The discharge behaviour of single vasoconstrictor motoneurones in human muscle nerves

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1. The discharge behaviour of fourteen single sympathetic vasoconstrictor efferents was studied using a tungsten microelectrode inserted percutaneously into a motor fascicle of the radial or peroneal nerve in eight awake supine subjects. Units were classified as vasoconstrictor because their firing properties correlated appropriately to changes in cardiac interval and arterial pressure.

2. On average, individual vasoconstrictor units discharged in only 21% of heart beats, with an overall mean frequency of 0·47 Hz. Usually only one spike was generated per cardiac cycle. Calculated from cardiac cycles in which a unit fired from two to seven spikes, the mean within-burst firing rate was 18·8 ± 2·5 Hz (mean ± S.E.M.); but instantaneous frequencies above 50 Hz were occasionally observed.

3. Measured from a defined R-wave of the ECG, the spike onset latency varied over 358 ± 33 ms, suggesting considerable variation of synaptic delays in the baroreflex arc. This latency had a relatively uniform temporal relationship with the burst onset or peak latency, compatible with a fixed recruitment order of individual sympathetic neurones.

4. In view of the low average firing rate of individual units we suggest that the variable instantaneous firing rates may optimize the contractile responses of vascular smooth muscle.

Baroreceptor-induced changes in heart rate and the arteriolar diameter in the skeletal muscle vascular bed contribute to the beat-to-beat control of arterial pressure in the resting state. The changes in vascular resistance are driven by increases or decreases in the activity of vasoconstrictor motoneurones (Jänig, Sundlöf & Wallin, 1983). With the development of microneurographic techniques for recording directly from peripheral nerves in awake subjects (Hagbarth & Vallbo, 1968), much has been learnt about the behaviour of the sympathetic nervous system in humans (for references see Vallbo, Hagbarth, Torebjörk & Wallin, 1979). For technical reasons, however, sympathetic neural activity is generally recorded only as multiunit discharges.

The only study on the discharge behaviour of single postganglionic sympathetic efferents in human subjects was published by Hallin & Torebjörk (1974), who recorded from cutaneous fascicles in the median and peroneal nerves. Their study of eight units demonstrated that these sympathetic motor axons generally present low levels of spontaneous activity at rest and, when activated in a reflexly evoked arousal burst, only fire from one to seven impulses, with maximal instantaneous frequencies of up to 35 Hz. Unfortunately, it was not possible to determine whether the recorded units were vasoconstrictor, vasodilator, sudomotor or pilomotor in function. The aim of the present study was to record from single vasoconstrictor motor axons supplying the skeletal muscle vascular bed in resting subjects, specifically to determine the baroreceptor-mediated influences of arterial pressure on the recruitment and firing properties of the units. The following questions were asked. What is the relationship between arterial pressure or heart rate and the recruitment latency, firing probability and number of spikes generated in a sympathetic burst? How many impulses does a vasoconstrictor motoneurone fire in a burst? What are the firing rates and how regular are they?

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METHODS

General procedures

Data were obtained from twelve experiments performed on six male and two female subjects ranging in age from 21 to 32 years. Each subject provided informed written consent to the procedures, which were conducted under the approval of the human ethics committee of the University of Göteborg. For the majority of experiments, in which recordings were made from the deep branch of the peroneal nerve, the subject lay supine on a bed with the thigh supported in a vacuum cast. However, when the radial nerve was studied, the subject reclined in a dental chair with his or her forearm supported. ECG surface electrodes were applied to the chest, an elastic band incorporating a strain gauge element was strapped around the thorax for recording respiratory movements and the sensor cuff of a servo pulse-plethysmography arterial pressure monitor (Finapres, Ohmeida, Englewood, CO, USA) placed on the middle phalanx of the long finger. A tungsten microelectrode (type 25-10-1 (Frederick Haer Corporation, Brunswick, ME, USA); or laboratory produced) was inserted through the skin, generally after a hole had been made by a hypodermic needle, and directed into a motor fascicle of the radial or common peroneal nerve while delivering weak pulses (0·2 ms, 1 Hz, 0·5–3 V) through the electrode; an uninsulated subcutaneous electrode served as the reference. Intrafascicular stimulation through the microelectrode evoked twitches of the innervated muscles but no paraesthesiae in the innervation zone. Mechanoreceptor activity could be recorded during stretch or percussion of the appropriate tendon or muscle but not during superficial stimulation of the skin. Once a suitable intrafascicular site was found a search was undertaken for spontaneous pulse-related sympathetic activity and the microelectrode manipulated until large unitary discharges appeared out of the multiunit bursts. When the selectivity of

