Central and Reflex Regulation of Sympathetic Vasoconstrictor Activity to Limb Muscles during Desynchronized Sleep in the Cat

By Giorgio Baccelli, Renato Albertini, Giuseppe Mancia, and Alberto Zanchetti

ABSTRACT

Desynchronized sleep (DS) in the cat is accompanied by a long-lasting (tonic) constriction of muscle blood vessels (conductance decrease 5-30%), on which are superimposed short-lasting (phasic) vasoconstrictor waves that occur simultaneously with bursts of rapid eye movements and body twitches. Both the tonic and the phasic vasoconstrictions are abolished after regional sympathectomy (conductance increase 5-10%). Tonic vasoconstriction can also be prevented by hind-limb deafferentation (bilaterial section of the dorsal roots from L5 down) or by transection of the spinal cord at L4 in such a way as to separate sympathetic innervation from afferent input from the hind limbs. These procedures do not affect the phasic vasoconstrictions. After lumbar sympathectomy or hind-limb deafferentation, iliac blood flow decreases during the tonic fall in blood pressure associated with DS by exactly the amount (1-2 ml/min) predicted by pressure-flow relationships observed during artificial lowering of iliac blood pressure. We conclude that tonic and phasic vasoconstrictions are both due to sympathetic discharges. However, phasic sympathetic discharges are driven by central descending influences, and tonic sympathetic vasoconstriction depends on reflex influences originating from the limbs themselves. When tonic sympathetic vasoconstriction is prevented, muscle blood vessels exhibit autoregulatory behavior during DS.

KEY WORDS

hind-limb deafferentation
spinal vasomotor reflexes
muscle afferent fibers
tonic and phasic vasoconstriction
iliac blood flow
autoregulation

The desynchronized phase of natural sleep in the cat (DS) is accompanied by a decrease in systemic arterial blood pressure (1-2) due in large part to a peripheral vasodilatation (3) mediated by the sympathetic nervous system (4). Recent work (5, 6) has shown that this peripheral vasodilatation is by no means diffuse to all vascular beds. Indeed, vasodilatation in the viscera is accompanied by vasoconstriction in the muscles, which parallels the muscle atonia typical of DS. As with other somatic and visceral phenomena associated with DS, during which short-lasting (phasic) changes are superimposed on long-lasting (tonic) ones (2, 3, 7, 8), tonic muscle vasoconstriction is periodically interrupted by phasic constrictor changes that appear simultaneously with bursts of rapid eye movements, body twitches, and changes in heart rate (5).

The present experiments attempted to clarify the mechanisms responsible for tonic and phasic muscle vasoconstriction during DS. We thought that this vasoconstriction could result from either central neural, reflex neural, or nonneural factors. A mechanism involving centrally evoked sympathetic vasoconstrictor discharges would mean that a behavioral condition like sleep can induce an extremely selective repatterning of sympathetic discharges, suppressing those directed to visceral vessels and increasing those controlling muscle blood vessels. Alternatively, an increase in sympathetic discharge to the muscular bed could result from a reflex mechanism originating from the muscles themselves and possibly induced by the tonic condition characteristic of DS. Finally, the sudden fall in muscle tone could also induce local vasoconstriction by nonneural pathways, e.g., a decrease in vasodilating metabolites.

In the present study, sympathectomy of the hind limbs, transection of the lower lumbar cord, and section of the lumbosacral dorsal roots were used to identify the importance of central neural, reflex neural, and nonneural factors. Our experiments indicated that both the long-lasting tonic and the short-lasting phasic muscle vasoconstrictions during DS resulted from sympathetic discharges. The
short-lasting sympathetic discharges appeared to be driven by central descending influences, whereas the long-lasting vasoconstriction in the limb muscles depended on reflex influences originating from the limbs themselves.

Methods

The data reported in this paper were obtained from 14 cats that had fully recovered (3–10 days) from each surgical procedure; the cats were studied under natural behavioral conditions. Blood flow to one hind limb was measured before and after one of the following procedures: ipsilateral lumbar sympathectomy, section of the dorsal roots from L5 down, or spinalization at L4. In 8 cats, blood flow to both hind limbs was recorded, and comparisons were made between the intact limb and the contralateral limb which had been subjected to either ipsilateral lumbar sympathectomy or section of the ipsilateral dorsal roots.

Preparation.—Under sodium pentobarbital anesthesia (35 mg/kg, ip), noncannulating electromagnetic flow probes (Statham, type Q, 1.5–2 mm, i.d.) were implanted on the external iliac arteries. A polyethylene catheter was placed in the aorta through the inferior mesenteric artery. A snare was placed around the abdominal aorta at a level above the orifice of the coeliac artery; closure of the aorta with this snare allowed the establishment of zero flow to the flowmeters. Electrodes were implanted in the skull, neck muscles, and muscles of one or both thighs for monitoring electroencephalographic and electromyographic activities. Cables from the flow probes, wires from the electrodes, threads from the aortic snare, and the arterial catheter were all exteriorized through the paravertebral muscles and protected in a leather jacket sewn to the skin of the back.

