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Organ-Specific Changes in Sympathetic Nerve Activity Induced By Intravesical Pressure Fluctuation In Anesthetized Rats

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It is well known that micturition possibly induces cardiovascular disorders. However, the role of the autonomic nervous system has not been clear yet. In this report, we attempted to clarify the mechanism through the comparison of the organ-specific changes in three different sympathetic nerve activities (i.e., cervical (CvSNA), renal (RNA), and hypogastric (HgNA)) with hemodynamics.

Male Wister rats were anesthetized and a ballon catheter was inserted into the urinary bladder. Following the increase of intravesical pressure at 90 cm H_2O with the use of water reservoir, arterial pressure (AP) and heart rate (HR) were elevated by 4.8% and 2.5%, respectively. All three nerve activities were also accentuated but the magnitudes of increase were different with each other. The values of relative increasing ratio were 145.3% in HgNA, 28.1% in RNA and 2.5% in CvSNA. In the study of blood flow, the elevation of intravesical pressure induced an increase in carotid arterial flow by 23%, however, after deflation, the flow was decreased by 12%.

Thus, organ-specific changes in sympathetic nerve activity during an elevation of intravesical pressure should develop redistribution in blood flow, which might induce cardiovascular disorders related to micturition.

Key Words
Organ-specificity,
Sympathesic nerve activity,
Intravesical pressure,
Micturition,
Anesthetized rats,
Redistribution.

INTRODUCTION

Although there are numerous reports dealing with the relationship between micturition and cardiovascular disorders such as angina pectoris, cerebrovascular accident, and transient syncope, the mechanism has been still obscure. In these symptoms, autonomic nervous system must play an important role as several articles suggested (1, 2). However, it has not been clear yet whether the response of sympathetic nerve activities are identical in all respects and, furthermore, how the changes in sympathetic nerve activities control hemodynamics during micturition.

In a spinal man or animal (1, 3). the changes in blood pressure and

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heart rate during micturition were produced through spinal reflex. Because of the contribution of the sympathetic nervous system, this mechanism was named as vesico-sympathetic reflex. These reports also have suggested the development of different responses of sympathetic nerve activity to the vesical load through the spinal reflex because of the difference of responses by spinal level.

It is well known that sympathetic nerve activity regulates the various functions of the target organs (4). Although several reports (4, 5) have shown the specific responses of sympathetic nerve activities to the given stimuli, the differences of the responses among several sympathetic nerve activities to vesical contraction have not been clearly shown by direct recording.

If the potential disarrangement of sympathetic activity could be induced by micturition, the serious changes of blood flow to important organs could be developed, and consequently, it might cause the pathological state such as cerebrovascular disorders.

From these points of view, in this report, we conducted our experiment by recording three sympathetic nerve activities (i.e., hypogastric, renal and cervical) regulating different organs. In the comparison of these three nerve activities with arterial blood pressure, heart rate, and carotid blood flow, we attempted to clarify the mechanism of the development of physiological and pathological states related to micturition.

MATERIALS AND METHODS

Male Wister rats weighing 300 to 400g were anesthetized with urethane (1.2g/kg in each body weight) which was given intraperitoneally. as shown in Fig. 1, arterial blood pressure was measured through a catheter inserted into the left femoral artery. By triggering the arterial wave, heart rate was obtained. The left femoral vein was cannulated for venous injection.

A latex balloon catheter (2ml of the capacity) was inserted into the urinary bladder through a small incision at the vesical apex. This catheter was connected to a reservoir which contained water in rat body warmth (38℃). Bladder pressure was measured by a transducer. By a change in the height of the reservoir, water could be drained into and out the ballon and also various pressure could be given to the urinary bladder.

When the balloon in the bladder was filled with adequate volume of water and disconnected to the reservoir using three way stop-cock, the automatic contraction of the bladder could be developed. In this report, this spontaneous elevation in the vesical pressure was defined as active load. On the other hand, passive elevation directly given by a change of the reservoir height was defined as passive load.