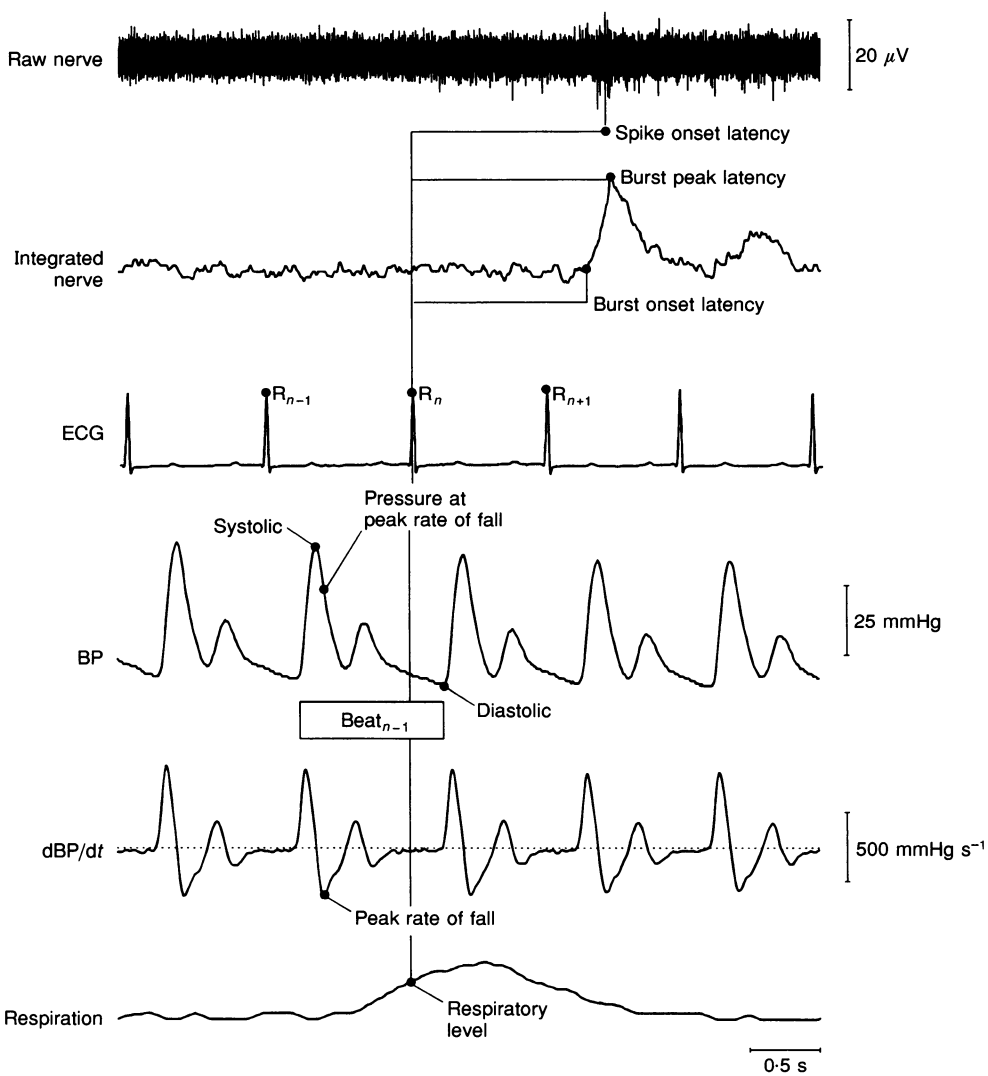

Figure 1. Variables measured for each putative vasoconstrictor motoneurone

To account for peripheral efferent conduction delays, sympathetic response latencies were determined from the ECG R-wave of beat n (the beat preceding that in which the sympathetic discharge was observed). In addition to the cardiovascular and respiratory parameters indicated, pulse pressure (systolic minus diastolic) and mean pressure (diastolic plus one-third pulse pressure) were also calculated over beat $n-1$. dBP/dt is the first time derivative of the blood pressure signal. In this and subsequent figures, negativity is downwards in the raw nerve record.

the electrode was particularly high the search for sympathetic activity was hampered by the difficulty in discerning multiunit bursts in the noise.

Data collection

Neural activity was amplified (5×10^4), filtered (0·3–3·0 kHz), digitized at 12·5 kHz (12 bits) and stored on magnetic and optical media via computer hardware and software (SC/ZOOM) developed by Anders Bäckström at the Department of Physiology, University of Umeå, Sweden. The amplified and filtered nerve signal was also led to an audiomonitor and through a resistance–capacitance circuit (time constant 100 ms). The latter output, the 'integrated nerve signal', was digitized at 800 Hz and stored as 8 bits. The ECG channel was also digitized at 800 Hz and the respiratory and arterial pressure signals at 100 Hz; each of these was stored as 8 bits. Data were sampled over 180 s, during which time subjects were requested to relax and to refrain from talking.

Data analysis

During off-line analysis of data files in which it was believed a single unit had been recorded, the morphology of every spike of the candidate unit was carefully checked using an algorithm-based unit retrieval system (see Edin, Bäckström & Bäckström, 1988) incorporated in the SC/ZOOM software.

Figure 1 illustrates the primary features that were measured for each unit. The first time derivative of the arterial pressure record was computed over three sampling points (30 ms), from which the rate of fall in blood pressure could be extracted. The computer measured the times at which an ECG R-wave occurred and the relative respiratory amplitude at each R-wave, the systolic and diastolic pressures of each beat, the peak rate of fall in arterial pressure and the absolute pressure at which the rate of fall was greatest (after correcting for the 30 ms phase advance of the derivative signal). The operator confirmed placement of a cursor at the following points: the peak of a

