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Activation and Inhibition of Muscle and Cutaneous Postganglionic Neurones to Hindlimb during Hypothalamically Induced Vasoconstriction and Atropine-Sensitive Vasodilation

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Summary. 1. Discharge patterns in postganglionic neurones to muscle and to hairy skin of the hindlimb of chloralose anaesthetized cats were investigated during electrical hypothalamic stimulation which induced either vasoconstriction or atropine sensitive vasodilation in the skeletal muscle.

2. Spontaneously active postganglionic neurones to muscle were activated both during hypothalamically induced vasoconstriction and active vasodilation. Stimulation of the hypothalamic vasodilator area induced mostly a sequence of activation-depression-activation in these neurones. Stimulation of cutaneous Group IV afferents elicited reflexes in these neurones; repetitive high frequency stimulation of large diameter afferents in the vago-depressor nerve produced depression of spontaneous activity followed by a post-inhibitory excitation. The characteristics of these neurones fit those that would be expected of vasoconstrictors.

3. Normally inactive postganglionic neurones to skeletal muscle could only be activated during hypothalamically induced atropine sensitive vasodilation. These neurones exhibit no reflexes on somatic stimulation. The axons of these neurones conduct faster than those of the spontaneously active postganglionic neurones. It is likely that they are cholinergic vasodilator neurones.

4. Most of the cutaneous postganglionic neurones to hairy skin were activated during stimulation of both the hypothalamic vasoconstrictor and the vasodilator areas. These neurones have the characteristics of cutaneous vasoconstrictor neurones. Part of the cutaneous not spontaneously active postganglionic neurones could neither be activated from the hypothalamus nor by somatic stimuli.

Key words: Vasoconstrictors – Vasodilators – Muscle – Hypothalamic stimulation – Atropine-sensitive vasodilation – Single unit analysis – Cat.

INTRODUCTION

Electrical stimulation of the hypothalamic defence area in anaesthetized cats induces an increased blood flow through skeletal muscle, together with an increased cardiac output and reduction of blood flow through the skin and intestines (see Hilton, 1965; Lisander, 1970). This pattern of cardiovascular response is part of the defence reaction and is thought to represent an "anticipatory" visceromotor reaction which prepares the organism to meet challenges from the environment (Bard, 1960; Abrahams *et al.*, 1964). The autonomic responses are generated by a widespread sympathetic discharge. An important component of these responses, at least in the cat, is thought to be activation of cholinergic sympathetic postganglionic neurones to the vascular bed of skeletal muscle (Eliasson *et al.*, 1951; Abrahams *et al.*, 1960) by which the resistance vessels are actively dilated. The existence of these sympathetic neurones and their pattern of response to stimulation of the hypothalamic defence area has been inferred indirectly on the basis of measurements of increased blood flow through skeletal muscle which can be blocked by atropine.

In the present paper, we report experiments which are based on the same considerations as those of Folkow and Gernandt (1952). Activity in single postganglionic neurones to muscle and skin, and blood

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flow through the hindlimbs were recorded simultaneously during hypothalamic stimulation. Atropine sensitive vasodilation was induced by electrical stimulation of the hypothalamic defence area, and muscle vasoconstriction by stimulation of an area rostral to the vasodilator area. Using this technique, the sympathetic postganglionic neurones to skeletal muscle could be classified into 2 types, one with the characteristics of vasoconstrictor neurones and one with those of vasodilator neurones. The discharge pattern of both types of neurones has been investigated during and after hypothalamically induced vasoconstriction and vasodilation in the hindlimbs, after somatic sensory stimuli, and after stimulation of the vago-depressor nerve. In addition, the effect of hypothalamic stimulation on the discharge patterns of cutaneous postganglionic neurones to hairy skin has been investigated. Some of the results have been communicated in preliminary form (Horeyseck *et al.*, 1972a, b; 1974).

METHODS

The experiments were performed on 17 adult cats (body weight 2.5–4.5 kg) anaesthetized with α-chloralose (50–70 mg/kg i.p.). All animals were artificially ventilated *via* a tracheal cannula and immobilized by i.v. injections of gallamine triethiodid (Flaxedil). The end expiratory CO_2 was adjusted to 3–4%. The rectal temperature was kept close to 38° C.

The blood pressure was recorded continuously from the right carotid artery by means of a Statham transducer. Blood flow was measured 1 cm proximal to the aortic bifurcation using an electromagnetic flow probe. About 80% of this blood flow represents the blood flow through the skeletal muscle (Mellander and Johansson, 1968). An increase of blood flow through the lumbar aorta induced by stimulation of the hypothalamic defence area should be due solely to the atropine sensitive vasodilation which occurs in skeletal muscle since the cutaneous vascular bed is concomitantly constricted (Eliasson *et al.*, 1951; Abrahams *et al.*, 1960). The increase of blood flow through the skeletal musculature of the hindlimbs would actually be larger than that measured through the lumbar aorta, because of the reduction in blood flow to the skin. The total peripheral vascular resistance (R) in the hindlimbs has been calculated as the ratio of mean blood pressure to blood flow.

Recordings from single muscle postganglionic fibres in the left lateral gastrocnemius nerve (LG) and single cutaneous postganglionic fibres in the left superficial peroneal nerve (SP) were made on teased preparations, as described by Horeyseck and Jänig (1974a, b). In order to identify these fibres as postganglionic the left lumbar sympathetic trunk (LST) was dissected at the level of lumbar L_4, L_5 or L_6, placed on a pair of platinum electrodes, and stimulated with single shocks of 2–5 V at pulse durations of 0.2 ms. For eliciting reflexes in the postganglionic neurones, the left sural nerve (SU) was dissected free at two locations and placed on two pairs of platinum electrodes for stimulation and for recording. The nerve was stimulated repetitively with 4 shocks at 30 cps and strengths which were maximal for the Group IV fibres. The stimulus strengths were 10–20 V with pulse durations of 0.5 ms. The left vago-depressor nerve was cut, placed centrally on a pair of platinum electrodes, and stimulated repetitively with 10 shocks at 100 cps. The stimulus strengths were 0.25–0.5 V with pulse durations of 0.2 ms; thus only large diameter afferents were excited.

