* during such a manoeuvre. At room temperature sudomotor bursts (with accompanying electrodermal responses) were less prominent and did not occur until the muscle work had lasted for a longer period (Fig. 4*B*). At an environmental temperature of 15 °C muscle work of similar strength and duration produced no neural or electrodermal signs of sudomotor activity, but a slight reduction of pre-existing bursts, presumably composed of vasoconstrictor impulses (Fig. 4*A*). At the low temperature the subject was shivering and some of the neural bursts shown in Fig. 4*A* may have been volleys of afferent impulses from low threshold cutaneous mechanoreceptors. Thermoregulatory sudomotor responses in the *median and peroneal nerves* to muscle work were also more prominent at high than at low environmental temperatures.

Quantitative neuro-effector relationships

Sudomotor system. As illustrated in Fig. 4, during profuse sweating no simple quantitative relationship could be seen between the size of individual sudomotor bursts and accompanying electrodermal responses. This was due partly to the fact that succeeding electrodermal deflexions merged when the sudomotor burst incidence was high, partly to the non-linear characteristics of the electrodermal apparatus

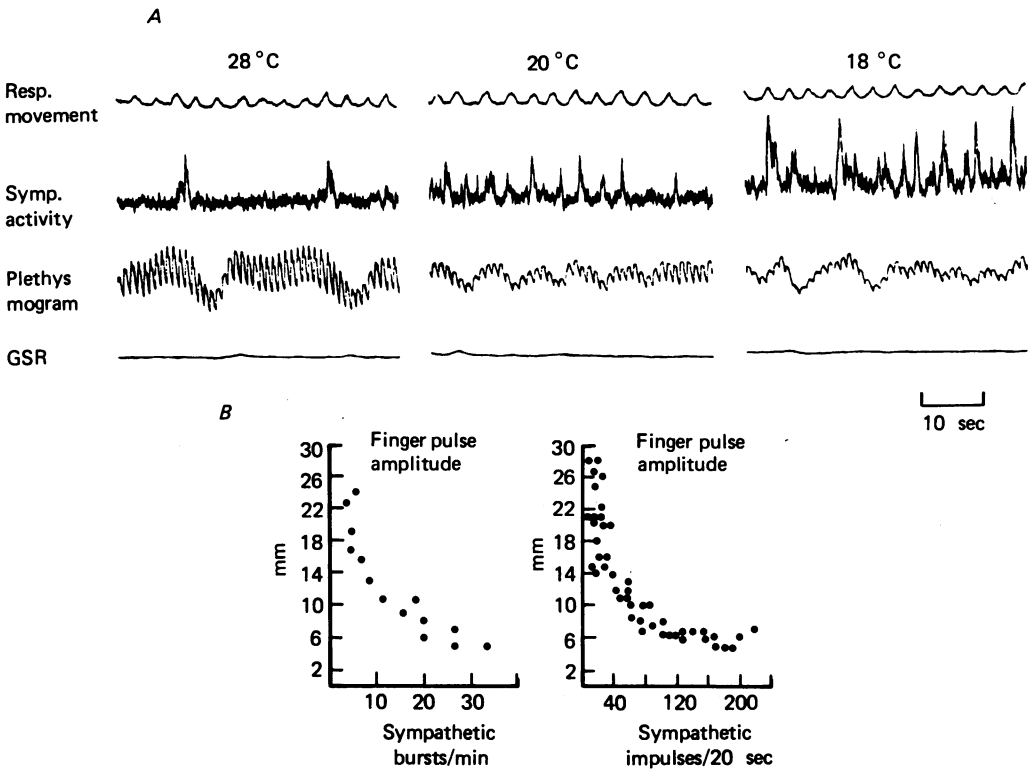

Fig. 6. Relationship between vasoconstrictor bursts and accompanying finger plethysmographic events. *A*, sympathetic activity recorded from median nerve at external temperatures of 28, 20 and 18 °C. Traces are from above: respiration, integrated neural signal, plethysmogram and skin resistance. *B*, left, diagram showing quantitative relationships between burst incidence/min (abscissa) and finger pulse amplitude (ordinate). Right, diagram showing quantitative relationship between sympathetic impulses per 20 sec (abscissa) and finger pulse amplitude (ordinate).

when measuring over wide ranges of absolute skin resistance. During the initial phases of thermoregulatory sweating, however, sudomotor burst incidence was low enough to allow a quantitative correlation between the mean voltage amplitude of individual sudomotor bursts and the amplitude of corresponding transient changes of skin resistance. As shown in Fig. 5, the relationship was linear with a considerable scatter.