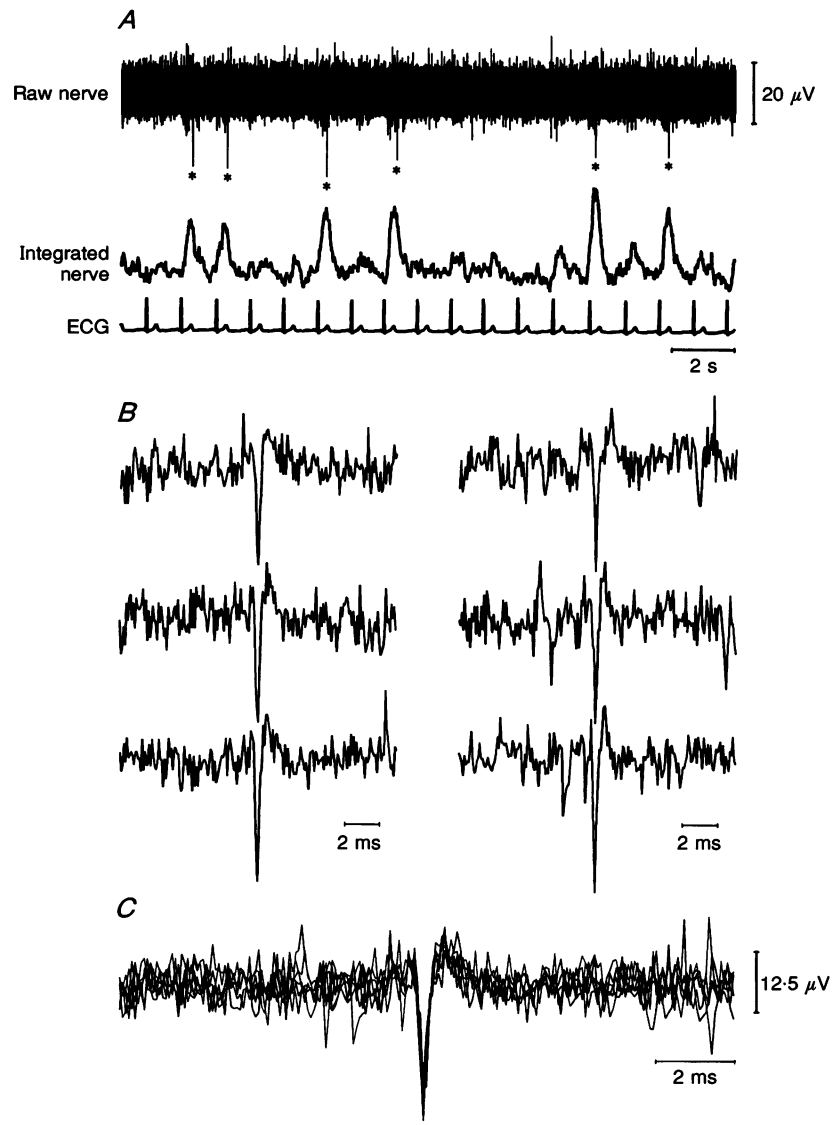

Figure 2. Recording of a single vasoconstrictor unit firing one spike per sympathetic burst
A, unitary recording from a motor fascicle of the peroneal nerve (unit nine in Table 1): one spike (*) was generated with each large sympathetic burst; rastered (*B*) and superimposed (*C*) action potentials suggest that the spikes originated from one axon.

burst (the highest point of the integrated neural signal), the first and last spikes the unit generated during the burst and the R-wave related to the burst. Cursors were also placed at the onset and end of each burst, at points where the integrated neural signal started to increase above the baseline level and where it returned. Judgement of these placements was facilitated by reference to points of zero crossing in the first time derivative of the integrated neural signal. From these event markers the computer calculated the following parameters for each sympathetic burst: the onset latency of the unit, the latency at which its peak discharge occurred, the onset and peak latencies of the integrated neural signal and its relative amplitude, the mean and peak frequencies of the unit, the duration of its discharge and that of the integrated record and the R–R interval of the beat before the unit was recruited and that of the beat during which the unit fired. Pulse pressure (systolic minus diastolic) and mean pressure (diastolic plus one-third pulse pressure) were also calculated.

All analyses are based on the 180 s period of data collected for each unit. Firing probability was calculated by the computer assigning either a '1' or a '0' to each heart beat, according to whether a unit fired or not. Statistical evaluation of the data was performed by the FYSTAT system, developed by Lars Bäckström, Department of Physiology, University of Umeå, and included linear-regression analysis, Student's paired t test, the non-parametric Mann–Whitney U test and the Kolmogorov–Smirnov test. Values are expressed as means ± S.E.M., and differences were considered statistically significant at $P < 0.05$.

RESULTS

Recording features

Stable recordings were obtained from four sites in motor fascicles of the radial nerve and from thirteen sites in the deep branch of the peroneal nerve. From these sites fourteen units that were extracted on the basis of spike amplitude and shape were accepted as being single sympathetic efferents after satisfying the behavioural criteria described below. Of the eight subjects in whom units were recorded, two subjects each provided three units, two provided two units and the remaining four subjects each provided one. Three candidate sympathetic units were rejected in spite of consistent spike morphology because they exhibited no significant relationships between firing properties and arterial pressure or cardiac interval. Eleven of the accepted units were recorded from the peroneal nerve (six subjects) and three from the radial nerve (two subjects); each unit generated action potentials in which the major component was a negativity which, theoretically, is compatible with an extra-axonal recording from a C fibre.

Figure 2*A* shows an example of spontaneous sympathetic activity recorded from a motor fascicle of the peroneal nerve. The activity occurs as pulse-synchronous bursts of multiunit discharges, the incidence and intensity of which vary from beat to beat. In some of these bursts a negative spike of considerably larger amplitude appeared; note that these large spikes contributed little to the amplitude of the integrated nerve signal, which is largely determined by the electrode picking up discharges of several sympathetic axons firing within each burst. Multiunit bursts were recorded in seven subjects, the number of bursts per minute ranging from 9 to 17 (12·6 ± 1·0) and the number of bursts per 100 heart beats ranging from 13 to 27 (21·0 ± 2·2). Because of the appreciable background noise, impulses seen on a contracted time base appear to vary in amplitude; however,

Table 1. Linear correlations between cardiovascular parameters and unit characteristics

		R–R interval			Diastolic pressure			Mean pressure			Pulse pressure			Rate of fall of pressure			Pressure at peak rate of fall		
Unit	n	N	P	L	N	P	L	N	P	L	N	P	L	N	P	L	N	P	L
1	13	+	+											+		−			
2	41												−						
3	27											+							
4	74	+	+		−	−	+			+								−	+
5	51		+	−											−				
6	56	+	+																
7	72	+	+		−	−		−	−										
8	43						+												+
9	44			−			+			+									
10	17		+			−			−						+	−		−	
11	15															−			
12	35	+	+		−	−		−	−		+	+							
13	38	+	+	−	−	−		−	−		+	+	−						
14	27	+	+		−	−	+	−	−		+	+							

Number of spikes (N), firing probability (P) and spike onset latency (L) generated by human vasoconstrictor motoneurones. n, number of recorded heart beats in which the unit fired. Positive correlations indicated by '+', negative correlations indicated by '−'. Only statistically significant linear correlations are shown. Units 1–3 from the radial nerve, the remainder from the peroneal nerve.

when rastered and superimposed on an expanded time scale one sees little variation in spike amplitude or shape (Fig. 2*B* and *C*), supporting the unitary integrity of the recording. All units fired with an obvious cardiac rhythmicity, as apparent in the unit of Fig. 2*A*.

Number of spikes generated per sympathetic burst

The number of spikes generated by the vasoconstrictor motoneurones varied between units and also between bursts. The occurrence of spikes was not high – when the data from all fourteen units were pooled, 79% of all heart beats lacked spikes altogether. Considering only heart beats associated with spikes, 68% of these beats had only one spike (see Fig. 4*B*). The maximum number of spikes that could be ascribed to a single motoneurone during a sympathetic burst was seven. An example of the discharge pattern of a unit that occasionally fired multiple spikes per burst is shown in Fig. 3: two impulses were generated in *A* and four in *B*. These spikes are shown on an expanded timescale in Fig. 3*C*; four smaller spikes from panel *B* are shown in Fig. 3*D*, but these exhibited so much variability in spike morphology that they were rejected. The superimposed spikes of the large unit (Fig. 3*E*) support the conclusion that these originated from a single axon. For seven units the number of spikes generated per cardiac cycle correlated significantly with one or several cardiovascular parameters. These data are summarized in Table 1.