Efferent sympathetic nerve activity was recorded from one of the bundles of cervical sympathetic trunk, renal nerve or hypogastric nerve on random selection basis. Each nerve was exposed under binocular microscope and placed on silver-silver bipolar electrode. The nerve potential was recorded using a high gain ampilifier and measured in arbitrary unit of in-

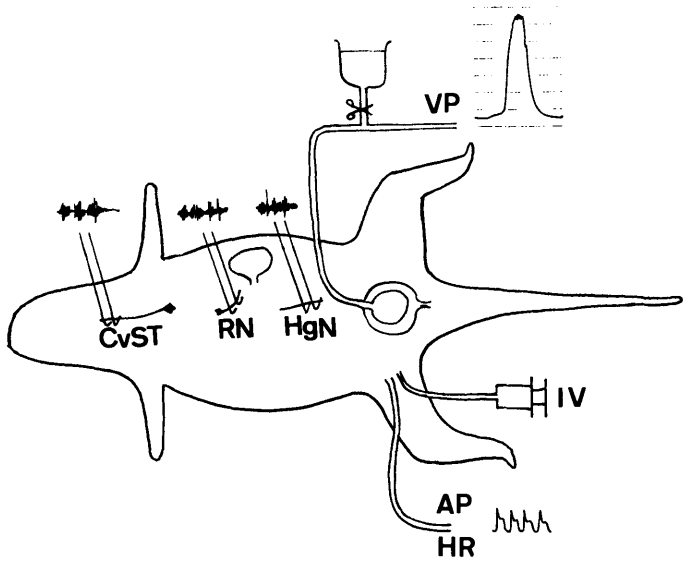


Figure 1. Schematic model of the experiment. A latex balloon was inserted into the urinary bladder and connected to a water reservoir in use of three way stop-cock. The catheter was connected to a transducer in order to mesure vesical pressure (VP). Arterial pressure (AP) and heart rate (HR) were also measured. Sympathetic nerve activity was recorded from one of the bundles of cervical sympathetic trunk (CvST), renal nerve (RN) or hypogastric nerve (HgN).

tegrated amplitude.

For the purpose of the investigation of blood flow to the head, in 8 rats, left carotid arterial blood flow was measured in use of an electromagnetic flow meter.

For statistical analysis, the relative percent change in each parameters was calculated in comparison with each values before the elevation in intravesical pressure. The results were graphed in terms of mean±S. E. M. Analysis of data was performed using ANOVA test for the examination of differences among three sympathetic nerve activities. The criterion for statistical significance was defined as $p<0.05$.

RESULT

1. Effects of Spontaneous Changes in Intravesical Pressure

When adequate volume (approximately 1ml) of water was filled in the balloon, spontaneous contraction of the bladder (active load) could be developed. As shown in Fig. 2, arterial blood pressure, heart rate and cervical sympathetic nerve activity were changed simultaneously in parallel with the fluctuation of intraves-

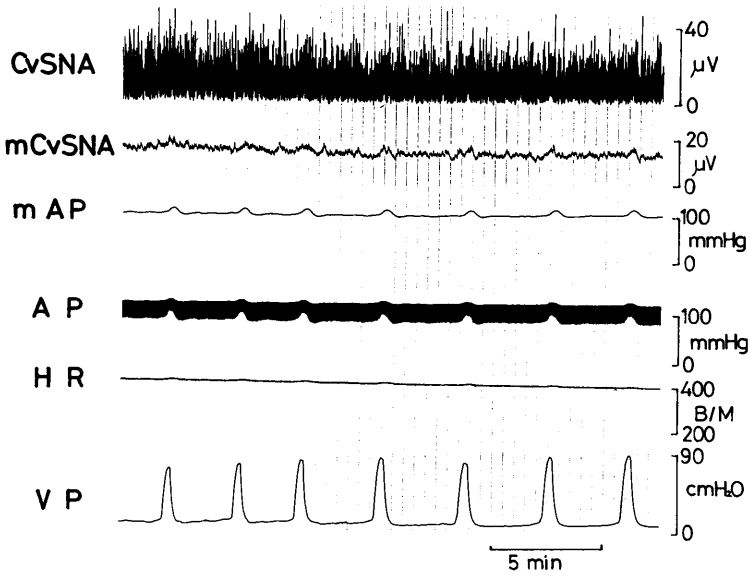


Figure 2. Typical record during spontaneous change in vesical pressure (active load). Simultaneous recording of sympathetic nerve activity, arterial pressure and heart rate. Note the spontaneous fluctuation of vesical pressure which was followed by changes of other parameters. Following abbreviations are used. CvSNA: cervical sympathetic nerve activity, mCvSNA: mean CvSNA, mAP: mean arterial pressure, HR: heart rate, VP: vesical pressure

ical pressure. It was clear that a rise in intravesical pressure was followed by an increase in sympathetic nerve activity, arterial pressure and heart rate.