For electrical stimulation of the hypothalamus, the head of the animal was fixed in a stereotaxic head holder and two to three concentric electrodes (diameter 200 μ; resistence 3 kΩ) were implanted into the left ventral hypothalamus. Maximal atropine sensitive vasodilation was elicited from the defence area of different animals, which is between frontal planes 8–13, lateral planes 0.5–2, and vertical level 4–6. Vasoconstriction in the hindlimbs together with increased blood pressure was usually induced from a hypothalamic area 2 mm rostral to this vasodilator area. For convenience the area from which vasodilation was elicited will be called the "vasodilator area" and the area from which vasoconstriction was elicited will be called "vasoconstrictor area". The corresponding stimuli will be called "hypodilation" and "hypoconstriction". Both areas were stimulated for 5–50 s at frequencies of 80–100 cps. The stimulus strengths were 3–10 V with pulse durations of 1 ms. Maximal vasodilation was usually produced with stimulation at 5 V and 80 cps for 5–8 s. These stimulus parameters had previously been reported to be optimal by Lindgren (1955). The minimum interval between the hypothalamic stimuli was 6 min.

During each experiment, a check was made to ensure that hypothalamically induced vasodilation could be abolished by atropine (0.5 mg/kg i.v.). After the experiments the positions of the tips of the electrodes in the hypothalamus were marked by electrical microcoagulation and the animals were perfused with formal-saline (10%). The whole brain was removed and sectioned with a razor blade until the electrode track and the microcoagulation were visible. The brain surface was then stained superficially with cresyl violet and photographed.

RESULTS

A. Spontaneously Active Neurones in the Postganglionic Supply to Skeletal Muscle

Most sympathetic postganglionic neurones to the lateral gastrocnemius muscle were spontaneously active and displayed reflex responses during somatic sensory stimulation (Koizumi and Sato, 1972; Horeyseck and Jänig, 1974a, b). The discharge pattern of a neurone of this type is illustrated by the large action potential in the experiment of Figure 1. The filament recorded from contained a second unmyelinated axon which was probably also of postganglionic origin (small action potential). The spontaneous activity of the neurone exhibited a marked rhythmicity which was synchronous with the frequency of the artificial respiration (Fig. 1B). Repetitive stimulation of the vago-depressor nerve caused a reduction of the spontaneous activity in the neurone for about half a second which was followed by a rebound excitation (Fig. 1C). Repetitive stimulation of the sural nerve with maximal strength for all afferent fibres induced reflex discharges in the neurone with a latency of 500–600 ms (Fig. 1D). These reflex discharges were followed and probably preceded by a depression of the spontaneous activity. These results are in accord with those of muscle postganglionic neurones observed in studies of Koizumi and Sato (1972) and Horeyseck and Jänig (1974a, b).

The behaviour of this neurone to electrical stimulation of a hypothalamic "vasoconstrictor" area and