Distribution of firing rates

When all interspike intervals were considered (including those between bursts) the average firing rate of all fourteen units was 0·47 Hz, calculated as the rate corresponding to the mean interspike interval. Mean firing rates within the sympathetic bursts ranged from 2·9 to 40·0 Hz for the thirteen units that fired two or more spikes per cardiac cycle; the population mean was 18·8 ± 2·5 Hz. However, as indicated in Fig. 4*A*, the range of instantaneous frequencies

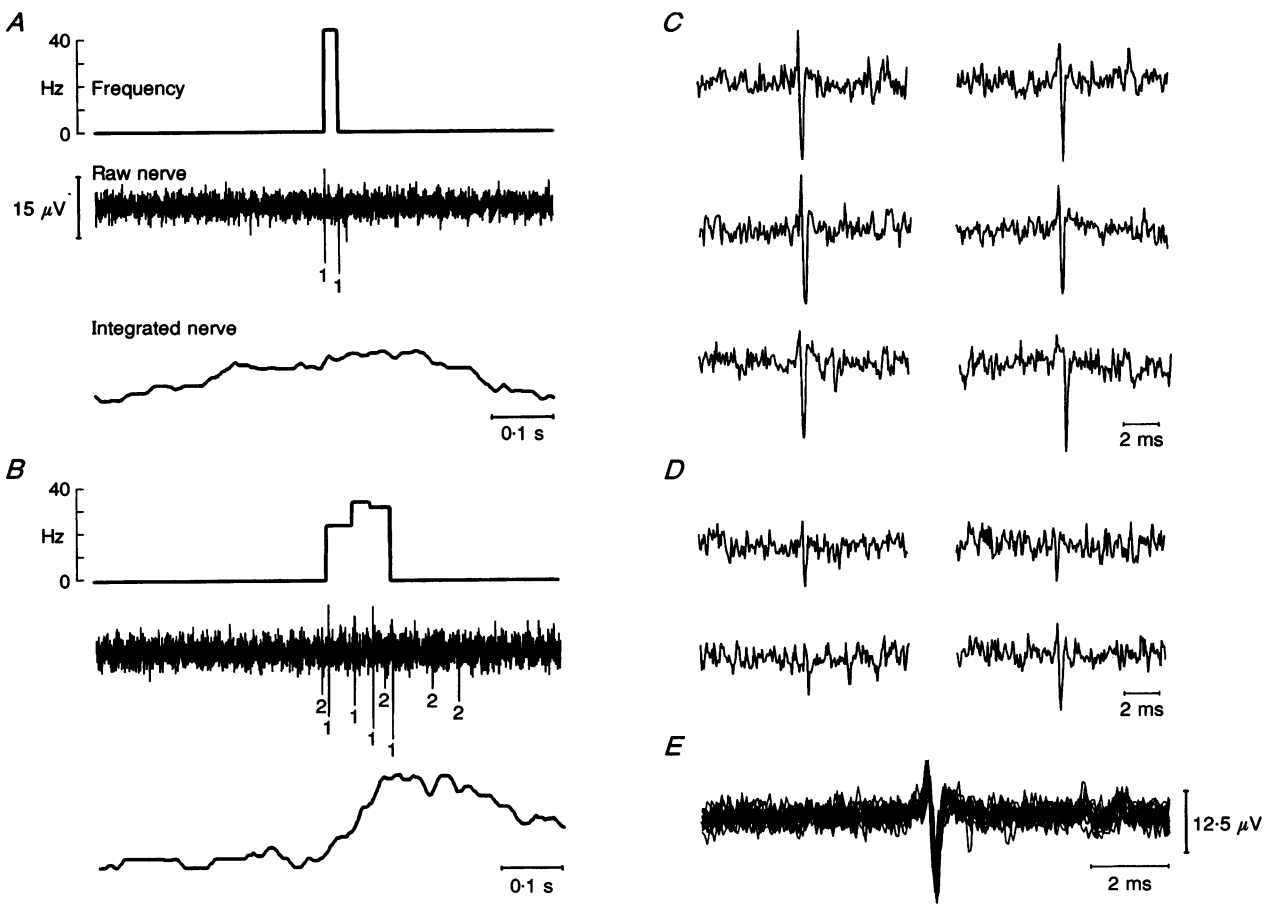

Figure 3. Recording of a single vasoconstrictor unit firing multiple spikes per sympathetic burst

A and *B*, peroneal nerve recordings of two sympathetic bursts in which a large unit (unit five in Table 1) could be discriminated from smaller spikes. *C*, the two large spikes in panel *A* and the four in *B* (unit one) are shown on an expanded timescale. *D*, four smaller spikes from panel *B* (unit two) that failed to meet criteria for acceptance as originating from a single unit. *E*, twenty superimposed spikes of the large unit, demonstrating the relative constancy of spike amplitude and shape that supported the conclusion that these spikes were generated by a single axon.

was very broad and the distribution was strongly skewed towards low firing rates, with a few very high values. The median value was 1·03 Hz and the lower and upper quartiles, 0·34 and 7·92 Hz, respectively. Instantaneous frequencies higher than 50 Hz (range 50·6–93·1 Hz; median 61·1 Hz) were generated by nine of the fourteen units. Often these short intervals were present in isolated doublets, but could also occur within or at the onset of a burst of multiple spikes. Although a large proportion of units occasionally produced high instantaneous frequencies, only 2·4% of all interspike intervals were shorter than 20 ms.

Correlations between spike-firing probability and cardiovascular parameters

Outflow of sympathetic vasoconstrictor impulses in muscle nerves is known to occur during falls in diastolic pressure, when baroreceptor-mediated inhibition diminishes (Sundlöf & Wallin, 1978). Therefore, determining whether the firing of a unit was related appropriately to changes in arterial pressure or cardiac interval provided a means of assessing whether a unit's behaviour was compatible with it being vasoconstrictor in function. As summarized in Table 1, the firing probability of ten units was related to one or more of the cardiovascular variables considered above. The firing of nine units showed a significant positive correlation to the R–R interval of the appropriate beat, i.e. the longer this interval the more likely the occurrence of a spike. For six units an inverse relationship between firing probability and diastolic pressure was significant, and for five units such a negative correlation was significant for mean arterial pressure; data from two units are presented in Fig. 5*A*.