2. Differences between Active and Passive Load to the Bladder

Fig. 3 shows the changes in mean arterial pressure, mean sympathetic nerve activity and two types of vesical load (passive load on each left, active load on each right). During either vesical loads, mean arterial pressure and sympathetic nerve activities were elevated. This figure also suggested the different responses of each sympathetic nerve activities to the given vesical load.

Because of the similar responses between active and passive loads and also difficulties to obtain same magnitude in the intravesical pressure during active load, results of passive vesical load at 90 cm H_2O was employed for the statistical analysis.

3. Statistical Analysis during Passive Load

Fig. 4 demonstrates the statistical changes in heart rate (HR), mean arterial pressure (AP), cervical sym-

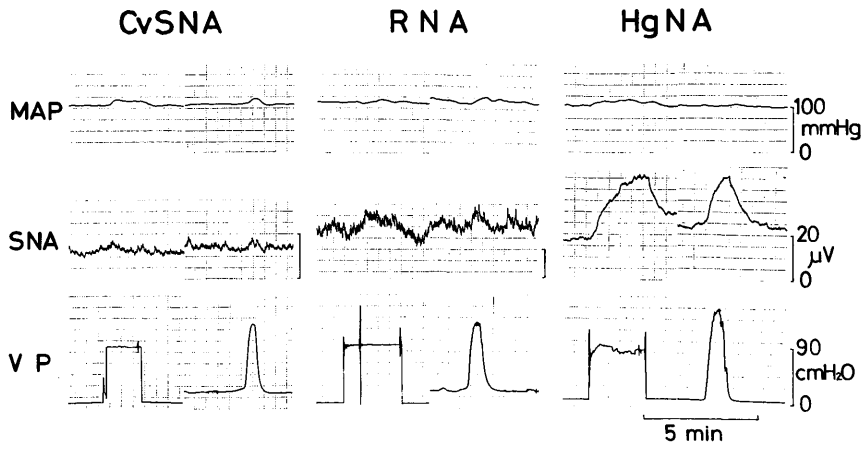


Figure 3. Comparison between passive (each left) and active load (eaci right). In either rises of vesical pressure, mean arterial pressure and sympathetic nerve activities were increased. Following abbreviations are used. RNA: renal sympathetic nerve activity, HgNA: hypogastric sympathetic nerve activity. Others are same as in Fig. 2.

pathetic nerve activity (CvSNA), renal sympathetic nerve activity (RNA) and hypogastric sympathetic nerve activity (HgNA). Each values are shown in relative percent change in comparison with the value before the load.

During a rise in intravesical pressure to 90 cm H_2O, all parameters were increased. Each increment ratios were 2.5% in heart rate, 4.8% in arterial pressure, 16.8% in cervical sympathetic nerve activity, 28.1% in renal sympathetic nerve activity and 145.3% in hypogastric nerve activity. These results clearly showed the different responses of three nerve activities to the same vesical load.

4. Blood Flow in Carotid Artery during a Change in Intravesical Pressure

The upper half of Fig. 5 represents a change in carotid arterial blood flow with simultaneous recording of heart rate and arterial pressure in a rat. During passive load of 90 cm H_2O to the bladder, carotid arterial flow was increased in parallel with heart rate and arterial pressure. Those statistical results in 8 rats were shown in the lower half of the figure. Vesical load of 90 cm H_2O increased carotid flow by 23% which was turned to a decrease by 12% after release from the load.

DISCUSSION

These results showed organ-specific increase in sympathetic nerve activity during vesical load. These also indicated that the sympathetic nerve which was closer to the bladder had

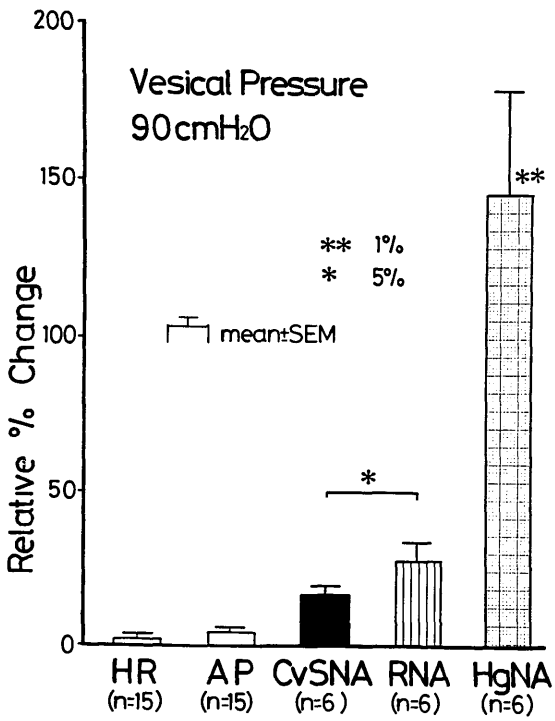


Figure 4. Statistical analysis of each parameters. During passive load at 90 cm H_2O, all parameters were increased but the increment ratio in each nerve activities were different. Values were described in the text. Same abbreviations are used as in Fig. 2 and 3.

