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SYMPATHETIC DISCHARGES IN THE HUMAN SUPRAORBITAL NERVE AND THEIR RELATION TO SUDO- AND VASOMOTOR RESPONSES

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SUMMARY

1. Sympathetic nerve activity occurring as bursts of multi-unit impulses was recorded with tungsten microelectrodes in the supraorbital nerve of awake healthy subjects. Within the fascicular innervation zone on the forehead, skin resistance was measured as an indicator of sweat gland activity, and skin blood flow was measured with laser-doppler flowmetry.

2. At room temperature, there was little or no background burst activity, but arousal stimuli or mental stress evoked bursts followed by a vasodilator response. Provided repeated arousal stimuli were delivered, individual bursts were followed by a decrease in skin resistance.

3. Body heating induced increasing background burst activity. After an initial period without associated electrodermal activity, there were decreases in skin resistance, which showed a positive linear correlation with the amplitude of the preceding burst. Individual bursts were followed by a vasodilator response with an average onset latency of 2·8 s and an average duration of 9·1 s, and rapid increases in blood flow coincided with a marked increase in burst activity. Arousal stimuli evoked bursts followed by both vasodilator and skin resistance responses.

4. During body cooling, there was no background burst activity, but signs of relatively weak, probably neurally mediated vasoconstriction were observed and arousal-evoked bursts were reduced or abolished, as were the associated vasodilator and skin resistance responses.

5. It is concluded that body heating induces active sympathetic vasodilatation in the skin of the human forehead, and that this is either sudomotor-mediated or caused by vasodilator fibres firing in synchrony with sudomotor fibres. A similar sympathetic mechanism probably underlies the vasodilator responses evoked by arousal stimuli and mental stress.

INTRODUCTION

Our knowledge of the sympathetic innervation of the human face is based largely on indirect estimations of skin blood flow and sweating, from which conclusions regarding the underlying neural mechanisms have been drawn (Hertzman & Dillon, 1939; Blair, Glover & Roddie, 1961; Fox, Goldsmith & Kidd, 1962; Drummond & Lance, 1987). In the present study of the human supraorbital nerve, sympathetic

neural activity was recorded with microelectrodes inserted percutaneously into individual nerve fascicles. Simultaneous recordings of skin blood flow with laser-doppler flowmetry, and of skin resistance (as an indicator of sweat gland activity), were obtained from the forehead. In addition to thermoregulatory responses, the effects of arousal stimuli and mental stress were studied. The aim was to gain understanding of the normal sympathetic outflow and the associated sudo- and vasomotor responses. Such knowledge may provide a basis for further studies on pathophysiological mechanisms of importance for vascular headache. Some preliminary results from the present study have been published in abstract form (Nordin, Thomander, Wallin & Hagbarth, 1987).

METHODS

Subjects

The data were obtained in thirty-four male and two female healthy subjects aged 20–59 years (31 ± 9 years, mean $\pm$ S.D.). The total number of experiments was sixty-five, including those with nerve recordings, effector organ recordings or a combination of the two. The number of subjects studied in different respects are given in the Results. Informed consent was obtained and the study was approved by the local ethics committee.

Recording techniques

Skin sympathetic activity. This was recorded by microneurography using methods similar to those described for nerves of the extremities (Hagbarth, Hallin, Hongell, Torebjörk & Wallin, 1972; Bini, Hagbarth, Hynninen & Wallin, 1980*a*, *b*). A lacquer-insulated tungsten microelectrode, with a shaft diameter of 0·2 mm and a tip diameter of about 5 μm, was inserted through the skin 1–15 mm above the eyebrow (left side in two-thirds of the experiments), and a reference electrode was inserted nearby. The search for the supraorbital nerve was aided by electrical stimulation via the microelectrode. Once an intrafascicular recording position had been obtained (as evidenced by the responses to tactile stimuli), arousal stimuli were used to elicit sympathetic reflex responses, and minor manipulations of the microelectrode were performed in order to find and improve a sympathetic recording site (cf. Hagbarth *et al.* 1972; Wallin & Fagius, 1988). The major difficulty was in impaling a nerve fascicle (prolonged attempts failed in nineteen experiments). Even small movements of the eyebrow easily displaced the microelectrode from the intrafascicular position, and the duration of a sympathetic recording ranged from a few minutes to 3 h.

The nerve signal was amplified in two steps (total gain usually 20000 ×) and band-pass filtered (500–5000 Hz), and the signal-to-noise ratio was improved by an amplitude discriminator which eliminated the central portion of the noise. The neurogram was audio-monitored.

Skin blood flow. This was measured with a laser-doppler flowmeter (Periflux 1d or 2b, Perimed AB, Sweden). This equipment gives no absolute values, but permits measurements of relative changes in blood flow (Holloway & Watkins, 1977; Nilsson, Tenland & Öberg, 1980; Johnson, Taylor, Sheperd & Park, 1984). In all cases, recordings were obtained on the forehead within an area between 2 and 7 cm above the eyebrow, and in the experiments with simultaneous nerve recording the probe was placed within the fascicular innervation zone. Electrical calibration for zero blood flow was performed, and an appropriate gain was selected. In the figures, the maximal output at a given gain level was set at 100%.