Influence of respiration on spike-firing probability

Sufficient data were available for analysing respiratory influences on sympathetic activity for seven units. With one exception, the probability of firing for each of these was lowest during late inspiration and early expiration. Data from two units are shown in Fig. 5*B*. This fits with observations of the normal respiratory modulation of multiunit sympathetic activity in human muscle nerves – burst amplitudes are smaller in late inspiration than in late expiration (Eckberg, Nerhed & Wallin, 1985; Seals, Suwarno & Dempsey, 1990; Seals, Suwarno, Joyner, Iber, Copeland & Dempsey, 1993; V. G. Macefield & B. G. Wallin, unpublished observation) – and the present observations provide direct evidence that this is manifested in many vasoconstrictor motoneurones dropping out during late inspiration.

Spike onset latencies

Mean onset latencies were significantly shorter for units recorded from the radial nerve (0·97 ± 0·03 s) than the peroneal nerve (1·23 ± 0·03 s; $P = 0·002$, Mann–Whitney), which fits with the different conduction distances to the two recording sites. In multiunit recordings, the R-wave of the ECG has been used as a convenient reference for measuring time relations of muscle sympathetic bursts. The peak of the burst is considered to reflect the point at which systolic inhibition of vasoconstrictor activity by the arterial baroreceptors commences (Sundlöf & Wallin, 1978; Fagius & Wallin, 1980; Fagius, Sundlöf & Wallin, 1987). It has been shown that this baroreflex latency varies greatly between

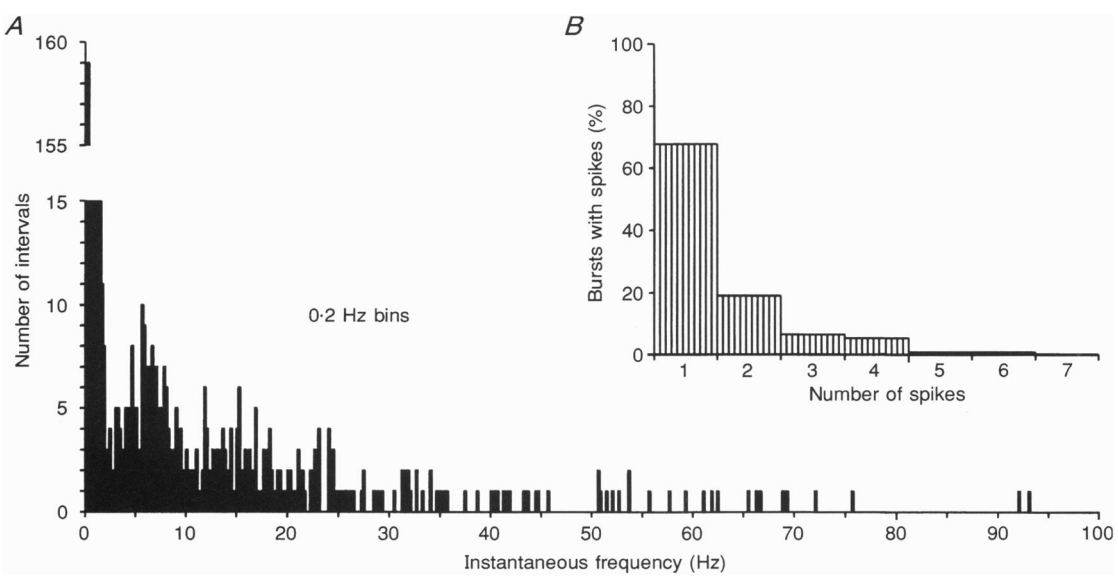

Figure 4. Distributions of instantaneous frequencies and spikes per beat for all vasoconstrictor motoneurones

A, the distribution of instantaneous frequencies is broad but clearly skewed towards lower firing rates. Data are based on all interspike intervals generated within a 3 min period by all fourteen units. *B*, the distribution of heart beats in which one or more spikes were generated. Data were obtained over a 3 min period for all units. The data base of *A* is all interspike intervals of all fourteen units pooled, while the data base of *B* is all the heart beats recorded with all the units.

bursts (Fagius *et al.* 1987), and that higher burst amplitudes are associated with shorter onset and peak latencies of the bursts (Wallin, Burke & Gandevia, 1994). In the present study we reasoned that the onset latency of an individual unit should likewise differ between cardiac cycles.

Figure 6*A* displays, as cumulative-probability distributions, the onset latency for the first spike in a heart beat as well as for the onset and peak of the multiunit bursts of the same records (measured from the integrated nerve signal). The onset latencies varied over the same range and, as illustrated in Fig. 6*B*, there was a strong covariation in the latency to the unit firing and the burst onset. The slope of the linear regression was identical to that of the line of identity; the relationship between spike onset latency and burst peak latency was less tight. The close correlation between spike and burst onset latencies was not a universal finding, however, and the latency of the unit shown in Fig. 2 was more related to the peak of the burst than to its onset; this unit appeared to have a higher recruitment threshold. Overall, for seven of the eight units in which multiunit activity could also be measured, the onset latencies covaried significantly with the onset and/or peak latencies of the bursts, suggesting a relatively fixed recruitment order of human vasoconstrictor motoneurones firing at rest. For a given single unit the range of variation for the onset latency of the first spike was 358 ± 33 ms. The ranges of variation for the onset and peak latencies of the corresponding multiunit bursts were similar (380 ± 47 and 393 ± 39 ms, respectively). The cardiac rhythmicity expressed by these vasoconstrictor motoneurones was quite tight, as reflected by the fact that the range of variation in cardiac interval was of comparable magnitude (279 ± 32 ms).

Correlations between spike onset latency and cardiovascular parameters

Ten of the fourteen units exhibited significant correlations between onset latency and at least one of the relevant cardiovascular parameters (Table 1). Compared with the correlations to unit firing described above, fewer cardiovascular variables were significantly related to spike onset latency. More importantly, the relationships to spike onset latency were opposite, which fits with the expected behaviour of vasoconstrictor motoneurones. For example, the lower the diastolic pressure the more likely a unit will fire (inverse relationship) but the shorter its onset latency (direct relationship).