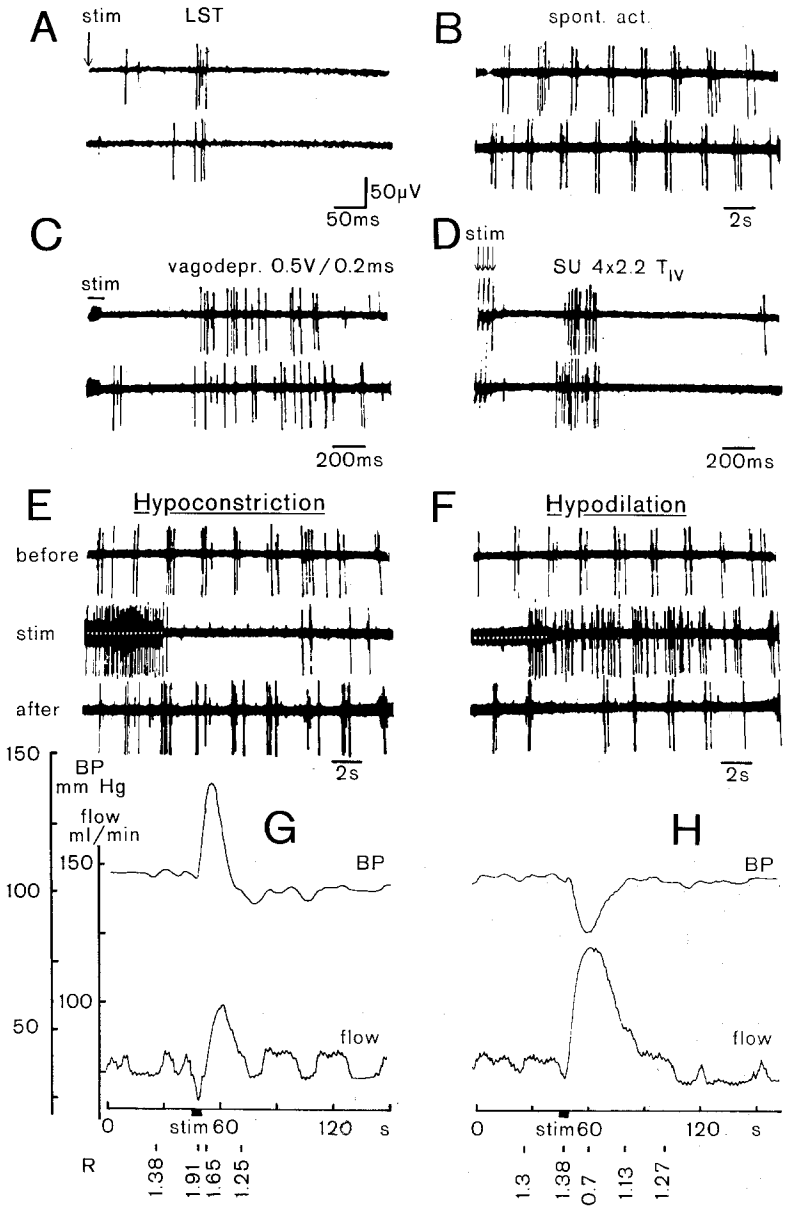

Fig. 1 A–H
Discharge pattern in a spontaneously active muscle postganglionic neurone. The filament recorded from, contained two spontaneously active postganglionic neurones (large and small action potentials). (A) Stimulation of the preganglionic axons, in the lumbar sympathetic trunk at L_4/L_5 with 5 V pulses of 0.2 ms duration. (B) Spontaneous activity, the axon with the large action potential discharged with 1.2 imp/s. (C) Stimulation of the vago-depressor nerve with 10 stimuli at 100 cps, and a stimulus strength of 0.5 V (0.2 ms pulses). 5 superimposed traces. (D) Stimulation of the sural (*SU*) nerve with 4 shocks at 30 cps, the stimulus strength was 2.2 times the threshold of the Group *IV* fibres (T_{IV}; 20 V pulses of 0.5 ms duration). (E–H) Bipolar stimulation of the hypothalamus between F_8 and F_{10} (V_6, L_2) and F_{10} and F_{12} (V_6, L_2) respectively, with 8 V at 100 cps for 5 s (broken lines) eliciting vasoconstriction (Hypoconstriction) or vasodilation (Hypodilation) in the hindlimbs. E and F show the neuronal activity before, during, and after stimulation. The time delay between the end of the second traces and the beginning of the third traces was about 1 s or less. *BP* Blood pressure; *flow* blood flow through the hindlimbs measured in the descending aorta; *R* resistance to flow of the vascular bed of the hindlimbs

of the hypothalamic "vasodilator" area is illustrated in Figures 1 E, G and Figures 1 F, H respectively. Stimulation of the constrictor area (hypoconstriction in Figure 1 E) for 5 s led to an increase of blood pressure and a decrease of flow through the hindlimbs resulting from an increase in peripheral vascular resistance R (Fig. 1 G). Stimulation of the "vasodilator" area (hypodilation in Figure 1 F) led to a decrease in blood pressure, but the reduction of resistance of the vascular bed was sufficient to result in an increased blood flow (Fig. 1 H).

During stimulation of the hypothalamic vasoconstrictor area the neurone was vigorously activated (Figure 1 E, trace 2); at the end of the stimulus this activation was followed by a depression of the spontaneous activity (Figure 1 E, trace 2). During electrical stimulation of the hypothalamic vasodilator area the activity of this neurone was depressed at the beginning of stimulation and activated at the end. After the end of the stimulus the activation continued for about 10 s (Figure 1 F, second trace).

The temporal pattern of activation of the spontaneously active postganglionic neurones during hypothalamic stimulation is further exemplified in Figure 2. Hypothalamic stimulation which induced vasoconstriction in the hindlimbs invariably activated these neurones throughout the period of stimulation. This activation was always followed by a depression of the discharge after the stimulation (Fig. 2A). Hypothalamic stimulation which produced vasodilation

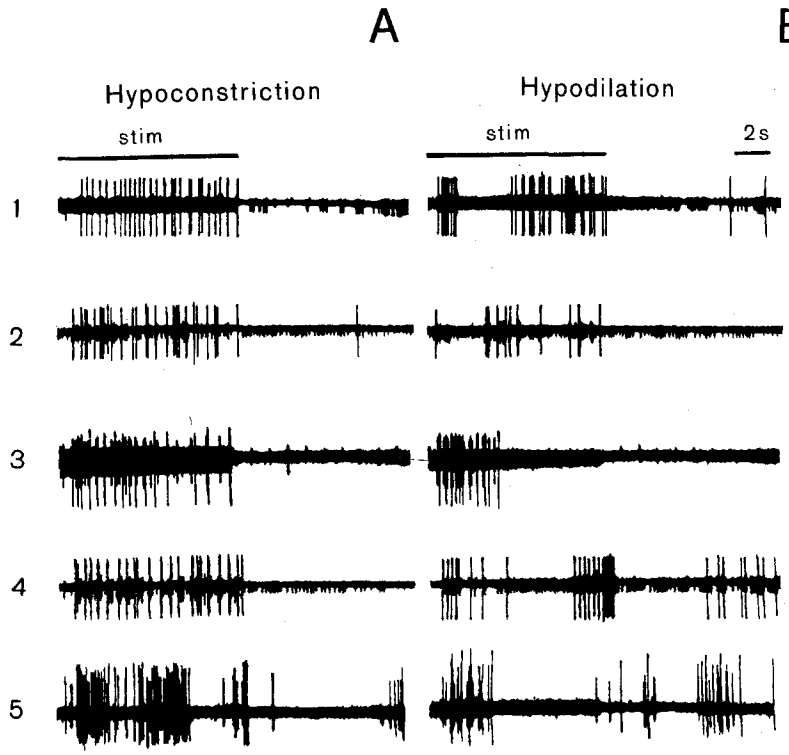

Fig. 2 A and B
Discharges in spontaneously active postganglionic neurones to muscle recorded from 5 filaments in 5 different experiments during hypothalamically induced vasoconstriction [Hypoconstriction in (A)] and vasodilation [Hypodilation in (B)] in the hindlimbs. The small action potentials in filaments 1, 2, and 4 are probably produced by axons from γ-motoneurones

in the hindlimbs led to discharge patterns which varied from neurone to neurone (Fig. 2B). Most neurones were activated at the beginning of the stimulation usually for 1–4 s. This was followed by a suppression of discharge which lasted either throughout stimulation or was followed after 4–6 s by an excitation which increased until the end of stimulation. The pattern of discharge was highly variable (Fig. 2B).