To sympathectomize the hind limb, the paravertebral ganglia were removed from L1 down. Removal was ipsilateral only, since this procedure provides complete sympathectomy (9). To obtain afferent denervation of the hind limb, the dorsal roots were cut intradurally from L5 down; the section was unilateral in three cats and bilateral in four. Transection of the spinal cord was performed at a level between the fourth and the fifth lumbar segment. All somatic innervation of the hind limb muscles depended on reflex influences originating from segments below this section; the limb was therefore disconnected from central motor regulation during sleep. On the other hand, all sympathetic innervation of the hind limbs leaves from the spinal segments above the section (9, 10), so centrally driven sympathetic control was unaffected.

Recording Procedures.—The following measurements were made on a 12-channel Grass P7 ink-writer: pulsatile aortic blood pressure (via a Statham P23e strain-gauge transducer), instantaneous blood flow through one or both external iliac arteries, heart rate (via a tachograph triggered by a pulsatile iliac flow signal), electromyograms from one or both hind limbs and from the neck, and one or two electroencephalograms. Aortic blood pressure and blood flow signals were also integrated (Grass TP10 amplifiers automatically reset at 2-second intervals) so that mean aortic blood pressure and mean blood flow could be recorded. Conductance indexes were calculated by dividing blood flow measurements by mean aortic blood pressure. Reasons for preferring conductance to its inverse, resistance, have been explained in a previous paper (11), in which methods for checking flow probe accuracy are also described.

Behavioral Procedure.—Each cat was placed in a large, sound-attenuated cage provided with a window for behavioral observations. In each cat, records were made during six episodes of DS for each of the experimental conditions studied. In DS, the cat looked completely relaxed, the electroencephalogram showed low-voltage fast activity, and bursts of rapid eye movements and body twitches occurred (5). DS also caused abolition of electromyographic activity in the neck and hind-limb muscles. Hind-limb atonia could not be used as a criterion for identifying DS in spinalized or rhizotomized cats, since these procedures themselves produce persistent hind-limb atonia throughout the wakefulness-sleep cycle.

Data Analysis.—As in a previous paper (5), analysis of the data was limited to periods of 2 minutes immediately before and immediately after both the beginning and the termination of DS. From the integrated tracings, blood pressure, iliac blood flow, and conductance values for 4 consecutive seconds out of every 12 were selected for analysis. Ten representative values at regular intervals of 12 seconds were therefore obtained for each 2-minute period. In every cat, one of the intervals during the second minute of DS was randomly selected. Pressure, flow, or conductance values measured at this interval in each of the six episodes studied were compared with base-line values obtained from the same cat at an interval randomly selected during the first minute of the 2-minute period before the onset of DS. Comparison was made using analysis of variance with two-way classification. Analysis of variance was always performed using absolute data, and the results appear in Tables 1–4. Furthermore, each value measured during each 12-second interval was averaged with values recorded at a corresponding time interval in all six DS episodes studied in every cat. In this way, the average time course of cardiovascular changes at the beginning and the end of DS could be studied by drawing graphs such as those in Figures 1–3. Although calculations and statistical analyses were made using only absolute data, the data in Figures 1–3 are reported as percents of base-line values for ease of graphical display.

Results

MECHANISMS OF THE LONG-LASTING TONIC IILAC VASOCONSTRICTION

Effects of Lumbar Sympathectomy.—In five cats, blood flow was recorded from the intact and the contralateral sympathectomized hind limb. As reported in Table 1, four of the five cats exhibited a statistically significant decrease in mean aortic blood pressure during DS. All showed a statistically significant, persistent decrease in blood flow to the intact hind limb. The decrease in blood flow was consistently greater than the decrease in aortic blood pressure; therefore, the conductance index decreased significantly, indicating vasoconstriction. The sympathectomized limb behaved differ-
ently. Blood flow decreased slightly, but the change was significant in only one cat (no. 3). Blood flow either did not change significantly or showed a significant increase in the other four cats. Iliac conductance in the sympathectomized limb was constantly increased. Although this increase was statistically significant in only one cat (no. 5), it became statistically significant \((P < 0.01)\) when all five cats were analyzed together. The time course of iliac vasoconstriction in the intact hind limb throughout DS and the absence of vasoconstriction in the sympathectomized hind limb are illustrated in Figure 1A (mean data from cat no. 3).