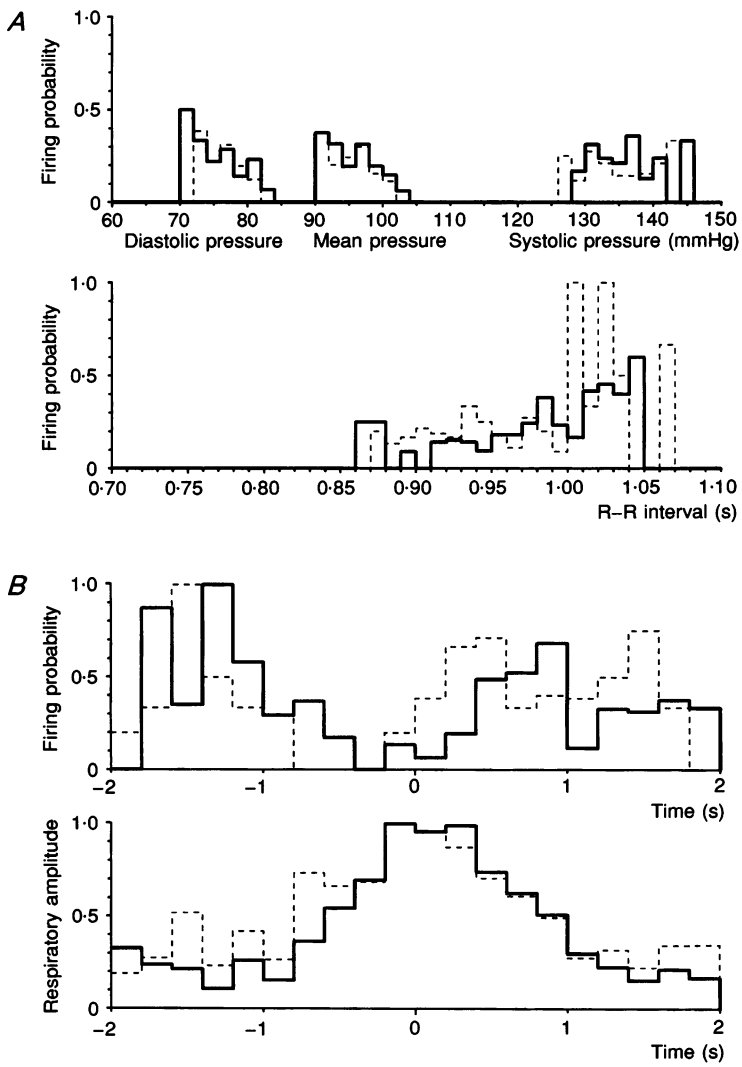

Figure 5. Baroreceptor-mediated changes in the firing probability of two units
A, correlation between firing probability and arterial pressure or cardiac interval for two vasoconstrictor motoneurones (units 4 and 7 in Table 1, indicated by continuous and dashed lines, respectively). The firing probability of both units was greater the lower the diastolic or mean arterial pressure and the longer the cardiac interval, whereas there was no correlation with the systolic pressure. Both units also showed a lower firing probability during inspiration (*B*), respiratory amplitude being measured at the time of the R-wave of the same beat from which latencies were measured (see Fig. 1). Data obtained over a 3 min period.

An inverse linear relationship between the appropriate cardiac interval and spike onset latency was significant for three units, four units exhibited a significant positive correlation of spike onset latency to diastolic pressure, one unit was directly related to mean arterial pressure and two were inversely related to pulse pressure. A significant negative correlation to the rate of fall in arterial pressure during each beat was observed for four units, whereas the latency of two units was directly related to the absolute pressure at which this rate of fall was maximal. Figure 7 shows examples of these relationships for two units: both showed a significant inverse relationship to the peak rate of fall in pressure, but the direct relationship to the corresponding absolute pressure failed to reach statistical significance.

DISCUSSION

This study has shown that individual vasoconstrictor motoneurones innervating resistance vessels in human skeletal muscle present low levels of spontaneous activity in resting conditions, in which most subjects were supine. The majority fire only one spike per sympathetic burst, and only when baroreceptor-mediated inhibition is diminished during spontaneous falls in arterial pressure.

Methodological considerations

Our primary criteria for assessing the unitary integrity of a recording relied on the relative constancy of amplitude and shape of a unit's action potentials. However, even if our criteria for single unit allocation were conservative, we cannot exclude the possibility that occasional impulses conducted in other fibres were allocated to the single neurone we studied if impulse shape and amplitude were identical. Such mistakes would be most likely to occur when multiple firing occurred in a single heart beat. Therefore, the maximum number of spikes in a beat and the highest instantaneous firing rates may not be absolutely correct. We can, however, exclude the opposite error, i.e. that impulses belonging to the unit we studied escaped detection altogether, simply because all impulses were well above the noise level. Moreover, units were accepted as single vasoconstrictor motoneurones only when their firing properties exhibited significant dependences on relevant cardiovascular parameters. This requirement led us to reject units that spike superimposition criteria suggested should be accepted. Whether or not the three units so rejected were vasoconstrictor motoneurones upon which baroreceptor stimuli were less effective cannot be decided.