In all the activity of 104 spontaneously active postganglionic neurones supplying skeletal muscle was investigated. All these neurones exhibited response patterns similar to those illustrated in Figures 1 and 2 (Table 1, column 2).

B. Non-Spontaneously Active Postganglionic Neurones Supplying Skeletal Muscle

About 10% of the postganglionic neurones dissected from the nerve to the lateral gastrocnemius muscle were not spontaneously active (see also Koizumi and Sato, 1972). Figure 3 illustrates a typical experiment on such a neurone. Stimulation of the preganglionic axons in the lumbar sympathetic trunk at L_4/L_5 initiated 2–3 discharges in this neurone (Fig. 3A), suggesting that this neurone represented a postganglionic sympathetic fibre. Repetitive stimulation of the vagodepressor nerve and of the sural (SU) nerve with strengths which were maximal for the unmyelinated,

Table 1. Total number of cutaneous and muscle postganglionic neurones investigated. + activation, − depression of spontaneous activity, ϕ no effect

Postganglionic neurones to					
Muscle			Skin		
1	2	3	4	5	6
Spont. act	yes	no	yes	no	no
Number of neurones	104	11	25	5	7
Somatic reflexes	+ −	ϕ	+ −	+	ϕ
Stim. vago-depressor nerve	− +	ϕ	− or − +	ϕ	ϕ
Hypoconstriction	+	ϕ	+	+	ϕ
Hypodilation (atropine sensitive)	+ − + or − + or + −	+	+	+	ϕ

Group IV afferents (Fig. 3B) had no effect on this neurone. During a hypothalamically induced vasoconstriction in the hindlimbs (increase of peripheral resistance R; Figure 3G) this neurone was only weakly activated (Figure 3C, trace 2; Figure 3E). But during vasodilation in the hindlimbs, induced from the hypothalamic vasodilator area (decrease of peripheral resistance R; Figure 3H), this neurone was vigorously

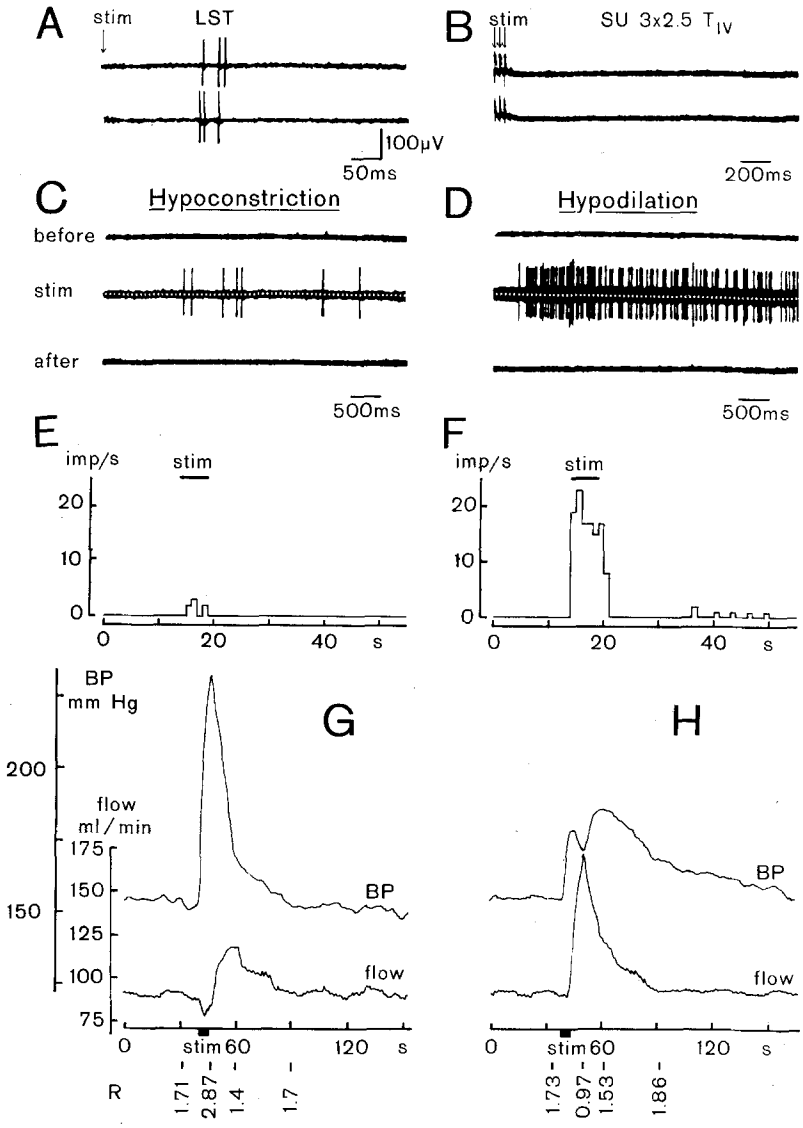

Fig. 3 A–H
Discharge pattern in a normally silent postganglionic neurone supplying muscle. (A, B) see Figures 1 (A, D, C, E, G) (Hypoconstriction) and (D, F, H) (Hypodilation) see Figures 1 (E, G and F, H) respectively. The stimulation periods in (C) and (D) are indicated by the broken lines. The time delay between the end of the second traces and the beginning of the third traces in (C) and (D) was about 1 s or less. The histograms in (E, F) show the activation of the neurone during vasoconstriction and vasodilation. The hypothalamus was stimulated with concentric electrodes at F_{12} (V_5, L_2) with 10 V at 100 cps for 5 s (Hypoconstriction) and F_8 (V_5, L_2) with 10 V at 100 cps for 5 s (Hypodilation)

