Anesthesiology
63:500–508, 1985

Circulatory Responses to Baroreflexes, Valsalva Maneuver, Coughing, Swallowing, and Nasal Stimulation during Acute Cardiac Sympathectomy by Epidural Blockade in Awake Humans

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Reflex circulatory responses are chiefly governed by the integrated functions of both sympathetic and parasympathetic nervous systems at any moment. To examine how sympathetic denervation of the important effector organ, the heart, modifies such reflex responses, the authors compared circulatory responses to arterial baroreflexes, the Valsalva maneuver (VM), coughing (C), swallowing (S), and nasal stimulation (NS) before and after cervical epidural blockade using 10 ml of 1.5% lidocaine in awake, healthy humans.

The cervico-thoracic sympathetic denervation (sensory block of C_4–T_7) caused a slight suppression of the baroreflex sensitivity assessed by increases in RR intervals to increased systolic blood pressure with a pressor test (phenylephrine) in all eight subjects studied; the mean slopes of the regression lines were 29.1 ± 9.8 ms · mmHg^{-1} before the blockade and 17.2 ± 6.3 ms · mmHg^{-1} after the blockade ($P < 0.05$). However, the baroreflex sensitivity to a depressor test (nitroglycerin) remained unchanged following the blockade. Furthermore, the responses in heart rate and blood pressure to VM (Phases II and IV) and the responses in heart rate to C, S, and NS were partially suppressed after the blockade ($P < 0.05$). Despite these suppressions, the overall responses to VM, C, S, and NS remained unchanged after the blockade. No predominant parasympathetic responses such as profound hypotension and bradycardia were observed during any maneuver after the blockade.

Since the vagus nerves were kept intact, these results indicate that acute sympathetic denervation of the central organs appears to preserve reflex circulatory responses to physical maneuvers such as producing high intrathoracic pressure, moderate changes in blood pressure or swallowing, though with some suppression of the cardiac acceleratory response. The results suggest that sympathetic control of heart rate functions as an inhibitor of the vagus rather than an active cardiac accelerator. (Key words: Anesthetic, local: lidocaine. Anesthetic techniques: epidural. Heart: cardiovascular reflexes; sympathectomy. Reflexes: baroreceptor; Valsalva maneuver; coughing. Sympathetic nervous system: reflexes; catecholamines.)

IT IS WELL KNOWN that numerous maneuvers such as tracheal intubation, insertion of a nasogastric tube, suctioning from nose or trachea, and coughing or bucking could elicit changes in heart rate and blood pressure. These reflex circulatory responses are governed chiefly by the balance of sympathetic and parasympathetic tone existing at any moment.[1–7] Since cardiac responses to neural stimulations in one autonomic division depend upon the level of activity in the other autonomic division,[8] high-level sympathectomy induced by epidural anesthesia could disturb the balance of autonomic functions. To assess the overall function of the autonomic nervous system, arterial baroreflex function and the Valsalva maneuver have been extensively employed.[5–7] The evidence that autonomic functions are impaired in anesthetized subjects[9–11] and in patients with circulatory disorders such as hypertension, congestive heart failure, coronary artery disease[12–17] is increasing.

Cardiac sympathetic denervation itself by epidural block does not appear to produce any remarkable cardiovascular perturbations.[18–20] Recently, however, Dohi *et al.*[21] reported that cardiac sympathectomy induced by epidural anesthesia partially suppressed baroreflex responses to a pressor test in lightly anesthetized, paralyzed humans. In their previous study[22] they also showed that it suppressed heart rate and blood pressure responses associated with mechanical stimulation to the carina. Although they observed no predominant vagotonic responses in either study,[21,22] it is possible that the presence of anesthesia and positive-pressure ventilation employed in the paralyzed humans of these studies could, to some extent, affect or modify the autonomic reflex responses.[4,7] Therefore, we undertook the present study in awake humans to examine how cardiac sympathectomy by high-level epidural block modifies autonomic circulatory functions, especially arterial baroreflex function (by pressor or depressor test and the Valsalva maneuver), which is a very important neural control system for the maintenance of cardiovascular stability in humans.

High-level epidural anesthesia also will interrupt sympathetic afferent and efferent impulses of the lungs and the great vessels where many important peripheral receptors affecting or modulating the circulatory reflexes exist.[23–25] Thus, we also examined the circulatory responses to other brief noninvasive maneuvers such as coughing,[6] swallowing, and nasal stimulation.[4,25] The last two may not directly stimulate arterial and cardiopulmonary baroreceptors, or lung irritant and stretch receptors.