Concordant results were obtained in two other cats not included in Table 1. The first, which had a flowmeter implanted around only one iliac artery, was studied before and after ipsilateral lumbar sympathectomy. In this cat, DS was accompanied by a statistically significant decrease in iliac conductance (from 0.36 ± 0.02 to 0.32 ± 0.01 ml/min mm Hg\(^{-1}\)) only when limb innervation was intact. After sympathectomy, the pattern was reversed; iliac conductance increased during DS from 0.44 ± 0.03 to 0.49 ± 0.01 ml/min mm Hg\(^{-1}\). The second cat had been prepared like the five cats listed in Table 1, but only the sympathectomized limb was studied because the contralateral flow probe failed to work properly. Consistent with the data from the other cats, the sympathectomized hind limb did not show any vasoconstriction during DS.

Two tests were performed to show that the effect of sympathectomy was due to interruption of an adrenergic vasoconstrictor influence rather than to interference with a tonic cholinergic vasodilatation suppressed during DS. Either methylatropine (0.5 mg/kg body weight) or bretylium (10 mg/kg followed by the same dose 2 hours later) was administered intravenously. In no instance did cholinergic blockade by methylatropine interfere with DS vasoconstriction in the hind limb with intact sympathetic innervation; however, the vasoconstriction was easily blocked by the antiadrenergic agent.

**Effects of Lumbar Spinalization.**—Transection of the spinal cord at L4 was performed in four cats. As stated in the Methods, after this procedure hind limbs were incapable of voluntary movements and atonic throughout the remaining experimental period. Sympathetic innervation was intact; a prompt vasoconstriction occurred in response to emotional stimuli such as the showing of an aggressive cat or a threatening dog as it does in intact cats. Previous work by our group (10) has demonstrated that these stimuli induce iliac vasoconstriction that survives L4 spinalization but disappears after local sympathectomy. Therefore, if iliac vasoconstriction during DS were due to centrally driven sympathetic discharges, it should

<table>
<thead>
<tr>
<th>Cat</th>
<th>Variable</th>
<th>Intact hind limb</th>
<th>Sympathectomized hind limb</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Mean blood pressure (mm Hg)</td>
<td>95.0 ± 3.6</td>
<td>87.0 ± 2.4*</td>
</tr>
<tr>
<td></td>
<td>iliac flow (ml/min)</td>
<td>35.2 ± 2.7</td>
<td>30.6 ± 2.3*</td>
</tr>
<tr>
<td></td>
<td>iliac conductance (ml/min mm Hg(^{-1}))</td>
<td>0.37 ± 0.02</td>
<td>0.35 ± 0.03*</td>
</tr>
<tr>
<td>2</td>
<td>Mean blood pressure (mm Hg)</td>
<td>88.3 ± 1.6</td>
<td>78.3 ± 1.6*</td>
</tr>
<tr>
<td></td>
<td>iliac flow (ml/min)</td>
<td>31.3 ± 0.6</td>
<td>25.0 ± 0.9†</td>
</tr>
<tr>
<td></td>
<td>iliac conductance (ml/min mm Hg(^{-1}))</td>
<td>0.36 ± 0.01</td>
<td>0.32 ± 0.01*</td>
</tr>
<tr>
<td>3</td>
<td>Mean blood pressure (mm Hg)</td>
<td>75.0 ± 0.6</td>
<td>61.0 ± 2.1†</td>
</tr>
<tr>
<td></td>
<td>iliac flow (ml/min)</td>
<td>31.5 ± 1.4</td>
<td>19.6 ± 2.3†</td>
</tr>
<tr>
<td></td>
<td>iliac conductance (ml/min mm Hg(^{-1}))</td>
<td>0.42 ± 0.02</td>
<td>0.32 ± 0.04*</td>
</tr>
<tr>
<td>4</td>
<td>Mean blood pressure (mm Hg)</td>
<td>93.7 ± 2.2</td>
<td>84.1 ± 2.3†</td>
</tr>
<tr>
<td></td>
<td>iliac flow (ml/min)</td>
<td>37.2 ± 2.5</td>
<td>30.9 ± 1.9*</td>
</tr>
<tr>
<td></td>
<td>iliac conductance (ml/min mm Hg(^{-1}))</td>
<td>0.40 ± 0.02</td>
<td>0.38 ± 0.02†</td>
</tr>
<tr>
<td>5</td>
<td>Mean blood pressure (mm Hg)</td>
<td>100.0 ± 2.9</td>
<td>99.0 ± 1.9</td>
</tr>
<tr>
<td></td>
<td>iliac flow (ml/min)</td>
<td>33.7 ± 1.0</td>
<td>27.7 ± 3.4*</td>
</tr>
<tr>
<td></td>
<td>iliac conductance (ml/min mm Hg(^{-1}))</td>
<td>0.34 ± 0.02</td>
<td>0.24 ± 0.04*</td>
</tr>
</tbody>
</table>

All values are means ± SE for six episodes of DS in each cat.