activated (Figure 3D, trace 2; Figure 3F). This activation outlasted the stimulus for 2 s. With prolonged stimulation of the vasodilator area for 20 s the activity in the neurone slowly decreased (Figures 4A, D, traces 2; Figures 4B, E). After this prolonged hypothalamic stimulation, the neurone remained active with a low frequency discharge for several min (Figures 4A, D, last traces).

After i.v. injection of atropine, which abolished the active vasodilation in the hindlimb musculature (Fig. 4F) and revealed a small vasoconstriction previously masked by the vasodilation (see increase of peripheral resistance R in Figure 4F), the postganglionic neurone was still activated by stimulation of the hypothalamic vasodilator area (Fig. 4D, E). This activation was somewhat smaller than that before the application of atropine, but otherwise similar in its overall pattern. Hypothalamic stimulation at a higher intensity which increased the activation of the neurone so that it was equal to that before application of atropine, did not elicit an active vasodilation in the hindlimbs.

Eleven normally silent postganglionic neurones were identified from the nerve to the lateral gastrocnemius muscle. Without exception these neurones were activated during a hypothalamically induced active vasodilation in the hindlimbs, and either unaffected or only weakly activated during a hypothalamically induced vasoconstriction. All eleven neurones were uneffected by somatic stimulation (Table 1, column 3).

It was striking that the action potentials produced by the axons of these neurones were always larger than the action potentials produced by the axons of

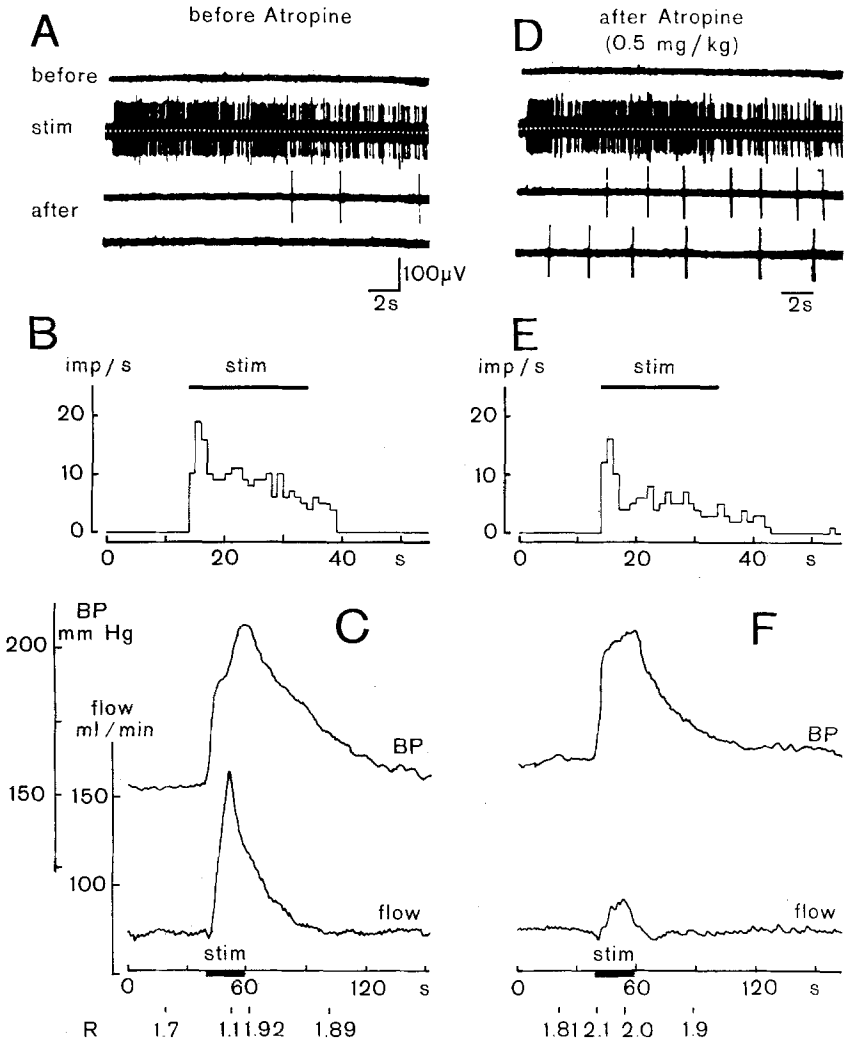

Fig. 4 A–F
Activation of a normally silent postganglionic neurone to muscle during stimulation of the hypothalamic defence area before (A, B) and after (D, E) i.v. application of 0.5 mg/kg atropine. Same neurone as in Figure 3. For further details see Figures 1 and 3

the spontaneously active postganglionic neurones when recorded from the same nerve filament. Furthermore, the latencies of the action potentials in these neurones after lumbar sympathetic trunk stimulation were significantly shorter than those in the spontaneously active neurones (Fig. 5A). This is shown for the axons of both types of neurones in Figures 5B, C. Although it cannot be explicitly excluded it is assumed that the neurone sample is not biased in favour of the fastest conducting axons because of the dissection method. The difference of the mean latencies of both classes of neurones is statistically highly significant ($P < 0.001$, t-test). From the latencies (Fig. 5B, C) the approximate conduction velocities of the postganglionic axons can be estimated. They differ by about 20% and are around 0.65 m/s for the spontaneously active neurones, and 0.8 m/s for those not spontaneously active, if some 3–5 ms are allowed for conduction in preganglionic fibres and for ganglionic transmission.