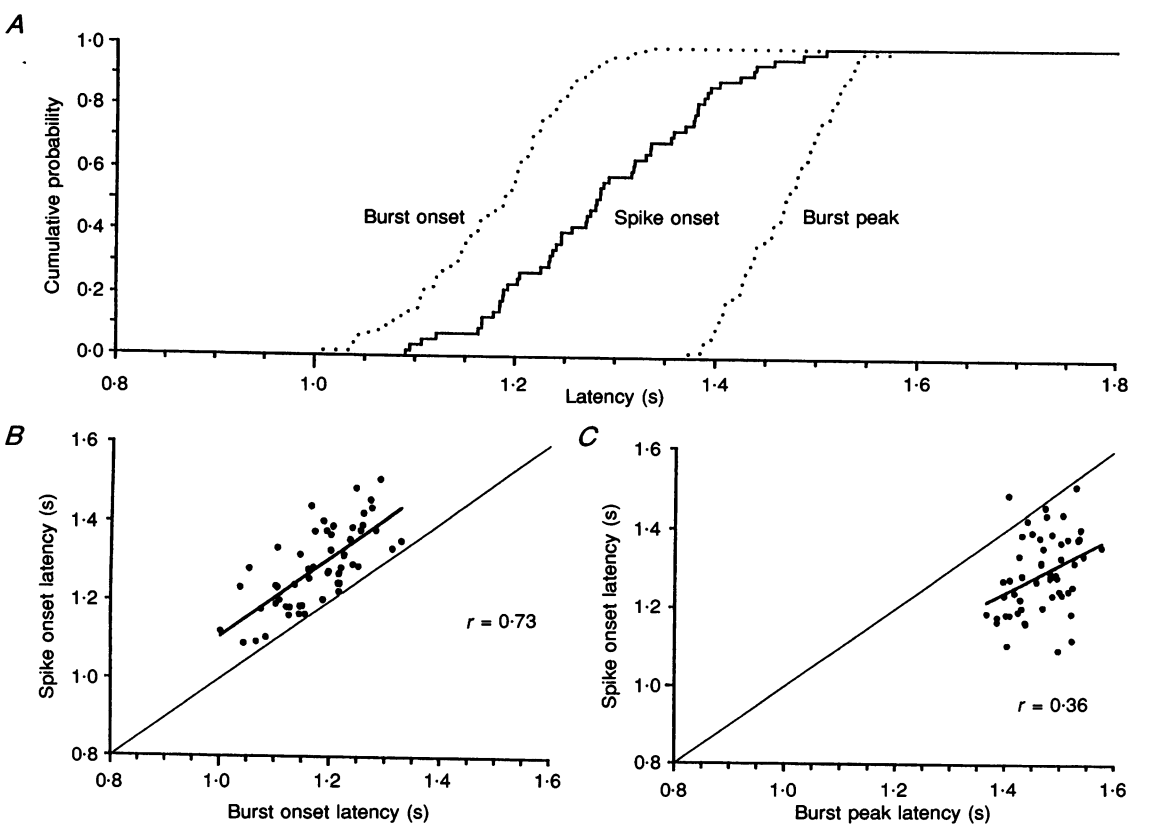

Figure 6. The fixed recruitment order of vasoconstrictor motoneurones
A, cumulative probability plot of burst onset, spike onset and burst peak latencies for one vasoconstrictor motoneurone (unit 4 in Table 1) recorded from the peroneal nerve. *B*, correlation analysis between spike onset latency and burst onset latency revealed a significant linear relationship between the two variables. Conversely, spike onset latency did not covary significantly with burst peak latency (*C*). Data obtained over a 3 min period.

Arterial pressure was measured indirectly by servo pulse-plethysmography from a finger, which is known to reflect adequately the profile of intra-arterial pressure *changes* but may be in error in terms of absolute pressures (Parati, Casadei, Groppelli, Di Rienzo & Mancia, 1989). In addition, the pressure pulse is distorted distally because of reflection of the pulse wave from the terminal branches of the arteries (Kroeker & Wood, 1955). Despite these limitations significant linear correlations were found between various components of the arterial pressure wave and the discharge properties of the units. It is possible that each of the units classified as vasoconstrictor would have expressed relationships to more of the measured pressure variables had pressure been monitored more centrally and intra-arterially.

Correlations between cardiovascular parameters and firing properties

The predictive criteria developed for the analysis of the present material were based on what is known about the incidence of sympathetic bursts in multiunit recordings from human muscle nerves. Firing probability and the number of spikes were significantly higher, and recruitment latencies shorter, the longer the R–R interval, the lower the diastolic or mean arterial pressure and the higher the pulse pressure and rate of fall in arterial pressure. These cardiovascular parameters were measured in the beat during which unloading of the arterial baroreceptors reduced the inhibitory feedback provided by these receptors to the vasoconstrictor motoneurone pool. Although not every relationship was expressed significantly by each motoneurone, each was clearly influenced by baroreceptor stimuli within the physiological range, during spontaneous falls in arterial pressure. Because neither spike onset latency, firing probability nor the numbers of spikes in a burst correlated to systolic pressure for any of the vasoconstrictor motoneurones, the significant relationships to mean arterial pressure and pulse pressure can be attributed to the partial reflection of diastolic events in these pressures, i.e. to falls in arterial pressure. It is not surprising, therefore, that an increase in cardiac interval was associated with a higher firing probability of vasoconstrictor motoneurones. A longer R–R interval will (1) cause arterial pressure to fall to lower values, which causes lesser baroreflex inhibition and (2) increase the probability of firing, simply because

