Kobe University Repository : Kernel

PDF issue: 2026-11-02

Effects of Peripheral Chemoreceptor Stimulation on Sympathetic Nerve Activities

Kujime,Kenichi
Sawatari,Hisayuki
Su,Michiyo
Ueba,Yasuyuki

(Citation)
Bulletin of allied medical sciences Kobe : BAMS (Kobe),4:33-38

(Issue Date)
1988-12-26

(Resource Type)
departmental bulletin paper

(Version)
Version of Record

(URL)
https://hdl.handle.net/20.500.14094/80070289

Effects of Peripheral Chemoreceptor Stimulation on Sympathetic Nerve Activities

Kenichi Kujime[1], Hisayuki Sawatari[2], Michiyo Su[3] and Yasuyuki Ueba[1]

Chemoreceptor stimulation induces various changes on hemodynamics. As we have reported before, when chemoreceptor was stimulated by hypoxia or hypercapnea, three different types of sympathetic nerve activity showed characteristic changes by each nerve. In that report, we concluded that this response might exert protective effects on important organs and was mainly produced in the central nervous system because denervation of peripheral chemoreceptor fiber induced minimal changes. However, the role of peripheral chemoreceptor should be demonstrated by direct stimulation of peripheral receptors.
In this report, our main purpose is to clarify the role of the peripheral chemoreceptor on the sympathetic nervous system by recording three different types of nerve activity in anesthetized rabbits.
When the carotid sinus was stimulated by local injection of lobeline, hypertension and bradycardia appeared. In the mean time, cardiac sympathetic nerve activity decreased. On the other hand, renal sympathetic nerve activity increased more than cervical sympathetic nerve activity did.
Thus, peripheral chemoreceptor stimulation induced organ-specific changes in the sympathetic nervous system. This response may control the hemodynamics much faster than the central chemoreceptor.

Key Words
Peripheral chemoreceptor,
Sympathetic nerve activity,
Rabbit,
Organ-specificity,
Lobeline.

INTRODUCTION

As we have reported before (1), hypoxia or hypercapnea induced characteristic changes in hemodynamics and organ-specific difference among sympathetic nerve activities. Because this response could not be abolished by the denervation of peripheral chemoreceptors, central chemoreceptor was seemed to play main role in this phenomenone. However, for further investigation of the role of peripheral chemoreceptors, it is necessary to examine the effects of direct stimulation of peripheral chemoreceptor.

Although several reports (1,2,3) have shown effects of simultaneous stimulation of central and peripheral chemoreceptor on the autonomic nervous system, effects induced by separated stimulation of peripheral chemoreceptor alone have not been cleared yet.

Since Heymans et al (4) first showed that simulation of the carotid bodies in dogs caused cardiac slowing, several

School of Allied Medical Sciences, Kobe University[1], Takasago Municipal Hospital[2], Department of Internal Medicine, Division I, School of Medicine Kobe University[3], Kobe, Japan.

reports have appeared which showed the effect of chemoreceptor on the hemodynamics. They used cyanide, lobeline and other drugs. In 1951, Bernthal et al (5) perfused the carotid bodies of dogs with hypoxic blood and they consistently obtained bradycardia in artificially ventilated dogs. De Geest el al (6) examined changes in ventricular contractility produced by perfusing one carotid body with blood having an oxygen saturation of 25%. These results suggested that peripheral chemoreceptor stimulation induces bradycardia by decreased cardiac sympathetic nerve activity.

Abboud FM et al (7) showed vasoconstriction in the skeletal muscle and vasodilation in the paw caused by peripheral chemoreceptor stimulation with nicotine or cyanide. They have indicated that peripheral chemoreceptor stimulation activates sympathetic nerve activity which controls the skeletal muscle.

Above results suggest that distribution of blood flow to organs is changed by stimulation of peripheral chemoreceptor and mediated by neural mechanism. Furthermore the blood flow control in each organ must be different. However, it is not clear yet how sympathetic nerve activities are changing during stimulation of peripheral chemoreceptor.

In this report we designed to clarify the role of peripheral chemoreceptor in the control of hemodynamics by recording three types of sympathetic nerve activities. The peripheral chemoreceptor was stimulated by local administration of lobeline. This investigation must lead to show the different role between peripheral and central chemoreceptor in the condition of hypoxia or hypercapnea.