* \(P < 0.05\), DS compared with control.
† \(P < 0.001\), DS compared with control.
‡ \(P < 0.01\), DS compared with control.

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have survived spinalization at L4. However, as shown in Table 2 and Figure 1B, transection of the spinal cord abolished the iliac vasoconstriction that was observed during DS when the spinal cord was intact (cat no. 3 and cat no. 6). Namely, iliac conductance decreased during DS when the spinal cord was intact and increased after cord section. These results were confirmed by the observation that in the two remaining cats of Table 2, which were studied only after spinalization, DS was accompanied by a statistically significant increase in iliac conductance. The increase in conductance became highly significant \( P < 0.01 \) when all four cats were analyzed together. Thus in all cats transection of the spinal cord prevented iliac vasoconstriction during DS. Comparison of the continuous lines in Figure 1B with the broken lines in Figure 1A shows that the effects of sympathectomy and spinalization were similar.

Effects of Bilateral Dorsal Root Section.—Bilateral section of the dorsal roots from L5 down was performed in four cats to test the possibility
that the effect of lumbar spinalization was due to interruption of sympathetic reflexes with their afferent limbs in the lower lumbar and sacral roots. Cats subjected to bilateral rhizotomy differed from spinalized cats; they showed centrally commanded movements of the hind limbs, but, like their spinalized companions, their hind limbs were completely atonic. Sympathetic outflow was unaffected as shown by the normal occurrence of iliac vasoconstriction during emotional stimuli. Table 3 summarizes the results of our observations.

In the three cats studied both before and after dorsal root section, control records showed that DS was accompanied by the usual statistically significant decreases in aortic blood pressure, hind-limb blood flow, and conductance. After bilateral rhizotomy, aortic blood pressure decreased during DS to the same extent, but the decrease in iliac blood flow was largely reduced. In every cat there was an increase rather than a decrease in conductance. A fourth cat (no. 9), in which recordings were first made after bilateral rhizotomy, also had no iliac vasoconstriction during DS. Once again, cumulative analysis of all four cats showed that after dorsal rhizotomy the increase in conductance was highly significant ($P < 0.01$).

Two of the rhizotomized cats were subsequently studied after spinalization at L4. Spinalization did not modify the pattern of iliac vasomotor changes resulting from the dorsal rhizotomy; the decrease in aortic blood pressure observed during DS was still accompanied by a small reduction in iliac blood flow and, as a result, by an increase in iliac conductance. The increase in conductance was comparable to that observed after bilateral rhizotomy alone.

Figure 2 shows the iliac vascular changes during DS in a cat (no. 1) with its spinal cord and dorsal roots intact (A), its dorsal roots sectioned (B), and both its cord and dorsal roots sectioned (C). Clearly the changes in B and C overlap both in magnitude and time course.

In one cat (no. 9), six DS episodes were recorded before and six were recorded after paw circulation had been interrupted by inflating a rubber sleeve around the paw with a pressure higher than the existing aortic blood pressure. This procedure has been shown to eliminate most of the neurally controlled cutaneous blood flow (11). The increase in muscle conductance observed during DS after bilateral rhizotomy and spinalization (+11.1 ± 4.2%) was not affected by elimination of the paw circulation (+12.0 ± 3.8%) and therefore mainly represents changes in the muscular vascular bed.

**Effects of Unilateral Dorsal Root Section.**—In three cats, hind-limb blood flow was recorded from both external iliac arteries, and the dorsal roots were sectioned on only one side. Throughout the wakefulness-sleep cycle, muscle atonia was limited to the hind limb ipsilateral to the cut dorsal roots; this atonia contrasted with the normal fluctuations observed in the tone of the contralateral muscle. As reported in Table 4, during DS not only the "intact" hind limb but also the hind limb ipsilater-