Vasoconstrictor system. During some median nerve recordings, room temperature was slowly decreased (from 28–18 °C) while all external stimuli giving electrodermal responses were minimized. Before cooling, pulsations in the finger plethysmogram

were maximal and as illustrated in Fig. 6*A* (left) only transient reductions of pulse amplitude occurred in response to occasional spontaneous vasoconstrictor bursts. Cooling produced an increased incidence of vasoconstrictor bursts, each of which initially was followed after 2–4 sec by a well defined transient reduction of pulse amplitude lasting 4–5 sec. When the intervals between bursts became shorter,

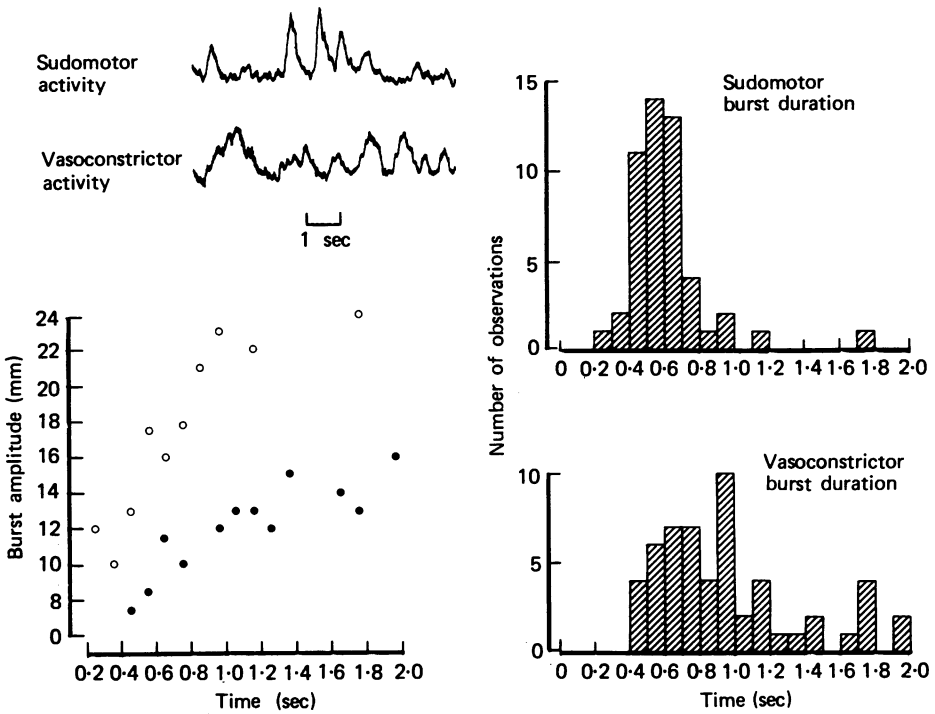

Fig. 7. Temporal dispersion of sudomotor and vasoconstrictor impulses. *A*, integrated neurograms from median nerve showing sudomotor activity at 45 °C, upper, and vasoconstrictor activity at 15 °C, lower. *B*, burst duration histograms of sympathetic activity at 45 °C, upper, and at 15 °C, lower. The histograms were obtained by measuring the duration of 50 sudomotor and 55 vasoconstrictor bursts as seen in the integrated neurograms. Mean duration for sudomotor bursts, 0·6 sec. Mean duration for vasoconstrictor bursts, 1 sec. *C*, relationship between amplitude and duration of sudomotor (○) and vasoconstrictor (●) bursts. Each dot represents the mean amplitude value of a population of bursts with the same amplitude.