MATERIALS AND METHODS

1. Surgical Procedures

Adult rabbits of unselected as to sex and ranging from 2.5 to 3.0 kg in weight were used. They were anesthetized with urethane (1200mg/kg) administered intraperitoneally. After a tracheotomy was performed, each rabbit was ventilated on mixture of oxygen and room air using a Harvard respirator pump. Gallamine (0.2mg/kg, i.m.) was injected initially to prevent movement and was repeated during the course of the experiment as required. Blood gas was measured on occasion and kept within the physiological range with supplement of bicrbonate or oxygen as necessary.

The right femoral vein was cannulated for intravenous administration of drugs. Blood pressure was recorded through a cannula inserted into the left femoral artery. A cannula was also introduced into the left lingual artery for injection of drugs to peripheral chemorecepor (8). On the same side all branches of the common carotid artery except the internal carotid artery were ligated. The rectal temperature was also monitored and maintained at 38°C with a heat pad.

2. Recording of Nerve Activity

Efferent sympathetic nerve activity was recorded from two of the bundles of left cervical sympathetic trunk, left renal nerve or right cardiac 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 amplifier and measured in arbitrary unit of integrated amplitude. These were recorded on chart paper simultaneously with arterial blood pressure and heart rate.

3. Protocol for Lobeline Administration

After all parameters were stabilized and the control level was recorded, Lobeline hydrochloride at a dose of

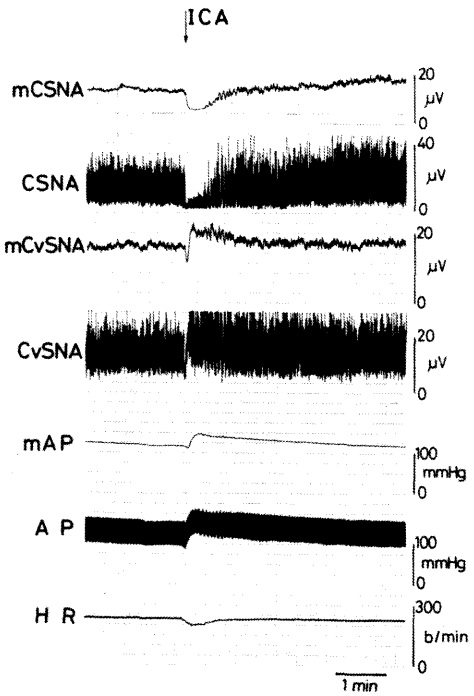


Figure 1. Typical changes induced by loveline injection
Following abbreviations are used. ICA : the point of intracarotid arterial injection. CSNA : cardiac sympathetic nerve activity. CvSNA : Cervical sympathetic nerve activity, AP : arterial pressure, HR : heart rate, m : mean.

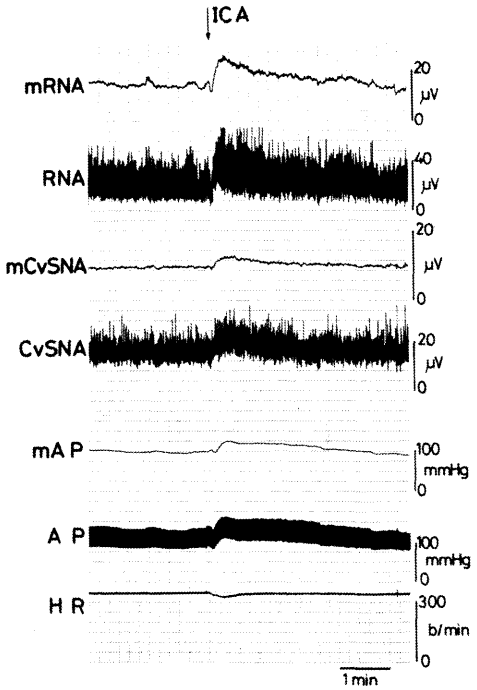


Figure 2. Typical changes induced by lobeline injection
RNA : renal nerve activity. Other abbreviations are same as in Fig. 1.

0.1mg per body was given to peripheral chemoreceptor through a catheter placed in the lingual artery. All parameters were recorded at least for 10 minutes continuously.

4. Data Analysis

The results are graphed in terms of mean $\pm$ S.E.M. Analysis of data was performed using Student's test and ANOVA test (9). The criterion for statistical significance was $P<0.05$.