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**Table 2**

<table>
<thead>
<tr>
<th>Cat</th>
<th>Variable</th>
<th>Spinal cord intact</th>
<th>Spinal cord cut at L4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Control</td>
<td>DS</td>
</tr>
<tr>
<td>3</td>
<td>Mean blood pressure (mm Hg)</td>
<td>75.0 ± 0.6</td>
<td>61.0 ± 2.1*</td>
</tr>
<tr>
<td></td>
<td>Iliac flow (ml/min)</td>
<td>31.5 ± 1.4</td>
<td>19.6 ± 2.3</td>
</tr>
<tr>
<td></td>
<td>Iliac conductance (ml/min mm Hg⁻¹)</td>
<td>0.42 ± 0.02</td>
<td>0.32 ± 0.04†</td>
</tr>
<tr>
<td>6</td>
<td>Mean blood pressure (mm Hg)</td>
<td>89.2 ± 2.3</td>
<td>76.5 ± 1.9‡</td>
</tr>
<tr>
<td></td>
<td>Iliac flow (ml/min)</td>
<td>44.1 ± 31.3</td>
<td>31.3 ± 3.6‡</td>
</tr>
<tr>
<td></td>
<td>Iliac conductance (ml/min mm Hg⁻¹)</td>
<td>0.50 ± 0.04</td>
<td>0.41 ± 0.04†</td>
</tr>
<tr>
<td>7</td>
<td>Mean blood pressure (mm Hg)</td>
<td>84.0 ± 1.0</td>
<td>75.4 ± 1.8†</td>
</tr>
<tr>
<td></td>
<td>Iliac flow (ml/min)</td>
<td>31.1 ± 0.3</td>
<td>31.5 ± 2.6</td>
</tr>
<tr>
<td></td>
<td>Iliac conductance (ml/min mm Hg⁻¹)</td>
<td>0.37 ± 0.01</td>
<td>0.42 ± 0.01†</td>
</tr>
<tr>
<td>8</td>
<td>Mean blood pressure (mm Hg)</td>
<td>87.8 ± 0.7</td>
<td>73.6 ± 3.5‡</td>
</tr>
<tr>
<td></td>
<td>Iliac flow (ml/min)</td>
<td>28.8 ± 1.6</td>
<td>28.6 ± 2.1</td>
</tr>
<tr>
<td></td>
<td>Iliac conductance (ml/min mm Hg⁻¹)</td>
<td>0.33 ± 0.02</td>
<td>0.40 ± 0.04†</td>
</tr>
</tbody>
</table>

All values are means ± se for six episodes of DS in each cat.

* $P < 0.001$, DS compared with control.
† $P < 0.05$, DS compared with control.
‡ $P < 0.01$, DS compared with control.
### Effects of Bilateral Dorsal Root Section (L5 Down) and Subsequent Lumbar Spinal Cord Transection on Circulation of an Otherwise Intact Hind Limb during DS

<table>
<thead>
<tr>
<th>Cat</th>
<th>Variable</th>
<th>Intact</th>
<th>DS</th>
<th>Lumbar cord section</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Control</td>
<td>DS</td>
<td>Control</td>
</tr>
<tr>
<td>1</td>
<td>Mean blood pressure (mm Hg)</td>
<td>95.6 ± 3.6</td>
<td>87.0 ± 2.4*</td>
<td>79.1 ± 0.5†</td>
</tr>
<tr>
<td></td>
<td>Iliac flow (ml/min)</td>
<td>35.2 ± 2.7</td>
<td>30.5 ± 2.3*</td>
<td>28.4 ± 0.8</td>
</tr>
<tr>
<td></td>
<td>Iliac conductance (ml/min mm Hg⁻¹)</td>
<td>0.37 ± 0.02</td>
<td>0.35 ± 0.03*</td>
<td>0.33 ± 0.02</td>
</tr>
<tr>
<td>4</td>
<td>Mean blood pressure (mm Hg)</td>
<td>93.7 ± 2.2</td>
<td>84.1 ± 2.3†</td>
<td>73.7 ± 3.3‡</td>
</tr>
<tr>
<td></td>
<td>Iliac flow (ml/min)</td>
<td>37.2 ± 2.5</td>
<td>30.3 ± 1.9*</td>
<td>29.3 ± 2.0</td>
</tr>
<tr>
<td></td>
<td>Iliac conductance (ml/min mm Hg⁻¹)</td>
<td>0.40 ± 0.02</td>
<td>0.36 ± 0.02†</td>
<td>0.32 ± 0.02</td>
</tr>
<tr>
<td>9</td>
<td>Mean blood pressure (mm Hg)</td>
<td>95.2 ± 2.5</td>
<td>94.5 ± 2.3†</td>
<td>75.1 ± 1.6‡</td>
</tr>
<tr>
<td></td>
<td>Iliac flow (ml/min)</td>
<td>36.7 ± 2.1</td>
<td>31.0 ± 3.1*</td>
<td>37.3 ± 2.0</td>
</tr>
<tr>
<td></td>
<td>Iliac conductance (ml/min mm Hg⁻¹)</td>
<td>0.36 ± 0.02</td>
<td>0.31 ± 0.03*</td>
<td>0.43 ± 0.03</td>
</tr>
</tbody>
</table>

All values are means ± SE for six episodes of DS in each cat.

* P < 0.05, DS compared with control.
† P < 0.01, DS compared with control.
‡ P < 0.001, DS compared with control.