Skin resistance. This was recorded with two silver–silver chloride electrodes (E221, in Vivo Metric Systems, USA; diameter 8 mm), which were placed 2–5 cm apart within the described area in the forehead. A purpose-made electrode medium with a low electrolyte concentration was used (NaCl 0·3 g, carboxymethyl cellulose 5 g, purified water *ad* 100 g; cf. Edelberg & Burch, 1962). A modified galvanic skin response (GSR) module (IGSR-ZA, van Gogh, Netherlands) working according to the constant-current principle (measuring current 5 μA) was used. It had an exponential rise time constant of 0·3 s and a decay time constant of 3·3 s. Hence, absolute values of skin resistance were not recorded, but only transient changes. In some subjects, skin resistance was also measured in the thenar region of the right palm.

In most experiments vasomotor responses in the right index finger were recorded with a photoelectric pulse plethysmograph. In three subjects arterial blood pressure was monitored continuously but non-invasively with a Finapres device (Ohmeda Monitoring Systems, USA).

Experimental procedure

The subject lay on his back on a couch, awake and as relaxed as possible. The room temperature was 22–25 °C and the subject wore trousers or shorts and a short-sleeved shirt.

Although various stimuli were used, normally the arousal stimulus was electrical (square waves, duration 0·3 ms), applied with a bipolar surface electrode over the median nerve at the wrist. The voltage was adjusted so that a twitch occurred in the thenar muscles; most subjects did not consider this painful.

For induction of changes in ambient temperature the subject lay with the whole body, except the head, in a box intended for hypothermic surgery (Auto-Hypotherm Super Automatic XM, Heljestrands AB, Sweden). During heating the subject was covered with a blanket and in the course of about 20 min the temperature was gradually increased to 45 °C, at which level it was kept for various lengths of time. During cooling, the temperature was reduced to 15 °C or lower, and this had a pronounced cooling effect since the air was circulated by a fan. The procedure was stopped when the subject felt uncomfortably cold and started to shiver. Mental stress was induced for periods of about 20 s by harassing the subject to do mental arithmetic.

Signal display and analysis

During the experiments the signals were monitored on a storage oscilloscope or a video display monitor. They were stored on tape (multichannel FM tape-recorder, Sangamo Sabre VI, USA) and later recorded on paper (Mingograph 800, Siemens-Elema, Sweden or ES1000, Gould Instruments, France). Sympathetic burst activity was analysed from mean voltage recordings which were obtained by full-wave rectifying the nerve signal and passing it through an 'integrator' with an exponential decay (time constant 0·1 s). The skin resistance recordings allowed responses of about 0·2 kΩ to be detected.

A universal waveform analyser (Data 6000A-611, Data Precision, USA) was used for analysis of the flowmeter signal. Mean blood flow at different ambient temperatures was calculated for 30–60 s periods, and changes were expressed in per cent of the control flow. Averaging was used to study the vasomotor effects of arousal stimuli and the relation between heat-induced burst activity and blood flow changes. In averaged traces, increases in blood flow were measured from the maximal value in the pre-stimulus (pre-burst) control period to the peak value of the response and expressed in per cent of the control value. Durations were measured from the start of the response to the return to the mean flow for the control period.

Values are reported as mean ± S.E.M. The significance of changes in blood flow data was tested by the Mann–Whitney U test and the Wilcoxon signed rank test. For other data Student's t test was used. Differences were considered significant at $P < 0{\cdot}05$. Relations between variables were tested by linear regression and linear correlation.

RESULTS

Recordings at room temperature

Figure 1*A* shows a typical example of an arousal response recorded from the supraorbital nerve. When stimuli were repeated at short intervals the response habituated, but electrical stimuli of the type described, delivered at intervals of 1 min or longer, reliably elicited a reflex response. The evidence for the sympathetic origin of the activity is given in the Discussion.

Sympathetic reflex responses to arousal stimuli were detected in all except one out of twenty-seven subjects in whom an intrafascicular recording position was obtained (and in forty out of forty-two experiments). The average onset latency (based on at

least five responses in a given subject) ranged from 0·37 to 0·53 s (0·45±0·01 s; $n = 21$). The correlation with body height was not significant ($r = 0·36$, $P = 0·14$, $n = 18$, range of body height 165–193 cm). The average burst duration was 0·56±0·01 s (intra-individual means in twenty-one subjects).

Provided the subject was relaxed, there was usually no 'spontaneous' burst activity at room temperature (Fig. 1*B*; occasional 'spontaneous' bursts occurred in only seven subjects). Mental arithmetic evoked sympathetic activity in all thirteen subjects studied, and during a 20 s period the maximal number of bursts was 10±2.