5. Drugs

The drugs used in this experiment

were as in the following. : Lobeline hydrochloride (Dainippon Seiyaku), Gallamine (Teikoku Sangyo Co), Urethane (Wako Chem. Co.).

RESULTS

Figures 1 and 2 show effects of administration of lobeline through internal carotid artery (ICA) on the changes in heart rate (HR), arterial blood pressure (AP) and sympathetic nerve activities. As demonstrated in Fig. 1, local injection of lobeline induced an increase in AP and cervical sympathetic nerve activity (CvSNA) in contrast to decreases in heart rate and cardiac sympathetic nerve activity (CSNA). Although AP, HR and CvSNA in Fig. 2 showed the same pattern as in Fig. 1, renal nerve activity (RNA) increased more markedly than CvSNA did.

Figure 3 depicts statistical results obtained after ICA injection. All values are shown in relative % change by setting each control value as 100%. Mean AP (mAP) increased and HR decreased by 6% and 7%, respectively. Although RNA and CvSNA increased, those increment ratios were statistically different (23% in RNA, 7% in CvSNA). In contrast to these two nerve activities, CSNA decreased by 48%.

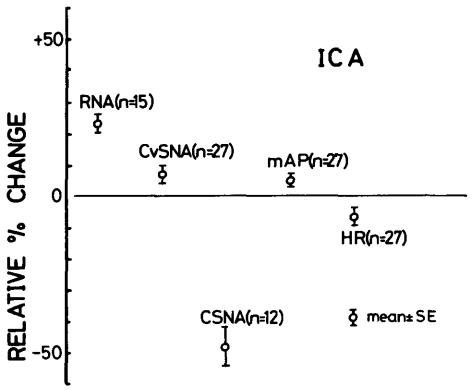


Figure 3. Statistical analysis of effects of lobeline
The control value was obtained at the point before the injection of lobeline. The effects of lobeline on each parameter were shown as relative % change by setting each control value as 100%. Sample numbers are shown in each parentheses. Values are shown as mean and its standard error.

DISCUSSION

1. Organ-Specific Changes in Three Nerve Activities

Thus, peripheral chemoreceptor stimulation induced organ specific changes in three different nerve activities.

During the last few years, an increasing number of reports (10) on organ-specific changes of sympathetic activity has considerably modified the classical concept that the sympathetic nervous system usually responds in a massive and generalized manner. This concept was based mainly on Cannon's work, and it had been endorsed for a long time by the results of electrophyiological studies on the sympathetic efferent functions.

As shown by Ninomiya et al (11,12), changes of arterial pressure and temperature differently affect sympathetic outflow to the skin, stomach, intestine, heart and kidney up to the degree of regionnally opposite changes of activity. We also demonstrates the organ-specific differences among sympathetic nerve activity induced by mic-

turition in the rat and human as well (13,14).

Bacelli et al (15) first suggested that integration of the arterial chemoreceptor reflex in cat was partly mediated through suprabulbar pathways. This suggestion was supported by the effects of arterial hypoxia on the heart rate in unanesthetized rabbits (16). These reports indicate that the integration of the responses may develop in the higher center such as the hypothalamus.

2. Role of Organ-Specificity

Our present results showed decrease in cardiac nerve activity concomitant with bradycardia. Because this nerve mainly controls heart rate and vagal nerve activity has minimal activity in the anesthetized animal, bradycardia must be developed by sympathetic neural mechanism in anesthetized rabbits. Bradycardia may resulted in the decrease of cardiac work and protective effects on cardiac hypoxia.

On the other hand, recorded sympathetic nerve activities, which cotrols the head and kidney, increased by different ratio. During hypoxia there is enhanced sympathetic constrictor activity in renal and intestinal beds, and inhibition of the sympathetic outflow to skin AV anastomoses (16,17). Blood distribution to the muscle or brain may be changed by this mechanism. This may show protective effects on the brain with an increase of the blood flow by less increase in the cervical sympathetic nerve activity (14).

Thus, these organ-specific responses in sympathetic nerve activity may exert protective effects on target organs in the hypoxia or hypercapnea.