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Vasoconstriction overwhelmed autoregulatory dilatation. An observation calculated using arterial conductance, an observation which indicates that local sympathetic activity was free of neural and hormonal influences, was observed in two cats that had been subjected to spinalization, bilateral iliac sympathectomy, and ileal atonia. Figure 4 (crosses and dotted lines) shows that a decrease in ileal blood flow from 26.2 ± 1.2 ml/min, when ileal blood flow was maintained at a low level, the cats continued to recline and showed no sign of excitement or discomfort. Figure 4 (crosses and dotted lines) shows that a decrease in ileal blood flow from 26.2 ± 1.2 ml/min, when ileal blood flow was maintained at a low level, the cats continued to recline and showed no sign of excitement or discomfort. Figure 4 (crosses and dotted lines) shows that a decrease in ileal blood flow from 26.2 ± 1.2 ml/min, when ileal blood flow was maintained at a low level, the cats continued to recline and showed no sign of excitement or discomfort. Figure 4 (crosses and dotted lines) shows that a decrease in ileal blood flow from 26.2 ± 1.2 ml/min, when ileal blood flow was maintained at a low level, the cats continued to recline and showed no sign of excitement or discomfort. Figure 4 (crosses and dotted lines) shows that a decrease in ileal blood flow from 26.2 ± 1.2 ml/min, when ileal blood flow was maintained at a low level, the cats continued to recline and showed no sign of excitement or discomfort. Figure 4 (crosses and dotted lines) shows that a decrease in ileal blood flow from 26.2 ± 1.2 ml/min, when ileal blood flow was maintained at a low level, the cats continued to recline and showed no sign of excitement or discomfort. Figure 4 (crosses and dotted lines) shows that a decrease in ileal blood flow from 26.2 ± 1.2 ml/min, when ileal blood flow was maintained at a low level, the cats continued to recline and showed no sign of excitement or discomfort. Figure 4 (crosses and dotted lines) shows that a decrease in ileal blood flow from 26.2 ± 1.2 ml/min, when ileal blood flow was maintained at a low level, the cats continued to recline and showed no sign of excitement or discomfort. Figure 4 (crosses and dotted lines) shows that a decrease in ileal blood flow from 26.2 ± 1.2 ml/min, when ileal blood flow was maintained at a low level, the cats continued to recline and showed no sign of excitement or discomfort. Figure 4 (crosses and dotted lines) shows that a decrease in ileal blood flow from 26.2 ± 1.2 ml/min, when ileal blood flow was maintained at a low level, the cats continued to recline and showed no sign of excitement or discomfort. Figure 4 (crosses and dotted lines) shows that a decrease in ileal blood flow from 26.2 ± 1.2 ml/min, when ileal blood flow was maintained at a low level, the cats continued to recline and showed no sign of excitement or discomfort. Figure 4 (crosses and dotted lines) shows that a decrease in ileal blood flow from 26.2 ± 1.2 ml/min, when ileal blood flow was maintained at a low level, the cats continued to recline and showed no sign of excitement or discomfort. Figure 4 (crosses and dotted lines) shows that a decrease in ileal blood flow from 26.2 ± 1.2 ml/min, when ileal blood flow was maintained at a low level, the cats continued to recline and showed no sign of excitement or discomfort. Figure 4 (crosses and dotted lines) shows that a decrease in ileal blood flow from 26.2 ± 1.2 ml/min, when ileal blood flow was maintained at a low level, the cats continued to recline and showed no sign of excitement or discomfort. Figure 4 (crosses and dotted lines) shows that a decrease in ileal blood flow from 26.2 ± 1.2 ml/min, when ileal blood flow was maintained at a low level, the cats continued to recline and showed no sign of excitement or discomfort. Figure 4 (crosses and dotted lines) shows that a decrease in ileal blood flow from 26.2 ± 1.2 ml/min, when ileal blood flow was maintained at a low level, the cats continued to recline and showed no sign of excitement or discomfort.
tation. Likewise, in both hind limbs of cats that had been subjected to unilateral dorsal rhizotomy, the pressure-flow relationships were much steeper than the control curve obtained from aortic constriction (C). On the other hand, in sympathectomized limbs (A) as well as in sympathetically intact limbs of cats subjected to either bilateral dorsal rhizotomy or low lumbar spinalization (B), the slope of the pressure-flow relationships was very similar to the relationships obtained by aortic constriction, indicating that the increase in iliac conductance calculated under these conditions resulted from vascular autoregulation.