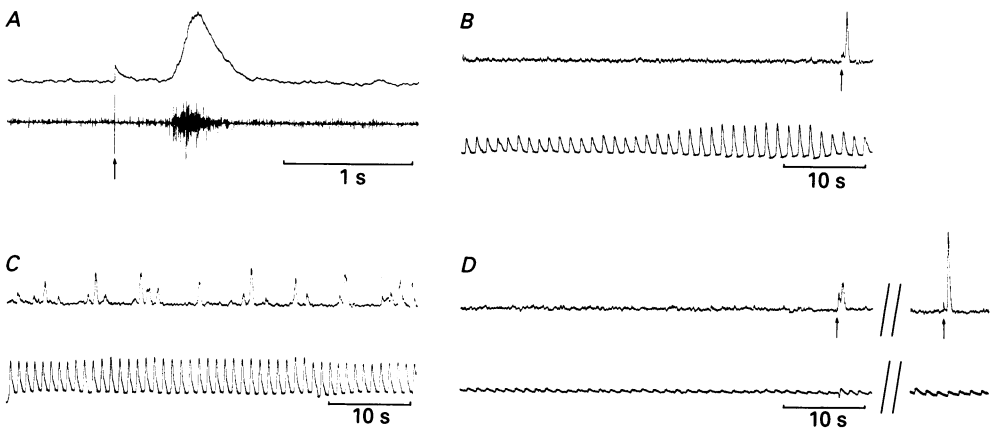

Fig. 1. Sympathetic recordings from the supraorbital nerve. The arrows indicate arousal stimuli (electrical stimulation over the median nerve). *A*, sympathetic reflex response as seen in the discriminated neurogram (lower trace) and in the mean voltage neurogram (upper trace). In all subsequent figures only the mean voltage neurogram is shown. Note that the stimulus artifact caused an initial peak in the neurogram, which could be used when measuring reflex latencies. *B–D* are recordings obtained in the same experiment at different ambient temperatures. The lower trace is the pulse plethysmogram from the right index finger. *B*, lack of background burst activity at 22 °C, but a large reflex response following an arousal stimulus. *C*, background burst activity at 45 °C. *D* (left). lack of background burst activity at 7 °C, although there was strong vasoconstriction in the hand. The arousal response was reduced in amplitude. Following re-warming to room temperature, the arousal response increased (*D*, right).

In nine out of fourteen subjects, a single arousal stimulus delivered after a period of rest caused no detectable change in forehead skin resistance, but repeated stimuli, each of which elicited a sympathetic response, resulted in the appearance of an electrodermal response (Fig. 2*A*). In two subjects there was a small initial response which increased in the subsequent trials. The maximal response amplitude in these eleven subjects was 3·8±1·0 kΩ, which was less than 10% of that observed from the palm of the hand (53±9 kΩ; $n = 10$, $P < 0·001$). In the remaining three subjects no skin resistance response was detected in the forehead, although repeated arousal stimuli were delivered.

More or less pronounced rhythmical changes in the forehead blood flow (average period duration 6·2±0·1 s) were noted in all except one out of twenty-four subjects studied with flowmeter recordings; these oscillations occurred even when there was no burst activity (Figs 3*A* and *D*, 6*E* and 7*A*). Arousal stimuli evoked marked

increases in forehead blood flow in eighteen subjects (Fig. 3*A*). This was noted even in the absence of any rise in blood pressure. In these subjects the magnitude of the most pronounced vasodilator response was 55±5%, when measured as described in the legend to Fig. 3*A*. In averaged traces obtained for eleven subjects (Fig. 3*B*), the

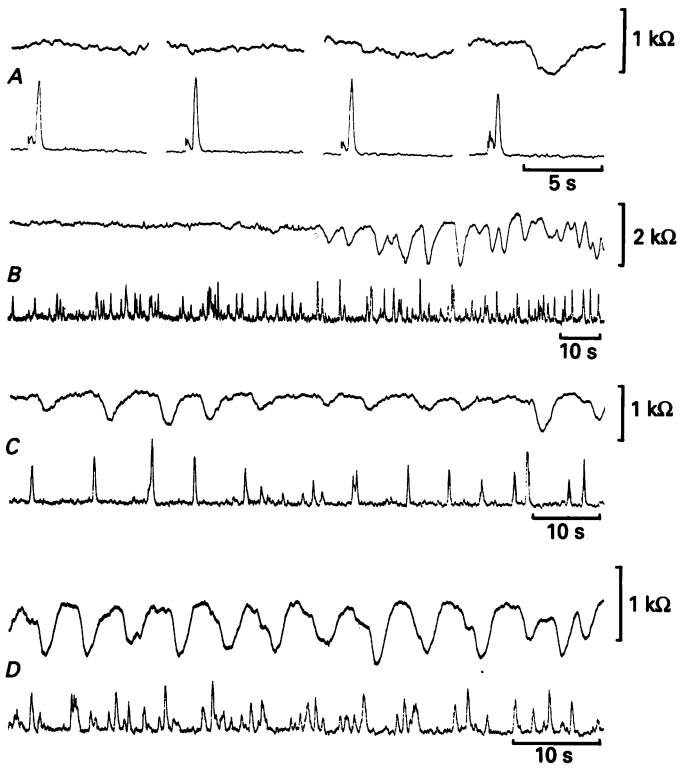

Fig. 2. Examples of the relation between sympathetic burst activity in the supraorbital nerve (lower trace) and skin resistance changes in the forehead (upper trace). *A*, repeated arousal stimuli at room temperature delivered during a period of 5 min and resulting in the appearance of a skin resistance response. The sympathetic reflex responses were of similar magnitude after each stimulus. The burst activity in *B–D* was heat-induced and occurred in relaxed subjects. *B*, bursts at 36 °C not accompanied by any electrodermal activity, followed by an abrupt appearance of decreases in skin resistance. *C*, relation between individual bursts and decreases in skin resistance in recordings obtained at 43 °C. *D*, rhythmical decreases in skin resistance at 45 °C, with each peak corresponding to a group of preceding bursts.