the larger response in the amplitude.

The afferent pathway of this response is the pelvic nerve which perceives the changes in intravesical pressure (6). This nerve tract enters the sacral spine and reaches to micturition center in S2-4 level. The firing in this tract produces spinal or supraspinal reflex (7, 8, 9). These evidences suggest that both supraspinal and spinal reflexes play an important role to provoke organ-specific changes in sympathetic nerve activity.

Can the organ-specific changes in sympathetic nerve activity induce disorders related to micturition? A rise in vesical pressure induced an increase in all three sympathetic nerve activities in our study. Because sympathetic nerve activity has a stimulatory action on the cardiovascular system, both arterial blood pressure and heart rate was raised as shown in Fig. 3 and 4. This could induce an increase in cardiac work and, in hypertensive patients (1), result in much more significant hypertensive response in arterial pressure during micturition.

As for the different responses of nerve activities to the vesical load, these three sympathetic nerve activities showed different magnitude of increment ratio. The increase ratio was most prominent in hypogastric nerve activity and least in cervical sympathetic nerve activity.

The independent increase in cervical sympathetic nerve activity should induce the contraction of the arterial wall and reduce the blood flow in the area dominated by the carotid artery. However, the blood flow in the carotid artery was increased as shown in Fig. 5. This suggested that redistribution of the blood flow was developed by higher activity in other sympathetic nerve activity than cervical sympathetic nerve activity.

How does this redistribusion affect on the hemodynamics in the head? Because the peripheral cerebral artery has autoregulatory function in the control of blood flow (10), the increased part in blood flow must be drained into other arterial tree in the head. However, the elevation in

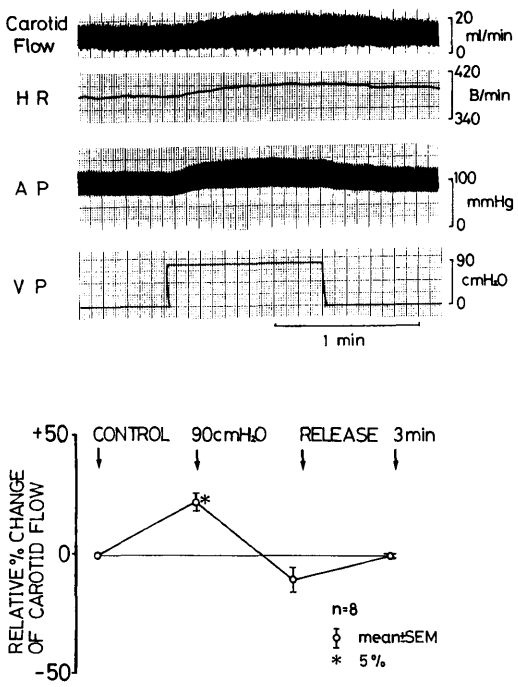


Figure 5. Upper half of the figure shows carotid flow, heart rate (HR), arterial pressure (AP) and vesical pressure (VP) in a rat.

Lower half of the figure shows relative percent change of carotid flow in comparison with the value before vesical load.

arterial pressure may give more tension to arterial wall and result in rupture of the wall.

It is also interesting to observe the change in the carotid arterial flow after the vesical load. When the balloon in the bladder was deflated, the carotid arterial flow was reduced in spite of the same value of arterial pressure as was observed in the control. This phenomenon may be due to failure of rapid adaptation of arterial tree to change in blood flow. If the autoregulatory function is failed more severely, such as in case of orthostatic hypotension (2), the shortage in cerebral blood flow may be developed more remarkably. This mechanism could be a cause of micturition syncope.

Thus, the changes in intravesical pressure induced the organ-specific responses in different sympathetic nerve activity. This phenomenon might develop redistribution in blood flow and also could be a factor to develop pathologic state related to micturition.

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