individual plethysmographic responses merged, resulting in a sustained decrease of pulse amplitude (Fig. 6*A*, middle and right). The results were quantified in two ways: (1) The number of bursts in the mean voltage neurogram/min was plotted against mean finger pulse amplitude; (2) the original neurogram was fed through an amplitude discriminator the setting of which permitted only high amplitude spikes to be transformed into standard pulses. This 'few unit' neurogram of standard pulses was then displayed together with the plethysmogram; the spikes were counted during sampling periods of 20 sec and plotted against the mean amplitude of corresponding pulsations in the plethysmogram which was delayed 3 sec in relation to the nerve activity to allow for the latency of the neuro-effector transfer. Fig. 6*B* shows examples

of both types of plots from a cooling experiment lasting about 20 min in which hyperbolic relationships were obtained.

Duration of sudomotor and vasoconstrictor bursts

Sudomotor bursts generally appeared more distinct with a shorter mean duration than the vasoconstrictor bursts (see the mean voltage neurograms Figs. 2*A*, *D* and 7*A*). The two histograms in Fig. 7*B* quantitate the difference in mean duration between sudomotor and vasoconstrictor bursts led off from the same recording site in the median nerve at temperatures of 45 and 15 °C, respectively. The diagrams in Fig. 7*C* show that for both types of bursts there was a linear relationship between burst amplitude and burst duration. However, for the sudomotor bursts, the amplitude rose more steeply relative to the duration, indicating a smaller temporal dispersion of sudomotor as compared to vasoconstrictor impulses.

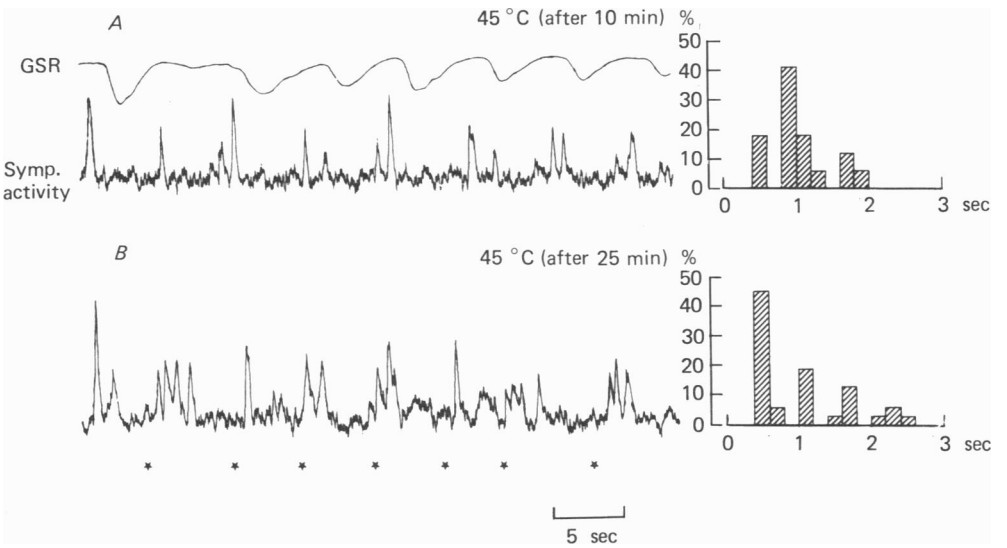

Fig. 8. Sudomotor rhythms. Sympathetic activity recorded from posterior cutaneous antebrachial nerve after exposure to an environmental temperature of 45 °C for 10 min (*A*) and for 25 min (*B*). *Left*, integrated neurograms showing rhythmically occurring sudomotor bursts. In *A*, upper trace, the accompanying electrodermal responses are also shown. *Right*, burst interval histograms. The histogram data were obtained during the 11th (*A*) and the 26th (*B*) min after 45 °C was reached. The asterisks in *B*, *left*, indicate the moments when the subject signalled the experience of heat waves, see text.