latency from the stimulus to the start of the response was 2·6±0·1 s, the duration of the response was 13·7±0·9 s and the magnitude of the increase was 37±5%. Vasodilator responses occurred even when there was no skin resistance response and were not potentiated by repeated arousal stimuli. Signs of vasoconstriction preceding the vasodilatation were observed in two subjects (Fig. 3*C*). In another six subjects, arousal stimuli known to elicit a sympathetic reflex response did not evoke any obvious blood flow response (Fig. 3*D*).

Mental arithmetic induced signs of forehead vasodilatation in all fourteen subjects studied, with a maximal blood flow increase of 74±14% (measured as described for

Fig. 3*A*). In all seven subjects in whom simultaneous nerve recordings were performed, the onset of the vasodilatation was preceded by the onset of burst activity, and when the neural activity ceased the blood flow returned to the basal level within 15 s. This was also true for the recordings in Fig. 4, which were obtained

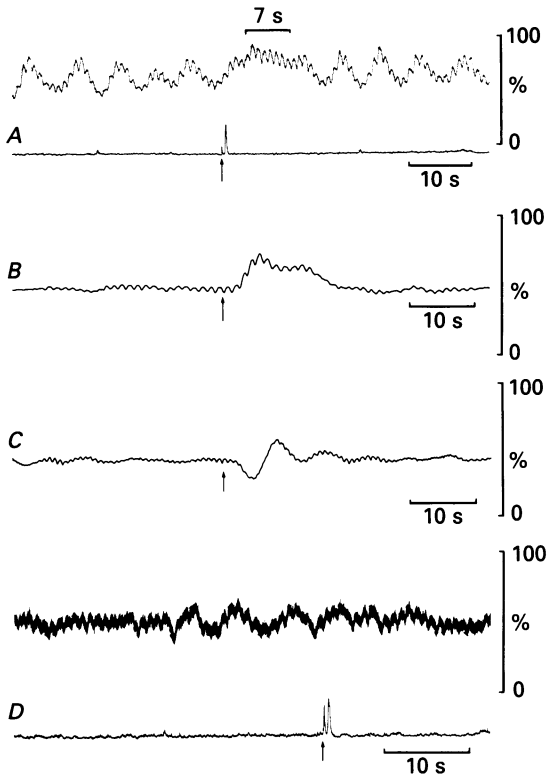

Fig. 3. Effects of arousal stimuli (indicated by arrows) on forehead blood flow at room temperature. Examples obtained in four different subjects. *A*, increase in blood flow interfering with the rhythmical variations. The lower trace is the supraorbital nerve recording with a sympathetic reflex response. To obtain an estimate of the response to an individual stimulus, the mean flow was measured for a period of the response corresponding to the cycle length in the pre-stimulus recording and adjusted to give a maximal mean value (in this case the mean for the indicated 7 s period was calculated). The rise in blood flow was expressed as a percentage of the mean for a 20–30 s pre-stimulus period. In this case it was found to be 39 %. *B*, vasodilator response obtained by averaging eleven trials. *C*, signs of initial vasoconstriction followed by vasodilatation; the trace was obtained by averaging eleven trials. *D*, absence of any obvious vasomotor response despite the occurrence of a sympathetic reflex response in the supraorbital nerve.

at somewhat above room temperature. The latency from the first major burst to the start of the vasodilator response was estimated to be $3{\cdot}0 \pm 0{\cdot}2$ s (eleven trials). Vasodilatation also accompanied the burst activity that occurred when the subject talked or felt embarrassed.

Recordings during body heating

Body heating induced increasing background burst activity in all thirteen subjects studied (Fig. 1*C*). This activity started at an ambient temperature of 33 ± 1 °C, and

in one subject it reached a maximal intensity of 60 bursts/min. The average burst duration was 0·64 ± 0·01 s (intra-individual means in eight subjects).

The initial part of Fig. 2*B* shows heat-induced sympathetic activity which was not associated with electrodermal activity in the forehead. However, a sudden decrease

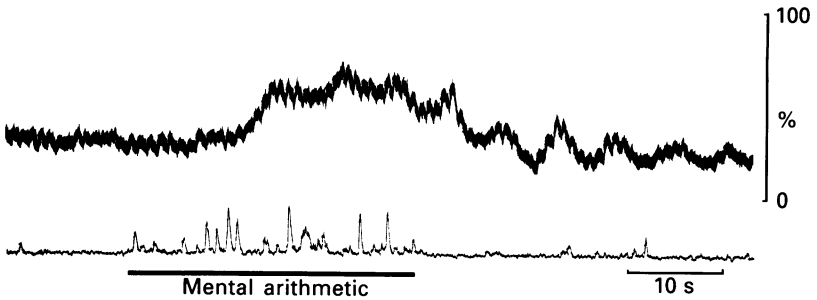

Fig. 4. Sympathetic activity in the supraorbital nerve evoked by mental arithmetic, accompanied by signs of pronounced vasodilatation in the forehead. Recordings obtained at 36 °C.