C. Postganglionic Neurones Supplying Hairy Skin

About 80% of the sympathetic postganglionic neurones to hairy skin are spontaneously active and disclose excitatory and inhibitory reflexes on somatic stimulation whereas the other 20% are not spontaneously active and are only partially activated by repetitive stimulation of cutaneous Group IV afferent fibres, or by noxious stimulation of the skin (Jänig *et al.*, 1972; Horeyseck and Jänig, 1974a, b). Postganglionic neurones from the superficial peroneal nerve were investigated in the same way as the muscle postganglionic neurones during hypothalamic stimulation. This is best illustrated by reference to Figure 6. The filament recorded from contained one axon producing a large action potential and two or three axons producing small action potentials (Fig. 6A). The spontaneous activity of the axon with the large action potential was 3.1 imp/s (Fig. 6B). Stimulation of the vago-depressor nerve depressed the spontaneous ac-

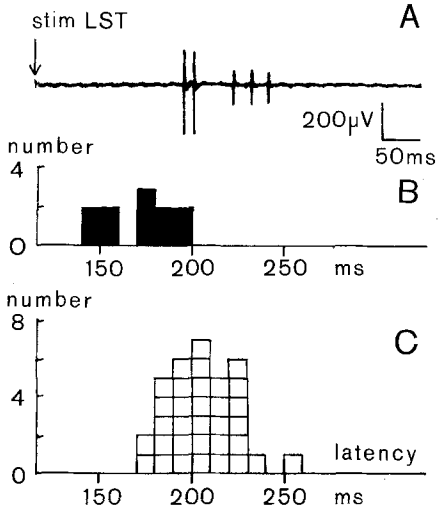

Fig. 5 A–C. Latencies of earliest discharges in spontaneously (□) and normally silent muscle postganglionic neurones (■) after stimulation of the lumbar sympathetic trunk. (A) Large action potential: silent postganglionic neurone. Small action potential: spontaneously active postganglionic neurone. (B) Latencies in normally inactive postganglionic neurones. Mean ± SD = 172 ± 18.5 ms. (C) Latencies in spontaneously active postganglionic neurones. All neurones are from experiments in which at least one not spontaneously active postganglionic neurone to skeletal muscle was found. Mean ± SD = 208 ± 22.5 ms

tivity in all neurones (Fig. 6C), repetitive stimulation of the sural (SU) nerve, with a stimulus strength which was maximal for the Group IV axons, elicited reflex discharges with a latency of 600–1000 ms (Fig. 6D). Stimulation of the hypothalamus which elicited either a vasoconstriction (Fig. 6G) or a vasodilation in the hindlimbs (Fig. 6H) both activated the neurones (Figures 6E, F, second traces). The hypothalamically induced vasoconstriction was followed by a large vasodilation (decrease of peripheral vascular resistance R), thus the response in Figure 6G was really a biphasic one. The activation was followed by a depression of the spontaneous activity for periods of 5–10 s. During stimulation of the hypothalamic vasodilator area the activation of the neurones was very uniform and regular (Figure 6F, second trace).

A total of 25 spontaneously active and 12 normally inactive cutaneous postganglionic neurones were investigated. The spontaneously active postganglionic neurones disclosed reflex patterns as shown in Figure 6 (see Table 1, column 4). Five normally quiescent neurones, which could be activated by somatic stimuli, were also activated by stimulation of the hypothalamic vasoconstrictor and vasodilator areas (Table 1, column 5). Seven otherwise inactive neurones which were not activated by somatic stimuli were uneffected by the hypothalamic stimulation (Table 1, column 6).

DISCUSSION

Sympathetic Outflow to the Skeletal Muscle

The sympathetic postganglionic outflow to the lateral gastrocnemius muscle consists, most probably, of only two types of postganglionic neurones: vasoconstrictors and vasodilators. The existence of any other type of postganglionic neurone to the skeletal muscle in any considerable number – although it cannot be excluded – is unlikely. The spontaneously active postganglionic neurones were inhibited after stimulation of the large diameter afferents in the vago-depressor nerve; this depression was followed by a postinhibitory excitation. The depression of the spontaneous activity was most likely caused by the excitation of the large diameter afferents from pressoreceptors, whereas the excitation may have been brought about by the excitation of large diameter afferents from the lung. Furthermore, the postganglionic neurones exhibited reflex responses to somatic stimulation and were activated during a hypothalamically induced vasoconstriction in the hindlimbs (Table 1, column 2). These characteristics fit those that would be expected of vasoconstrictor neurones.

The normally inactive neurones supplying skeletal muscle could only be activated during a hypothalamically induced, active atropine-sensitive vasodilation. They were either not activated or only weakly activated during a hypothalamically induced vasoconstriction. They possess the characteristics of the cholinergic sympathetic vasodilator neurones to skeletal muscle, as defined indirectly from investigations of the regulation of blood flow through the skeletal muscle (see Table 1, column 3). According to previous studies (for ref. see Lisander, 1970) vasodilator neurones should be activated from the hypothalamic defence area and not be spontaneously active. Further, they should not take part in the baroreceptor reflex and should be cholinergic. Therefore we assume that these non-spontaneously active postganglionic neurones to skeletal muscle have a vasodilator function.