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Received from the Department of Anesthesiology, The University of Tsukuba Hospital and Institute of Clinical Medicine, University of Tsukuba, Sakuramura, Ibaraki 305, Japan. Accepted for publication June 11, 1985.

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Methods

Subjects

Eight young healthy unpremedicated male volunteers (medical students), 22 or 23 yr old (64 ± 5 kg in weight, 174 ± 4 cm in height), were studied. All of them were free from cardiopulmonary and neurologic disorders. The study was approved by the Clinical Investigation (Jutaku Kenkyu) Committee of the University of Tsukuba Hospital.

Procedures

An intravenous cannula was placed for infusion of lactated Ringer's solution, 5 $ml \cdot kg^{-1} \cdot h^{-1}$; a radial artery catheter was inserted for direct measurements of arterial blood pressure (AP) and for blood samplings. AP was measured through an appropriate transducer (Statham, P23®, Gould-Statham) and an amplifier. Heart rates (HR) were calculated on a beat-to-beat basis electronically (1321 Tachometer®, Sanei Co., Tokyo) through ECG. ECG, AP, and HR were recorded throughout the study (Sanei).

Following control measurements, each person was placed in the lateral decubitus position, and after sterile preparation and draping of each volunteer, 1–2 ml of 1% lidocaine was injected intradermally and subcutaneously at the C7–T1 intervertebral space for cervical epidural anesthesia. A 17-G Tuohy needle was inserted into the epidural space using the hanging drop technique. After identification of the epidural space, 10 ml of 1.5% lidocaine without epinephrine was injected into the space over 30 s. Each person then was placed in the supine position. The level of analgesia was measured using the pin-prick method 15 min after the injection and at the termination of the following tests (approximately 30–40 min after the epidural injection).

Protocol

After a 15-min rest and obtaining resting AP and HR, the following tests were performed on each subject in the supine position. Each person was allowed to return to resting blood pressure between each test.

Baroreceptor Reflex. The pressor test was performed by a bolus intravenous injection of phenylephrine, 1 ml of 250 μg. The depressor test was performed by a bolus injection of nitroglycerin, 1 ml of 500 μg. In both tests the doses were chosen following several attempts to increase or decrease AP by about 20% in this age group.

Valsalva Maneuver. The volunteers performed the Valsalva maneuver by blowing into a tube connected to an aneroid manometer and maintaining a pressure of 40 mmHg for 15 s.[13] Each person was instructed to take as deep a breath as possible before blowing and, after release of the Valsalva maneuver, was asked to relax and breath quietly, but neither talk nor move. The maneuver was performed twice. The responses to the Valsalva maneuver were divided into the four sequential phases according to Elisberg.[13] They are as follows: Phase I, an evanesent increase in AP and reduction of HR immediately after the onset of straining; Phase II, a decrease, and later partial recovery of AP and a speeding of HR during the period of straining; Phase III, a sudden brief further reduction of AP and an increase of HR immediately following the release of straining; Phase IV, a terminal increase in AP above control levels and slowing of HR.

Coughing Test. Each person was asked twice to make three forceful coughs within 5 s on command (as had been done previously in the supine position). Care was taken to encourage all people to cough with vigor. Each person lay still after coughing.

Swallowing. Each person was asked to swallow his saliva twice.

Nasopharyngeal Stimulation with Cold Water. During quiet breathing, each person was given 2 ml of cold water intranasally with his or her eyes closed.

After the establishment of cervical epidural anesthesia, the above tests were repeated in a manner similar to those performed before the block.

Arterial blood gas analyses were performed before and after the block. Three samples of arterial blood also were taken for measurements of plasma concentrations of epinephrine and norepinephrine before and after the block: one for control, and one immediately after the pressor test, the other immediately after the depressor test. Plasma concentrations of catecholamines were measured by high-pressure liquid chromatography using the system based on the trihydroxyindole reaction.[26]

Data Analysis

The pressor and the depressor test data were analyzed using least-squares linear regression analysis on the linear regions between blood pressure and RR interval. The slopes of the regression lines (in ms of RR interval change per mmHg increase or decrease in systolic pressure) for each test were constructed in each person before and after the block. With bolus administration of phenylephrine, two pressure peaks were seen in all persons. The early one with a reflex decrease in heart rate was used to calculate the pressor test slope. Only the individual regression slopes with correlation coefficients greater than 0.85 were adapted.