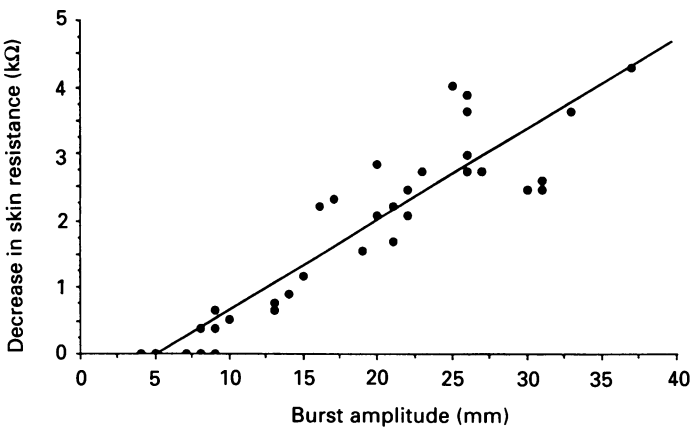

Fig. 5. Correlation in one subject between the amplitude of sympathetic bursts recorded from the supraorbital nerve during body heating and the amplitude of the corresponding decreases in skin resistance in the forehead. Bursts with short intervals, which rendered the exact assessment of the electrodermal response amplitude impossible, were not included in the analysis. The linear regression line is shown ($r = 0{\cdot}91$, $P < 0{\cdot}001$).

in skin resistance did occur later, and each subsequent major burst was followed by a skin resistance response. The period of burst activity prior to the appearance of electrodermal activity was 6 ± 2 min ($n = 7$). Once they had appeared, skin resistance responses also occurred after bursts evoked by arousal stimuli and mental stress.

Periods with sparse background burst activity (as in Fig. 2*C*) were analysed for the correlation between burst amplitude and the amplitude of the corresponding decrease in skin resistance. As shown in Fig. 5, there was a positive linear correlation. Similar strong correlations ($r = 0{\cdot}84$–$0{\cdot}93$, $P < 0{\cdot}001$) were found for the other four subjects studied.

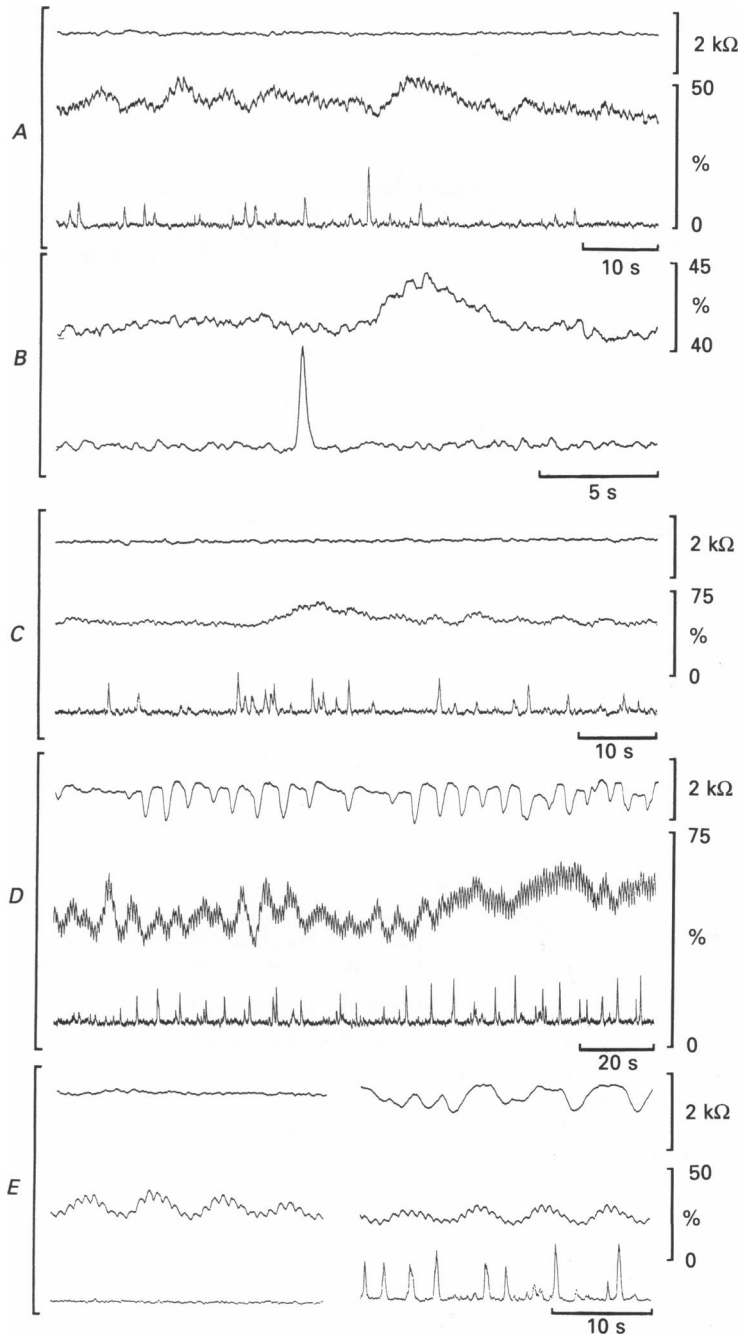

Fig. 6. For legend see facing page.