MECHANISMS OF THE SHORT-LASTING (PHASIC) ILIAC VASOCONSTRICTION

The mechanisms underlying the short-lasting...
Percent changes in mean blood pressure, iliac blood flow, and iliac conductance in cat no. 10 during DS. A: Hind-limb afferents intact. B: After unilateral section of the right dorsal roots from L5 down. C: After subsequent section of the left dorsal roots from L5 down. Solid circles and continuous lines refer to the left hind limb (L), and open circles and broken lines refer to the right hind limb (R). The inserts at the bottom are electromyograms (EMG) from the left and right hind limbs. Notice the slight difference in the time scale compared with the graphs above. All other explanations are the same as those in Figure 1.

Log-log diagram of pressure-flow relationships just before the onset of DS (right end of each line) and during DS (left end) under different experimental conditions. A: Solid circles are mean values (bars are SE) of pressure and flow measured in the intact hind limb of five cats; open circles indicate the means simultaneously measured in the contralateral sympathectomized limb. B: Solid triangles are mean values for the intact limbs of four cats subjected to transection of the spinal cord at L4, and solid stars indicate mean data for intact limbs of four cats subjected to bilateral section of their dorsal roots from L5 down. C: Squares indicate means from three cats subjected to unilateral section of their dorsal roots from L5 down; solid squares refer to the contralateral hind limb, and open squares refer to the deafferented hind limb. The dotted lines between crosses, repeated in A, B, and C, represent the average pressure-flow relationship in the sympathectomized limbs of two cats subjected to bilateral dorsal root section and L4 spinalization when iliac blood pressure was artificially reduced by tightening a snare around the abdominal aorta.
(phasic) iliac vasoconstrictions that occur simultaneously with bursts of eye movements or limb twitches were investigated by the same techniques used to study the long-lasting (tonic) vasoconstriction. Phasic changes were studied in five otherwise intact cats with one limb intact and the contralateral limb sympathectomized, in two cats before and after lumbar cord transection, and in three cats before and after dorsal rhizotomy. On the whole, more than 300 phasic changes were analyzed under one or another experimental condition. Figure 5 summarizes our results by showing observations from cat no. 1. Like the tonic vasoconstriction, the phasic waves were also completely abolished in the sympathectomized hind limb (A). However, at variance with the tonic phenomenon, the phasic vasoconstrictor waves persisted unmodified in the nonsympathectomized limb after dorsal root section from L5 down (B) and even after subsequent spinal cord transection at L4 (C). Identical results were obtained in all other cats in which phasic vasoconstrictions were analyzed.

**Discussion**

The results of these experiments show that both the long-lasting tonic muscle vasoconstriction occurring throughout DS and the short-lasting phasic waves of muscle vasoconstriction accompanying the rapid eye movements and the body twitches of DS are due to discharges along adrenergic sympathetic fibers. The mechanisms mediating the tonic and the phasic sympathetic discharges are, however, different. The phasic waves appear to be centrally driven; they survive limb deafferentation or spinal cord transection separating the sympathetic outflow from the afferent inflow from the hind limbs. It is likely that these phasic discharges of sympathetic constrictor fibers to muscle blood vessels are triggered by the vestibular nuclei, as has been shown to be the case for rapid eye movements (12), somatic twitches (12), bursts of tachycardia (8), and mydriatic waves (8). The sympathetic discharge responsible for the tonic muscle vasoconstriction seems to depend on reflex rather than central actions. Disappearance of iliac vasoconstriction after bilateral deafferentation of the hind limb or after spinal cord transection at L4 indicates that hind-limb reflexes are involved. Of course, this observation could also be compatible with a nonneural origin of iliac vasoconstriction: if the vasoconstriction were due to a decrease in the production of vasodilating metabolites in the muscles when atonia supervenes at the onset of DS, deafferentation and L4 spinalization obviously would prevent the vasoconstriction by rendering the muscle permanently atonic. That this mechanism is not the one which mediates iliac vasoconstriction is indicated, however, by two kinds of findings. (1) Vasoconstriction is abolished by lumbar sympathectomy, which does not produce atonia. (2) Vasoconstriction is still found after unilateral deafferentation in the deafferented limb, although this limb is fully atonic; vasoconstriction is abolished only when dorsal root section is extended to the other side. These observations can only be explained by postulating a reflex mechanism originating bilaterally from the limbs.

The next question is whether muscle vasoconstriction during DS is due to the activation of a vasoconstrictor reflex or whether it results from inhibition or cessation of a preexisting vasodilator reflex.

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**FIGURE 5**

Examples of phasic vasoconstrictions during DS in cat no. 13. One limb had intact sympathetic innervation (IIF) and the other was sympathectomized (SIF). A: Hind-limb afferents intact. B: After bilateral section of the dorsal roots from L5 down. C: After subsequent transection of the spinal cord at L4. OM = ocular movements, HR = heart rate, BP = instantaneous aortic blood pressure, i.IIF and i.SIF = instantaneous iliac blood flow to the intact and the sympathectomized hind limb, respectively, and j.BP, j.IIF, and j.SIF = 2-second integrals of these three values. On the top, time is given in 5-second intervals.