3. Comparison Between Local and Central Chemoreceptor Stimulation

In our previous report (1), it was showed that hypoxia or hypercapnea induced the same characteristic changes in hemodynamics and sympathetic nerve activity. In that report, even after the denervation of peripheral chemoreceptors, the response was still persisted instead of smaller grade of the change. Thus, peripheral and central chemoreceptors show identical responses to sympathetic nerve activity and hemodynamics.

Because central chemoreceptor is stimulated by a change in pH of cerebro-spinal fluid (18), it may be present some delay between the stimulant and the response. This suggested that peripheral chemoreceptor will be activated much faster than central chemoreceptor because of its neural mechanism. And the receptor must play an important role in short-term control of the hemodynamics in the situation of hypoxia or hypercapnea during an exercise or other conditions.

CONCLUSION

Peripheral chemoreceptor stimulation induced organ specific changes in the sympathetic nervous system. Although the response was almost identical to the report of the central chemoreceptor, peripheral response may control the hemodynamics much faster than the central chemoreceptor.

REFERENCES

1. Kujime K, Matsukawa K, Ninomiya I : Effects of hypoxia and hypercapnea on sympathetic nerve activities. J Physiol Soc Japan 46:493, 1984
2. Iriki M, Kozawa E:Factors controlling the regional differentiation of sympathetic outflow-Influence of the chemoreceptor reflex. Brain Research 87:281-291, 1975
3. Korner PI:Circulatory adaptations in hypoxia. Physiol Rev 39:312-367, 1959
4. Heymans C, Bouckaert JJ, Dautrebande L. et al:Au sujet du mechanisme de la bradycardie provoquee par la nicotine, la lobeline, le cyanure, le sulfure de sodium, les nitrites et la morphine, et de la bradycardie asphyxique. Arch Intern Pharmacodyn 41:261-289, 1931
5. Benthal T, Greene W Jr, Revzin M:Role of carotid chemoreceptors in hypoxic cardiac acceleration. Proc Soc Expt1 Biol Med 76:121-124, 1951
6. De Geest H, Levy MN, Zieske H:Carotid chemoreceptor stimulation and ventricular performance. Am J Physiol 209:546-570, 1965
7. Abboud FM, Heistad DD, Mark AK et al:Differential responses of the coronary circulation and other vascular beds to chemoreceptor stimulation. p427-442 The peripheral arterial chemoreceptors Cambridge Univ Press 1975
8. Kujime K, Sawatari H, Sasaki J et al:Digitalis toxicity and baroceptor in rabbits. Bull Allied Med Sci (Kobe) 1:21-30, 1985
9. Snedecor, G.W. and Cochran, W.G.:Satistical method. USA, Iowa State University Press., 1980, P253-272.
10. Simon E, Riedel W:Diversity of regional sympathetic outflow in integrative cardiovascular control:patterns and mechanisms. Brain Research 87:323-333, 1957
11. Ninomiya, I. and Irisawa, H. :Summation of baroceptor reflex effects on sympathetic nerve activities. Am. J. Physiol. 216:1330-1336, 1969
12. Irisawa H, Ninomiya I, Woolley G:Efferent activity in renal and intestinal nerves during circulatory reflexes. Jap J Physiol 23:657-666, 1973
13. Kujime K, Sawatari H, Su M et al:Mechanism of hemodynamic changes induced by micturition in humans subjects. Bull Allied Med Sci (Kobe) 3:45-52, 1987
14. Kujime K, Sawatari H, Ueba Y et al:Organ-specific changes in sympathetic nerve activity induced by intravesical pressure fluctuation in anesthetized rats. Bull Allied Med Sci (Kobe) 2:13-20, 1986
15. Baccelli G, Guazzi M, Libretti A et al:Respiratory influences upon depressor and pressor responses to stimulation of the aortic nerve in the decerebrate cat. Experimentia 20:95-96, 1964
16. Korner PI, Uther JB:Dynamic characteristics of the cardiovascular autonomic effects during severe arterial hypoxia in the unanesthetized rabbit. Circulation Res 24:671-685, 1970
17. Chalmers JP Korner PI:Effects of arterial hypoxia on the cutaneous circulation of the rabbit. J Physiol London 184:685-697, 1966
18. Robin ED, Whaley RD, Crump CH et al:Acid-base relations between spinal fluid and arterial blood with special reference to control of ventilation. J Appl Physiol 16:473-484, 1961