The latency from the onset of a major burst to the onset of the corresponding decrease in skin resistance was $0{\cdot}86 \pm 0{\cdot}03$ s (intra-individual means in seven subjects). With short burst intervals the skin resistance responses merged, but with intervals of 1·5 s or longer two peaks were usually discernible. After prolonged heating, the electrodermal activity often occurred in a rhythmical fashion, with intervals of 5–7 s (Fig. 2*D*). Each decrease in skin resistance at this stage corresponded to a preceding group of bursts.

Simultaneous blood flow and nerve recordings during body heating were obtained in ten subjects. Before the occurrence of sympathetic background activity, there was no significant change in mean blood flow compared with that at room temperature ($P = 0{\cdot}87$). Once the sympathetic activity had started, however, a vasodilator response was seen after individual large bursts in seven of the subjects (Fig. 6*A*). In averaged traces (Fig. 6*B*), the latency measured from the start of the burst to the onset of the response was $2{\cdot}8 \pm 0{\cdot}1$ s, the duration of the response was $9{\cdot}1 \pm 1{\cdot}0$ s and the magnitude of the increase was 11 ± 3%.

Periods of more intense sympathetic activity in the above seven subjects were accompanied by an increase in blood flow, which soon subsided when the burst activity decreased (Fig. 6*C*). Recordings in one subject showed that this was not caused by any corresponding change in blood pressure. As exemplified in Fig. 6*D*, in five of the ten subjects there was a rapid increase in blood flow (by 61 ± 9% in 1 min) coinciding with a marked increase in sympathetic activity. This started 25 ± 8 min after the appearance of burst activity, and the blood flow then remained at a higher level. A comparison was made between the sympathetic activity during two 1 min periods, the first immediately before and the second during the rapid rise in blood flow: the average number of bursts increased from 19 ± 4 to 29 ± 5 ($P < 0{\cdot}01$), and the total sympathetic activity, expressed as the sum of all burst amplitudes, also increased significantly ($P = 0{\cdot}01$). The relative increase in total sympathetic activity was 98 ± 13%.

Vasodilator responses following individual bursts were already seen at a stage when there was no electrodermal activity (Fig. 6*A* and *C*; observations in five out of seven subjects studied). Once the electrodermal activity had begun, there was no evidence that any particular type of burst caused vasodilatation without a skin resistance response. This was the case both in periods with individual bursts or groups of bursts followed by vasodilator responses (not illustrated; observations in

Fig. 6. Examples obtained during body heating of the relation between sympathetic activity in the supraorbital nerve (bottom trace), blood flow in the forehead (middle trace) and skin resistance changes in the forehead (upper trace, not shown in *B*). All sympathetic activity was heat-induced and occurred in relaxed subjects. *A*, recordings obtained at 36 °C, showing that a large sympathetic burst was followed by a rise in blood flow. *B*, averaged traces illustrating the time course of the vasodilator response, obtained for the same subject by triggering on thirty-five bursts. *C*, in the same subject a period with more intense burst activity at 40 °C was accompanied by a rise in blood flow. *D*, a rapid rise in blood flow at 44 °C coinciding with an increase in sympathetic activity. Note that the bursts were also followed by skin resistance responses. *E*, recordings obtained in another subject at 24 °C (left) and 45 °C (right), illustrating burst activity followed by skin resistance responses but without any increase in mean blood flow.

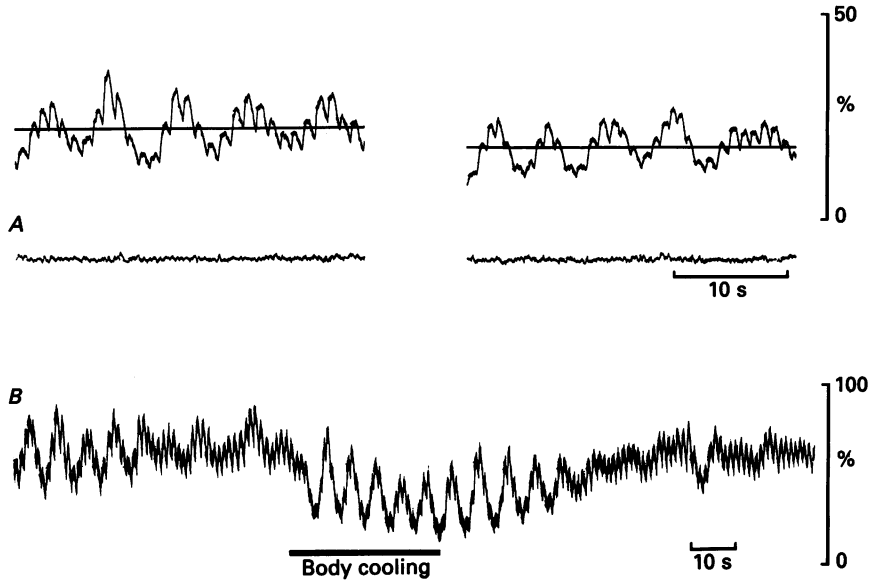

Fig. 7. Effects of body cooling on forehead blood flow. *A*, recordings obtained at 24 °C (left) and 11 °C (right), illustrating a reduction in mean blood flow (straight line) despite a lack of sympathetic bursts in the supraorbital nerve recordings under both conditions. *B*, reduction in blood flow and enhanced rhythmical blood flow variations induced by a period of body cooling starting at 19 °C. Attempts to obtain a nerve recording in this subject failed.