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Pressor, vasoconstrictor afferents from muscle are known to exist (13-17), but they are supposed to be excited by exercise (18, 19). It is difficult to envisage how they could be activated during DS at a time when all muscle activity disappeared. Vasoconstrictor afferents analogous to similar afferents in renal (20) and mesenteric nerves (21) which are excited by local venous congestion could originate from receptors in muscle blood vessels; however, evidence suggesting venous congestion in muscle during DS is lacking.

Vasodilating, depressor afferents from hind-limb muscles are known to exist (13-17); they have been identified with low-threshold group III fibers (13, 16) and shown to act by inhibiting sympathetic vasoconstrictor discharges (15-17). Dilatation of muscle blood vessels has also been described (15). This reflex inhibition of muscle vasoconstrictor tone could be inhibited during DS by the same supraspinal mechanisms that are known to inhibit somatic polysynaptic reflexes during the same stage of sleep (22). Alternatively, the decrease in muscle tone typical of DS could remove the stimulus maintaining the vasodilating reflex. DS atonia is accompanied by suppression of fusimotor discharge (23), and this suppression implies a depressed discharge of muscle spindle afferents. Some recent data by Koizumi and Sato (24) support the hypothesis that group II fibers, to which secondary spindle afferents belong, might inhibit sympathetic vasoconstrictor fibers. Of course, vasodilating afferents could originate from undefined muscle endings inactivated by atonia or from receptors in muscle vessels, e.g., arterial baroreceptors could be deactivated by the fall in blood pressure associated with DS.

A final difficulty to be discussed is that previous work (13-16) on depressor muscle afferents indicates a generalized inhibition of vasoconstrictor tone, as expressed by the very term “depressor.” On the other hand, our experiments require the existence of a regional reflex, since it would be difficult to explain in any other way the complete abolition of DS vasoconstriction in the hind limbs when only the hind limbs are deafferented and inputs from all other muscles are preserved. Among known vascular reflexes, the only one which postulates a vasodilatation limited to the region from which afferent stimuli originate seems to be the so-called Lovén reflex (25). However, even though Bayliss (26) has described such a reflex arrangement for the hind limbs, no support for the existence of the Lovén reflex has come from more recent, better controlled experiments (15). The study of spinal vascular reflexes is only at its beginning, and further investigation might reveal a more specific and topical organization than that commonly accepted at present. Some electrophysiological evidence is already accumulating; Sato (cited in ref. 17) has shown a segmental organization of reflex depression of spinal sympathetic activity.

Without more crucial evidence, we can only conclude that during quiet wakefulness and synchronized sleep a bilateral afferent inflow from the hind limbs seems to maintain a tonic inhibition of the sympathetic vasoconstrictor outflow to the limbs and that during DS this tonic inhibition is suppressed either because of active inhibition by brainstem mechanisms, or, more likely, because changes in the hind limbs themselves (e.g., atonia or vascular hypotension) make the receptors stop firing. In this context, the tonic constriction of muscle blood vessels is not a real exception to the vasodilatation simultaneously occurring in other vascular beds (5). It does not result from an opposite influence of DS mechanisms on sympathetic discharges to different beds but simply represents the consequence of a peculiar reflex control of muscle circulation, which exists prior to DS and which DS mechanisms or, more probably, DS phenomena happen to influence.

Other aspects of vasomotor regulation in the iliac bed were clarified by comparing pressure-flow relationships observed when arterial blood pressure spontaneously decreased during DS with the relationships found in a denervated bed when arterial blood pressure was mechanically reduced to a comparable level by aortic constriction. First, our data showed that the increase in iliac vascular conductance observed when either the efferent or the afferent limb of the vasomotor reflex is cut is identical to the increase in conductance occurring when aortic pressure is mechanically decreased and is therefore the expression of local autoregulation. This example of autoregulation in skeletal muscle blood vessels during natural behavior is analogous to the vascular autoregulation that has previously been shown to occur in the denervated kidney during DS (27). Second, the autoregulatory response that we observed in denervated skeletal muscle blood vessels of unanesthetized cats during either DS or aortic constriction is remarkably similar, quantitatively, to that previously calculated by Jones and Berne (28) under better controlled but necessarily more artificial conditions. Finally, the sympathectomized limb shows autoregulative vasodilatation during DS despite the si-
multaneous onset of muscle atonia, which should reduce oxygen consumption and production of metabolites. Autoregulative vasodilatation under these experimental conditions can hardly be attributed to metabolic factors and might rather be due to myogenic mechanisms (29, 30).

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References
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