These inactive postganglionic neurones comprised about 10% in the present sample. According to Bolme and Fuxe (1969) the cholinergic vasodilator neurones innervate only arteriolar resistance vessels with diameters of 30–100 μ, an innervation pattern which contrasts with the widespread supply of adrenergic neurones to the vascular bed. If it is correct that these neurones innervate only strategically important sections of the resistance vessels and can control the total flow resistance by depressing the pacemaker activity in these sections, a small number of cholinergic vasodilator neurones could, in fact, be sufficient to override the myogenic tone and to induce an active vasodilation.

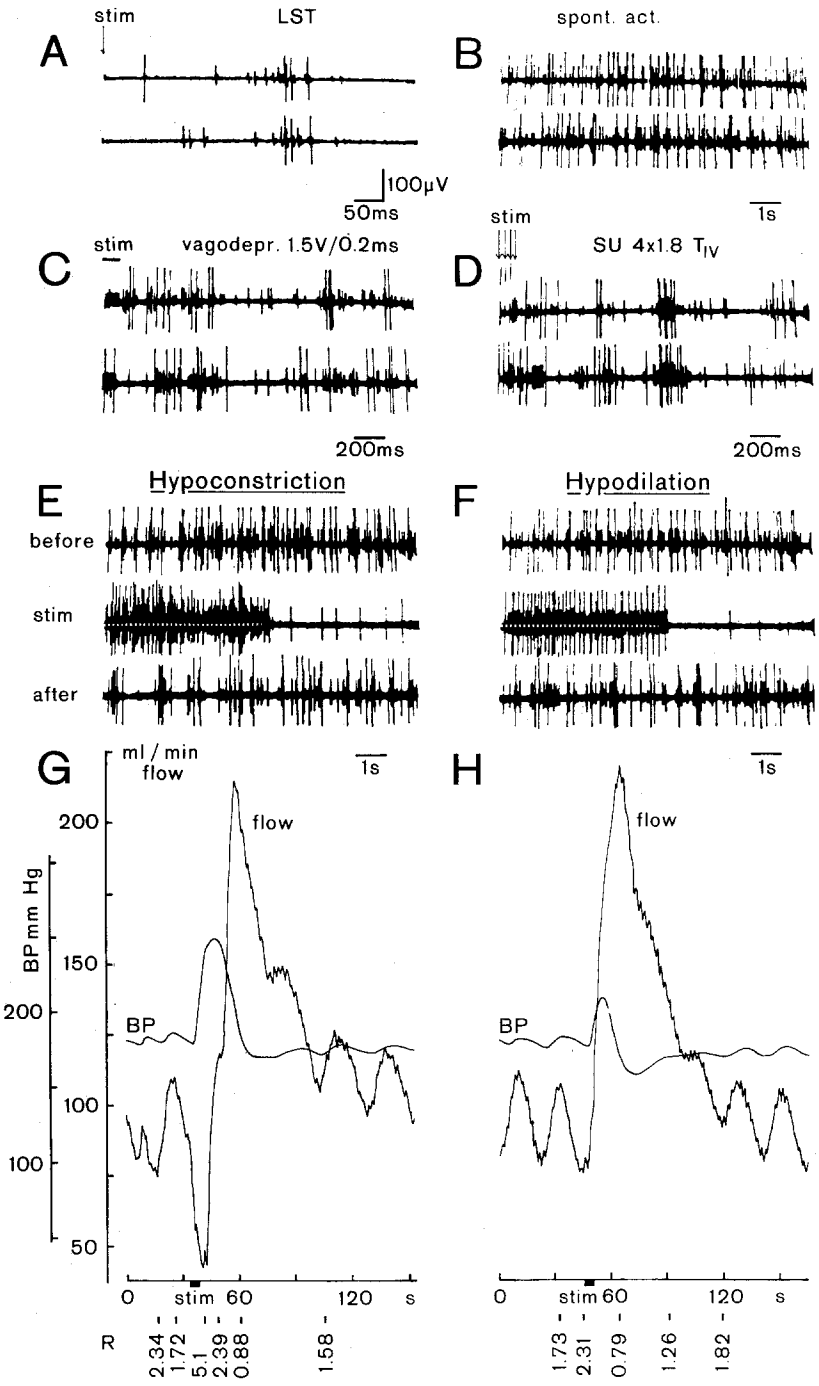

Fig. 6 A–H
Discharge pattern in spontaneously active cutaneous postganglionic neurones supplying hairy skin. The filament recorded from contained one axon producing the large action potential and 2–3 axons producing the small action potentials. For details see Figure 1. The hypothalamus was stimulated bipolarly between F_8 and F_{10} (V_5, L_2) with 6 V at 100 cps for 5 s (Hypoconstriction) and between F_{10} and F_{12} (V_5, L_2) with 5 V at 100 cps for 5 s (Hypodilation)

Conceptually, it is somewhat difficult to understand that the normally silent postganglionic neurones cannot be activated by somatic stimulation. If they are primarily activated from the hypothalamic defence area as vasodilators they would be expected to be activated by somatic noxious and non-noxious stimulation (Abrahams *et al.*, 1960). However, this failure is probably due to the use of chloralose anaesthesia, which is known to suppress such reflex response (Abrahams *et al.*, 1960).