SSA rhythms

As previously shown (Hagbarth *et al.* 1972) respiratory rhythms are sometimes reflected in the skin nerve sympathetic activity and such s.s.a. rhythms were seen also in the present study (Fig. 6*A*). By measuring the intervals between successive bursts and plotting the data in non-consecutive form a number of other inherent s.s.a. rhythms were also discerned.

Sudomotor rhythms. Successive sudomotor bursts in recordings such as Figs. 2*D* and 4*C* occurred at certain preferred intervals which were integer multiples of a period of about 0·6 sec. In another recording of sudomotor activity in the ante-

brachial nerve at 45 °C, soon after sweating had started, the bursts occurred in short sequences, separated by silent periods with a duration of 4–5 sec (Fig. 8*A*). As shown by the interval histogram (to the right) the predominant burst intervals during the sequences were 1·0–1·2 sec, whereas other intervals centred around 0·6 and 1·8 sec. 15 min later when the sweating was more pronounced the predominant burst interval was 0·6 sec with fewer bursts occurring at intervals of 1·2, 1·8 and 2·4 s (Fig. 8*B*).

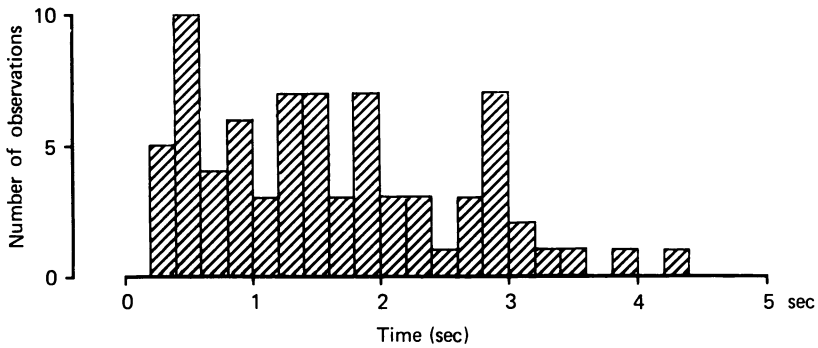

Fig. 9. Vasoconstrictor rhythms. Data obtained from a median nerve recording at an ambient temperature of 15 °C as in Fig. 2*A*. Burst interval histogram calculated as in Fig. 8 over an analysis period of 2 min.

As shown in Fig. 8*A* grouping of bursts at intervals of 4–5 sec was accompanied by similar rhythmical fluctuations in skin resistance. The subject reported that as long as this slow rhythmicity persisted he felt 'waves of heat sensations' which appeared regularly just before the sequences of sudomotor bursts, as indicated by the asterisks below the neurogram in Fig. 8*B*.

Vasoconstrictor rhythms. Successive vasoconstrictor bursts were found to occur at preferred intervals similar to those for the sudomotor bursts, the predominant intervals with strong vasoconstrictor tone being about 0·6 sec. However, interval histograms for the vasoconstrictor bursts did not show the succeeding peaks at the integer multiples of 0·6 as distinctly as for sudomotor bursts (cf. Fig. 8*B* right and Fig. 9). This difference was probably related to the fact that in the mean voltage neurograms it was easier to determine the exact intervals for the sudomotor than for the longer lasting vasoconstrictor bursts.

DISCUSSION

Discrimination between sudomotor and vasoconstrictor impulses. There is histological evidence that along their course in a peripheral nerve individual C axons repeatedly pass over from one Schwann cell bundle to another so that the axon composition of individual Schwann cells changes continuously (for references see Ochoa, 1976). This agrees with the present findings indicating that within a given nerve there are no specific intrafascicular sites from which only sudomotor and no vasoconstrictor sympathetic impulses can be recorded or vice versa. At least in nerves supplying hands and feet strong sympathetic impulse volleys are, at normal temperature conditions, always accompanied by both vasomotor and electrodermal responses,

indicating that both types of fibres were within the uptake range of the electrode (Fig. 1*A*). The fact that some of the smaller volleys obtained from the same recording site seemed to be dominated by either sudomotor or vasomotor impulses merely indicates that the two sets of fibres can be activated independently of each other (Fig. 1*C*, *D*).