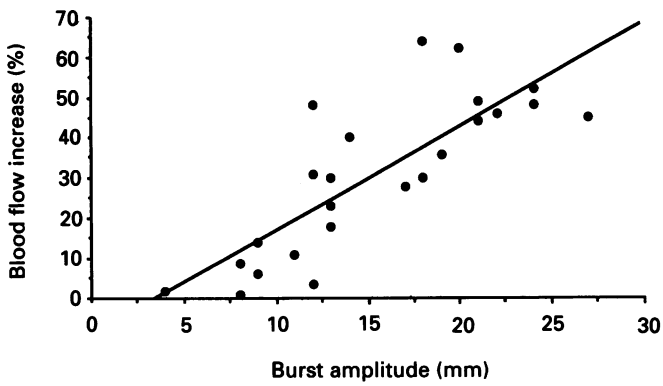

Fig. 8. Correlation in one subject between the amplitude of arousal-evoked sympathetic bursts recorded from the supraorbital nerve and the magnitude of the corresponding increase in forehead blood flow. Responses obtained at room temperature, during body cooling and in the initial phase of body heating were included. The linear regression line is shown ($r = 0{\cdot}80$, $P < 0{\cdot}001$).

four subjects), and in periods with more intense burst activity and a rapid rise in blood flow (Fig. 6*D*; observations in five subjects).

However, as shown in Fig. 6*E* (and observed also in another subject), burst activity during body heating occurred in some cases without any immediate signs of

vasodilatation. In the subject illustrated, intensified sympathetic activity associated with a rapid rise in blood flow was noted after further heating.

The subjects with arousal-evoked vasodilatation at room temperature showed responses of about the same magnitude during the initial phase of heating, but at high blood flow levels induced by prolonged heating, the relative increases in blood flow evoked by arousal stimuli were reduced.

Recordings during body cooling

No signs of background burst activity were observed during body cooling in the eight subjects studied, although the microelectrode was in a good sympathetic recording site (as evidenced by the responses to arousal stimuli) and there were plethysmographic signs of a strong vasoconstrictor outflow to the hand (Fig. 1*D*).

During cooling from room temperature, the mean blood flow decreased in all ten subjects studied, the relative reduction ranging from 9 to 60% ($30 \pm 5\%$; $P < 0.01$). This occurred despite the absence, both at room temperature and during cooling, of any background burst activity (Fig. 7*A*; simultaneous blood flow and nerve recordings in four subjects). When the cooling fan was restarted at a low temperature after having been switched off for a few minutes, the blood flow decreased rapidly and the blood flow oscillations were enhanced (Fig. 7*B*). Averaging of recordings obtained in eight subjects showed that this decrease began after 2·4 s.

As exemplified in Fig. 1*B* and *C*, the amplitude of the arousal-evoked sympathetic response was reduced by cooling ($P < 0.01$ for each of seven subjects except one, for whom $P = 0.06$). The average relative reduction in amplitude was $66 \pm 8\%$. The vasodilator response was also reduced significantly ($P \leqslant 0.01$) by cooling in each of seven subjects studied with several arousal stimuli. The magnitude of the average response was $34 \pm 5\%$ at room temperature and $8 \pm 3\%$ during cooling. As shown in Fig. 8, there was a positive linear correlation between the amplitude of the arousal-evoked sympathetic response and the magnitude of the corresponding vasodilator response ($r = 0.76$, 0·69, 0·68 and 0·54 in the other subjects studied; $P < 0.001$ in all except one for whom $P = 0.01$). In two subjects, moderate cooling induced an initial vasoconstrictor response, which was not observed at room temperature. The skin resistance responses were abolished by strong cooling.

DISCUSSION

For other skin nerves in man, it is well established that bursts of the type recorded from the supraorbital nerve consist of impulses in postganglionic sympathetic C fibres (Hagbarth *et al.* 1972; Wallin & Fagius, 1988). As expected from the difference in conduction distance, the sympathetic reflex latency found for the supraorbital nerve was shorter than those reported for nerves of the extremities (Fagius & Wallin, 1980). As in the case of skin and muscle sympathetic activity in all human nerves investigated (Wallin & Fagius, 1988), the present neural activity occurred as well-defined bursts. The possibility of a weak resting discharge between the bursts cannot be ruled out, but in nerves of the extremities such activity is not pronounced (Hallin & Torebjörk, 1974). Since a sympathetic multi-unit recording is not selective for any particular type of sympathetic fibre in other skin nerves (Hagbarth *et al.* 1972; Bini

et al. 1980*a*, *b*), it seems justified to consider the present recordings as representative of the sympathetic fibres within the supraorbital nerve.