Sympathetic Outflow Supplying Hairy Skin

The sample of cutaneous postganglionic fibres from the superficial personeal nerve investigated in the present paper most probably contains no sudomotor fibres

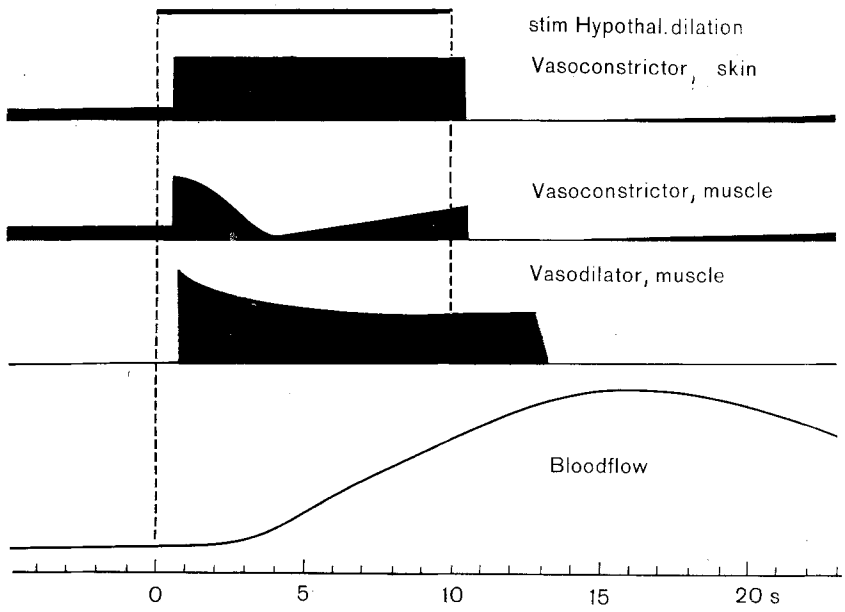

Fig. 7
Schematic diagram on the temporal relation between aortic blood flow, activation of the cutaneous postganglionic neurones and of the spontaneously and normally inactive muscle postganglionic neurones during stimulation of the hypothalamic defence area, eliciting active vasodilation. The diagram is based on the data from 10 spontaneously active muscle (vasoconstrictor) neurones analyzed in 10 experiments, 10 normally silent muscle (vasodilator) neurones analyzed in 6 experiments and 10 cutaneous (vasoconstrictor) neurones analyzed in 5 experiments. In all experiments an atropine sensitive vasodilation could be elicited by hypothalamic stimulation

and no pilomotor fibres. Sudomotor fibres are absent, since the portion of the superficial peroneal nerve from which the postganglionic axons were dissected innervates only hairy skin, and since the hairy skin of the cat does not contain sweat glands (Langley, 1891). Pilomotor fibres are absent since repetitive electrical stimulation of the lumbar sympathetic trunk produced no piloerection on the lower hindlegs, but only piloerection on the tail and the back of the cat (Langley and Sherrington, 1891; see also Grosse and Jänig, 1976).

The sample of cutaneous postganglionic fibres investigated consists of three classes (Table 1, columns 4–6). The properties of the spontaneously active neurones fit those of vasoconstrictor neurones: they exhibit reflexes on somatic stimulation, are depressed after vago-depressor stimulation, and are activated during hypothalamically induced vasoconstriction as well as atropine sensitive vasodilation in skeletal muscle. The same is also true for part of the non-spontaneously active postganglionic neurones (Table 1, column 5). Thus it is likely that these neurones also have vasoconstrictor function. Seven of the non-spontaneously active postganglionic neurones to hairy skin were not activated either by somatic stimuli or by any hypothalamic stimulation. It is unlikely that this behaviour was due to partial damage of the lumbar sympathetic trunk (LST) since experience showed that damage to the LST by the present dissection method usually involved all preganglionic fibres. These "silent" postganglionic neurones are possible candidates for vasodilator neurones which are supposed to induce active vasodilation of cutaneous vessels. It may be that these neurones are histaminergic (Beck, 1961, 1964; Graham and Lioy, 1973) and can be activated by warm stimuli applied to the spinal cord (Schönung *et al.*, 1972).

Temporal Relation between Activity in Postganglionic Neurones and Change of Blood Flow during Stimulation of Hypothalamic Vasodilator Area

The temporal relation of the activation of spontaneously active cutaneous and muscle postganglionic neurones, and normally silent muscle postganglionic neurones to active vasodilation in the hindlimbs, during stimulation of the hypothalamic vasodilator pathway, is illustrated schematically in Figure 7. The neurone types were tentatively called vasoconstrictor and vasodilator neurones according to their patterns of activity. The latency of the responses in the vasoconstrictors to stimulation of the hypothalamic defence area was approximately 200 ms and shorter than that in the vasodilator neurones. The mean latency of the blood flow increase was 2.5 s and the mean rise time 11–12 s. Prolongation of the hypothalamic stimulus for more than 10 s did not change this rise time. The functional interpretation of this pattern implies a vasoconstriction in the skin and a vasodilation in the skeletal muscle. The vasodilators and the vasoconstrictors to muscle are to some extent antagonistically activated from the hypothalamic vasodilator pathway. Most vasoconstrictor neurones are initially activated for about 1–3 s, this activation is followed by a period of reduced activity which is lower than the prestimulus activity; after this period the activity

slowly increased till the end of the stimulation. This temporal sequence varies from experiment to experiment and also in the same experiment between individual neurones (*cf.* Fig. 2). It cannot be decided from these investigations whether this complex pattern is an artefact and due to current spread or some other effect of electrical stimulation of the hypothalamus or whether it has some functional meaning. However, when compared with the activation of the vasoconstrictors produced from electrical stimulation of the hypothalamic vasoconstrictor areas and of the cutaneous vasoconstrictors activated from the hypothalamic vasodilator area, it appears that this partial depression of the spontaneous activity is a requirement for the cholinergically induced vasodilation, and indicates therefore some distinct antagonistic neuronal organization between the vasodilator and the vasoconstrictor pathways in the hypothalamus. A similar organization has been proposed by Coote *et al.* (1973).

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