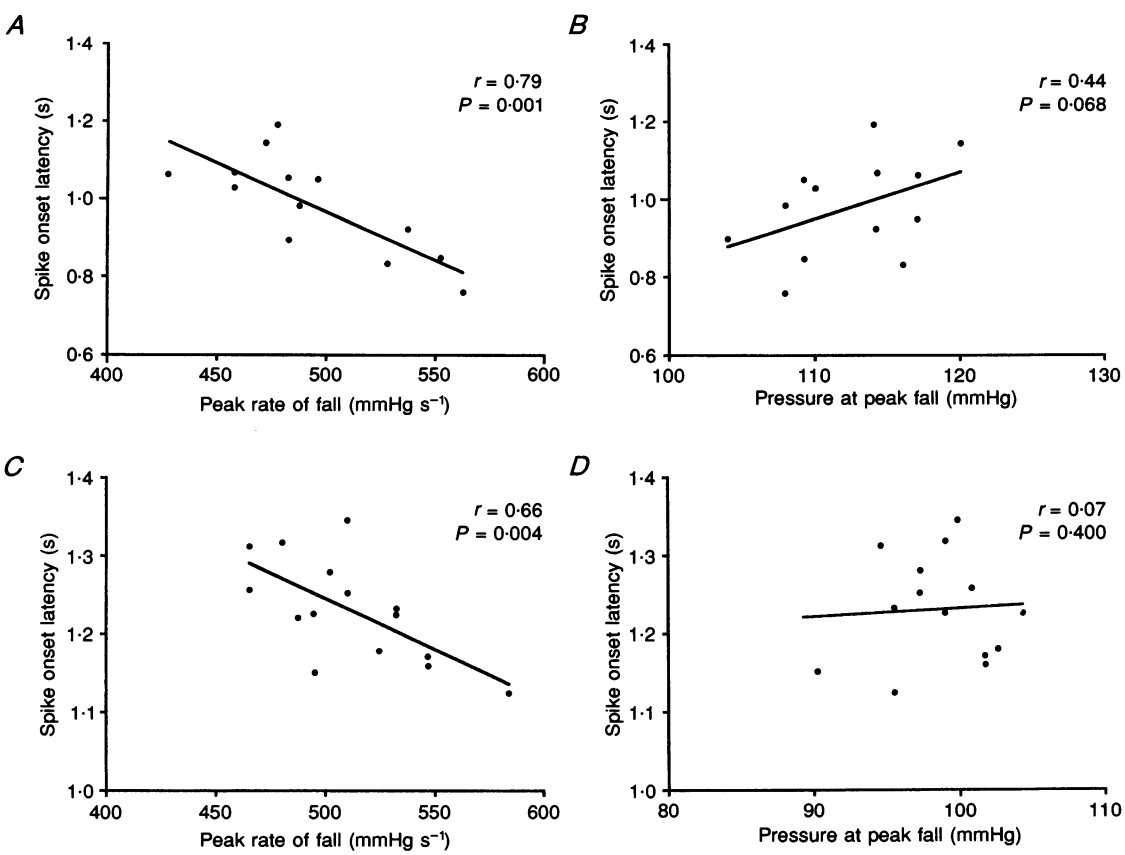

Figure 7. Baroreceptor-mediated changes in spike onset latency for two units
Linear correlation analysis for two units between spike onset latency and the peak rate of fall in arterial pressure (*A* and *C*) or the corresponding absolute pressure (*B* and *D*). *A* and *B* from a radial unit (unit 1 in Table 1) and *C* and *D* from a peroneal unit (unit 11 in Table 1). Both units expressed a significant inverse relationship between latency and the rate of fall in pressure, but the direct relationships to the corresponding absolute pressures failed to reach significance. Data obtained over 3 min periods.

the interval between systolic inhibitions increases. We made no attempt to compensate for the latter effect on the probability values. The dependence on falling pressure is highlighted by the fact that the rate of fall in pressure, or the absolute pressure at which this rate was maximal, were found to influence the firing properties of some of the vasoconstrictor motoneurones. Interestingly, we did not find a single cardiovascular parameter to which the firing properties of all units were correlated. This result suggests that certain vasoconstrictor motoneurones may be preferentially responsive to a particular component of the baroreceptor-mediated modulation of firing.

Latency variations

Recently an inverse relationship was described between the amplitude of an integrated burst and its (peak) baroreflex latency (Wallin *et al.* 1993). The underlying mechanism was suggested to be either variations of central synaptic delays or recruitment of fibres with higher conduction velocities in large amplitude bursts. Our finding of large latency variations for single units ($0{\cdot}36 \pm 0{\cdot}03$ s) indicates fairly large variations of synaptic delays. The locus of the variability is unclear but both supraspinal and/or spinal synapses may be involved. To our knowledge similar variations have not been described previously for the sympathetic limb of the arterial baroreflex, but for the vagal limb large variations in central delay have been reported in cats and rats (McAllen & Spyer, 1978; McCloskey & Potter, 1981). In addition, Coote & Macleod (1974) reported a variation of approximately 60–70 ms for the central sympathetic delay of a cardiac sympathetic reflex evoked by intercostal nerve stimulation.

Definition of single unit onset latency

As illustrated in Fig. 1, the haemodynamic event related to the peak of the mean voltage burst is the systolic pressure wave of cardiac cycle 'n', which induced the onset of inhibition. Spike (and burst) onset latency, on the other hand, is determined by the withdrawal of baroreceptor inhibition during the diastole of cycle '$n-1$'. Unfortunately, the exact time for this inhibition cannot be defined and, therefore, using the R-wave of cycle 'n' as the trigger point for the spike onset latency represents an approximation. However, the error is probably small since the R-wave occurs in the last part of the relevant diastole, i.e. at a fairly fixed time in relation to the triggering haemodynamic event.

Firing rates of single vasoconstrictor motoneurones at rest

The most significant and solid conclusion of the present study is probably that many vasoconstrictor motoneurones to human skeletal muscles rarely fire more than one impulse per heart beat in resting conditions. This conclusion could not have been reached in microneurographic recordings of multiunit sympathetic bursts, which have been the standard approach to recording from postganglionic sympathetic fibres in human peripheral nerves. The maximum number observed within a burst was seven, which is also what Hallin & Torebjörk (1974) found during reflexly evoked bursts of single cutaneous sympathetic motoneurones. It is interesting to note that the level of spontaneous activity in intact, unanaesthetized humans found in our experiments is comparable to that of single vasoconstrictor motoneurones recorded from muscle nerves in the anaesthetized cat (0·5–3 Hz; Jänig, 1985), as well as from renal, splenic and mesenteric nerves in the cat (0·03–6·4 Hz, median 0·9 Hz; Meckler & Weaver, 1988; Stein & Weaver, 1988). It should be noted, however, that our subjects had low levels of spontaneous multiunit activity (range 9–17 bursts min^{-1}). Higher levels are common, for example in older subjects (Sundlöf & Wallin, 1978), and therefore single unit frequencies may also be higher in such subjects. In the present material short interspike intervals, with instantaneous frequencies greater than 50 Hz, were produced by nine units, but only 2·4% of all intervals were so short. Single vasoconstrictor motoneurones in the renal, splenic and mesenteric nerves of the cat also generate high instantaneous firing rates, up to 59 Hz, and the frequency distribution is similarly broad (Meckler & Weaver, 1988; Stein & Weaver, 1988). Such erratic instantaneous frequencies may be physiologically appropriate; electrical stimulation of sympathetic nerves has shown that irregular interstimulus intervals are more effective than regular stimuli for contracting arterioles in the muscle vascular bed of the cat, the optimal pattern being a 32 Hz stimulus applied at 4 s intervals (Andersson, 1983). Similar results have been found between the effects of continuous and burst stimulation of mesenteric (Nilsson, Ljung, Sjöblom & Wallin, 1985) and gastric (Polenov, Lensman, Zasorin & Kolobanov, 1991) microvessels in the rat.

To summarize, the present study has shown that the normal inhibitory influences provided by arterial baroreceptors are expressed by individual vasoconstrictor motoneurones supplying the muscle vascular bed as changes in the probability of firing, the onset latency of the first spike in a sympathetic burst and the number of spikes in a burst. The motoneurones appear to be recruited within a burst according to a fixed order and the majority fire not more than one spike in a burst. When multiple spikes are produced the frequency distribution is broad, with interspike intervals shorter than 20 ms occasionally being produced, but is clearly skewed towards the low end of the range. Such an erratic firing pattern may be physiologically appropriate for improving the contractile responses of the arterioles, thereby optimizing the capacity of the sympathetic nervous system to buffer acute falls in arterial pressure.

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