The question may be raised whether a given sympathetic impulse volley can be safely classified as being of sudomotor or vasomotor origin, depending on whether it is succeeded by an electrodermal response or a plethysmographic response in the skin field to which it is destined. It seems safe to conclude that vasoconstrictor impulses are present in those sympathetic bursts which are succeeded by transient reductions in the plethysmographic pulse waves (as in Fig. 2*A*, *B*) and that sudomotor impulses are present in those neural bursts which are succeeded by transient reductions in skin resistance (as in Fig. 2*D*). Providing the skin electrode positions were correct (and the gain of the electrodermal response unit was sufficient) the absence of a response following a burst must be regarded as a good criterion that the burst contained few or no sudomotor impulses. However, the absence of a plethysmographic response following a sympathetic burst does not necessarily imply that this burst contained no vasomotor impulses. The transient plethysmographic responses following individual vasoconstrictor bursts were clearly seen only in the finger plethysmograms, not in the plethysmographic recordings from the forearm skin (cf. Hertzman, 1959), where increasing vasoconstrictor outflow was accompanied only by sustained reduction of pulse amplitude. Further studies are needed to explain this regional difference in the dynamic responsiveness of the plethysmograms. However, for median nerve sympathetic bursts a high gain plethysmogram from a finger supplied by the impaled nerve fascicle can probably be regarded as a fairly reliable indicator as to whether or not the bursts contain vasomotor impulses.

Thermoregulatory control of sudomotor and skin vasoconstrictor fibres. The present findings (Figs. 1 and 2*B*) confirm previous microneurographic observations (Delius *et al.* 1972*c*; Normell & Wallin, 1974) that in most subjects there is at normal temperature spontaneous vasoconstrictor activity in human skin nerves supplying hands and feet, an activity which increases in response to cooling and decreases in response to moderate warming. It was also confirmed that with a further rise in external temperature the sympathetic activity in these nerves increases again when the sudomotor fibres are recruited into action (cf. Normell & Wallin, 1974). These changes in the central excitatory drives on the two systems were reflected also in the sudomotor and vasoconstrictor responsiveness to arousal stimuli at different ambient temperatures.

The role played by cutaneous thermoreceptors in thermoregulation is widely accepted (McCook, Randall, Hassler, Mihaldzic & Wurster, 1970) and the sympathetic responses to ambient temperature changes, seen in the present study, were probably to a large extent dependent on exteroceptive clues. At least, this must be true for the very sudden cessation of sudomotor activity which occurred as soon as the ambient temperature started to fall after a peak value of 43 °C. On the other hand, thermosensitive interoceptors probably contributed to the sudomotor responses elicited by muscle work, even though the strength of these responses where also highly dependent on the ambient temperature (Fig. 4).

Sudomotor and skin vasoconstrictor rhythms. The sudomotor and skin vasoconstric-

tor post-ganglionic fibres showed a marked tendency to synchronous firing, a tendency resulting in more or less rhythmical bursts of multiunit sympathetic impulses. The temporal entrainment of the neural impulses may in part be due to the fact that many post-ganglionic fibres may fire in response to one single preganglionic impulse. However, since s.s.a. bursts tend to appear in a bilaterally synchronous fashion in both arm and leg skin nerves (Bini *et al.* 1980), suprasegmental structures must be involved in the temporal modulation of the sympathetic neural outflows from the spinal cord (cf. Sundlöf & Wallin, 1977). As found in the present study, one can, besides respiratory rhythms also recognize a series of harmonically related faster rhythms, in the vaso- and sudo-motor outflow to the skin, including a rhythm at about 100/min (Figs. 8 and 9). According to previous studies, brain stem centres have an intrinsic capacity to generate respiratory and cardiac rhythms, but such rhythms can also be driven by afferent impulses from the periphery, signalling heart beats or respiratory movements (Koepchen, 1962; Biscoe & Purves, 1967; Taylor & Gebber, 1975). The demonstration of the 100/min s.s.a. rhythm in man reopens the question whether the arterial baroreflex in any way contributes to the rhythmical modulations of the sympathetic outflow to the skin (cf. Hagbarth *et al.* 1972).