There is no reason to doubt that the neural bursts which were followed by a decrease in forehead skin resistance represented impulses in sudomotor fibres (cf. Lader & Montagu, 1962; Hagbarth *et al.* 1972; Bini *et al.* 1980*a*, *b*). Furthermore, the present findings indicate that sudomotor bursts that are not followed by any detectable electrodermal activity may occur. Since skin resistance responses were induced by repetitive burst activity, their initial absence may be explained by the lack of background burst activity at room temperature. On electrical stimulation of sudomotor fibres in a peripheral nerve which had been cut or blocked proximally, an analogous potentiation of the electrodermal response by repeated stimuli was observed in the cat (Lang, 1967) and in man (Wallin, Blumberg & Hynninen, 1983).

Evidence for active sympathetic vasodilatation in the forehead

The oscillations in the forehead blood flow were not caused by any sympathetic outflow in the supraorbital nerve. They are known to occur asynchronously in different parts of the forehead and the underlying mechanism is probably rhythmical active vasomotion influenced by local factors (Salerud, Tenland, Nilsson & Öberg, 1983).

Two main observations in the present study indicate that the increase in forehead blood flow during body heating is achieved by active sympathetic vasodilatation. First, individual sympathetic bursts were followed by a vasodilator response. Secondly, rapid increases in blood flow coincided with a marked increase in sympathetic activity. The findings are in accordance with the observed effects of supraorbital nerve blocks on forehead vasodilatation during body heating (Fox *et al.* 1962), and with observations in patients with a unilateral lesion in the sympathetic pathway to the face (Drummond & Lance, 1987).

In the forearm, sweating and vasodilatation occur simultaneously during body heating (Roddie, Sheperd & Whelan, 1957), but it is not known whether active sympathetic vasodilatation in human skin is mediated by sudomotor neurones or by separate vasodilator neurones (see Rowell, 1983). In the cat, there are data suggesting the existence of postganglionic sympathetic vasodilator neurones (Bell, Jänig, Kummel & Xu, 1985). The present results indicate that the vasodilator fibres to the forehead, if there are any separate such fibres, fire in synchrony with the sudomotor fibres. This is not unlikely since sympathetic vasoconstrictor and sudomotor fibres often discharge synchronously in other human skin nerves (Bini *et al.* 1980*a*, *b*). In addition, the results show that a sudomotor outflow can occur without any immediate rise in forehead blood flow, but this does not rule out the possibility that the vasodilatation is sudomotor-mediated.

The arousal-evoked vasodilatation is probably caused by a similar sympathetic mechanism, as judged from its time course and the positive correlation between its magnitude and the amplitude of the sympathetic response. However, other vasomotor mechanisms must be involved, since vasoconstriction or absence of vasomotor responses was occasionally observed. In the glabrous skin of fingers and toes, the arousal-evoked vasoconstriction seen at room temperature or in a warm environment is reverted to a vasodilatation by body cooling (Oberle, Elam, Karlsson

& Wallin, 1988). Since the forehead vasodilatation was reduced by cooling, a different vasodilator mechanism may be responsible. A neurally mediated reflex vasodilatation of a presumably sympathetic nature has been demonstrated in hairy skin of the human foot (Blumberg & Wallin, 1987).

Mental stress or a feeling of embarrassment evoked a sympathetic outflow in the supraorbital nerve which was consistently accompanied by forehead vasodilatation. Since the time course was similar to that after heat-induced sympathetic activity, the observations add further support to the conclusion that emotional blushing is mediated by the sympathetic nervous system (Drummond & Lance, 1987).

Absence of vasoconstrictor activity in the supraorbital nerve

The lack of vasoconstrictor bursts in the supraorbital nerve recordings represents a clear difference compared with skin fascicles of the human median and peroneal nerves (Bini *et al.* 1980*a*, *b*). In conformity with the present findings, vasoconstrictor tone at room temperature is absent in nerves supplying hairy skin of the human forearm and hand (Bini *et al.* 1980*b*).

Despite the lack of detectable background burst activity in the supraorbital nerve during body cooling, there were signs of forehead vasoconstriction which was neurally mediated, as judged from its short onset latency. Inhibition of vasodilator tone might be contributory, but according to the present recordings such activity is usually absent at room temperature. Another possible explanation is that there may be vasoconstrictor fibres to the forehead that do not run in the supraorbital nerve. Since sympathetic fibres run along the internal carotid artery before passing to the ophthalmic nerve (Parkinson, Johnston & Chaudhuri, 1978), it is conceivable that some of them accompany the ophthalmic artery to reach the forehead with its terminal branch.

The high rate of success with which sympathetic activity was recorded in the present study underlines the significance of our previous failures, with the same technique, to detect sympathetic activity in the human infraorbital and facial nerves (Nordin, Hagbarth, Thomander & Wallin, 1986; Nordin & Thomander, 1989). By exclusion, these negative findings suggest that all sympathetic fibres reach the infraorbital nerve territory by joining branches of the external carotid artery (cf. Gardner, 1943).

The relatively weak vasoconstriction in the forehead, as observed in this study, may contribute to the great heat loss from the head in a cold environment (Froese & Burton, 1957). Other parts of the face (ear, lip, nose) probably have more pronounced vasoconstrictor innervation (Blair *et al.* 1961; Fox *et al.* 1962).

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