The fast rhythms referred to above, which were similar for the sudomotor and vasomotor systems, can hardly be attributed to oscillatory tendencies in thermoregulatory servos. However, the sudomotor rhythm at about 15/min, illustrated in Fig. 8. may have resulted from such an oscillatory tendency in the closed servo-loop of the sudomotor thermoregulatory system: a rise in skin temperature giving rise to an outburst of sudomotor impulses causing sweat production and a lowering of skin temperature sufficient to cause a reflex suppression of the sudomotor outflow. If so, this suggests a high dynamic sensitivity of the cutaneous thermoreceptors engaged in thermoregulation.

Quantitative relations between vasoconstrictor neural activity and accompanying finger plethysmographic events. An approximately hyperbolic reduction of mean finger pulse amplitude with increasing levels of sympathetic vasoconstrictor activity in median nerve skin fascicles agrees well with previous animal data. Folkow (1952) found a pronounced increase of vascular resistance for the cat's hind limb when raising sympathetic impulse frequency from 1–4 impulses/sec but only minimal effects when going from 10 to 15 impulses/sec. Similar hyperbolic stimulus–response curves have since been found for many different vessels (e.g. Ljung, Bevan, Pegram, Purdy & Su, 1975). Although the general shape of the relationship between sympathetic impulse frequency and finger pulse amplitude is in good agreement with previous data it is difficult to compare absolute firing frequencies since diagrams like Fig. 6*B* (right) were not based on single unit recordings.

Possible functional relationship between rhythm generating mechanisms and neuro-effector transfer functions. As shown in single unit recordings from sympathetic C-fibres in human cutaneous nerves, the increase in sympathetic outflow during a given manoeuvre is both due to an increase in the mean firing rate of previously active units and to a recruitment of previously silent units. The highest mean firing rate observed for any given unit was 70 impulses/min, the single unit discharges being grouped together with impulses in neighbouring sympathetic fibres contributing to the multi-unit bursts (Hallin & Torebjörk, 1974). These findings are compatible

with a particular functional role of the central rhythm-generating mechanisms: by causing temporal entrainment of the impulses (cf. Figs. 8 and 9) individual sympathetic fibres are prevented from reaching mean firing rates far exceeding the 100/min rhythm. At least for the vasoconstrictor system, this may be of functional importance since it may help to restrict the mean firing rates of individual vasoconstrictor fibres to the low ranges within which there is optimal gain in the neuro-effector transfer functions.

Temporal dispersion of sudomotor as compared to vasoconstrictor impulse bursts. Duration histograms (Fig. 7*B*) and amplitude – duration plots (Fig. 7*C*) show the sudomotor impulse bursts to be more synchronized than the vasomotor ones. This may imply either a differently timed central drive or a different peripheral conduction velocity for these two fibre systems. The former hypothesis seems less likely since, as described above, both sudomotor and skin vasoconstrictor post-ganglionic neurones seem to be governed by similar rhythm-generating mechanisms. The latter hypothesis on the other hand, is consistent with experimental evidence obtained in animals. Jänig & Kümmel (1977), measuring the conduction velocity of single sympathetic fibres in cats, reported that sudomotor fibres conduct at a higher mean rate than vasoconstrictor ones. More recently, direct measurements of the conduction velocity of pure vasoconstrictor and sudomotor bursts in humans also gave results consistent with this hypothesis (Fagius & Wallin, 1980). Furthermore, the different conduction rates cannot be explained in terms of a passive effect of temperature since in our experiments the arm on which the recordings were performed was kept outside the box at a constant temperature, and similar differences were evident also among those sporadic vaso- and sudomotor bursts occurring at normal temperature.

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