HR and AP responses to Valsalva maneuvers were analyzed by the method described by Elisberg *et al.*[13] After release of the Valsalva maneuver (Phase IV), the correlation coefficient and the slope of the linear regression line were calculated for the systolic arterial pressures and

TABLE 1. Mean Values of Heart Rate (HR), Systolic Arterial Pressure (AP), Values of Arterial Blood Gas Analyses, and Plasma Concentrations of Epinephrine and Norepinephrine before and after the Cervical Epidural Block (mean ± 1 SD)

	Before Block	After Block (C3.9 ± 0.4–T6.8 ± 0.9)
HR (beats/min)	66 ± 8	58 ± 7*
AP (mmHg)	122 ± 8	117 ± 9*
Pa_{O_2} (mmHg)	94 ± 3	90 ± 3
Pa_{CO_2} (mmHg)	41 ± 1	42 ± 2
pH_a	7.43 ± 0.01	7.42 ± 0.02
BE (mEq/l)	2.8 ± 1.0	3.2 ± 0.7
Epi. (ng/ml)	0.03 ± 0.01	0.03 ± 0.02
Norepi. (ng/ml)	0.10 ± 0.03	0.11 ± 0.04

* $p < 0.05$ *versus* before block.

RR interval.[15] Baroreflex sensitivity during the Valsalva maneuvers was defined as the change in RR interval in ms per mmHg change in systolic arterial pressure.

The responses in HR and AP to coughing, swallowing, and nasal stimulation were assessed by their magnitude of change from resting values before and after the epidural block.

Paired Student's *t* test was used to determine statistical significance before and after the block. Analysis of variance also was used for difference in initial values before each test to obtain a more precise evaluation of the results. A value of $P < 0.05$ indicated statistical significance. All values were expressed as means ± 1 SD.

Results

The mean values of analgesic level measured by the pin-prick were $C_{3.9\pm0.4} - T_{6.8\pm0.9}$ (with a range from C3–C5 to T5–T8). No one complained of respiratory difficulty except for bilateral nasal congestion, which was accompanied by positive Horner's signs in all subjects after the block. There were small individual variations in motor blockade of the upper extremities following the cervical epidural block. HR and AP decreased significantly after the block; the mean values of their per cent decreases from control were 10.5 ± 3.4% and 3.6 ± 7.2%, respectively. There was no significant difference in arterial blood gases and the plasma concentrations of epinephrine and norepinephrine before and after the block (table 1). The mean values for hematocrit and plasma concentrations of Na and K were 40.7 ± 3.0%, 141.5 ± 2.5 mEq·l^{-1}, and 3.6 ± 0.1 mEq·l^{-1}, respectively.

TABLE 2. The Changes in Heart Rate (HR) and Systolic Arterial Pressure (AP) to Nitroglycerin and Phenylephrine before and after the Cervical Epidural Block

	Before Block		After Block	
	AP (mmHg)	HR (beats/min)	AP (mmHg)	HR (beats/min)
Depressor test				
Before	130 ± 12	61 ± 7	130 ± 14	59 ± 7
After	102 ± 18	85 ± 5	105 ± 16	78 ± 9
Pressor test				
Before	128 ± 13	67 ± 10	123 ± 10	61 ± 11
After	148 ± 20	42 ± 9	145 ± 15	44 ± 6

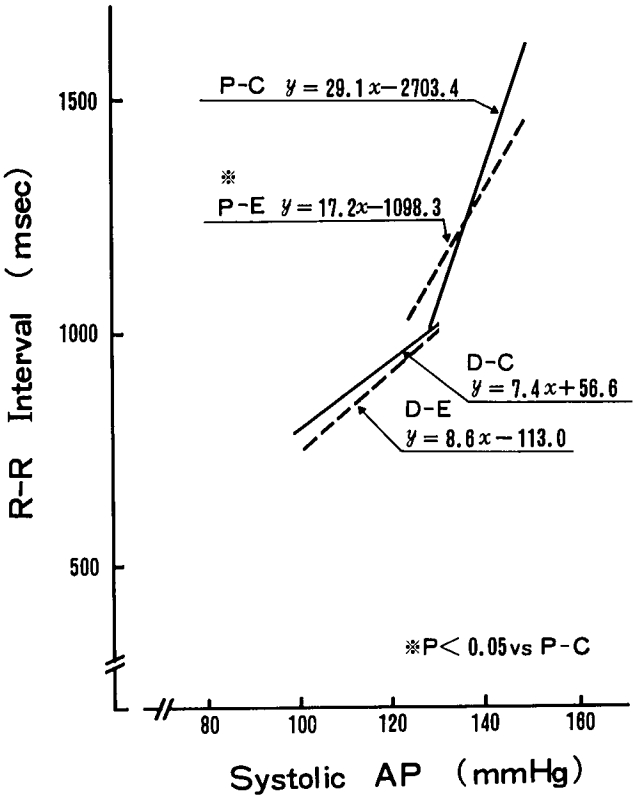

FIG. 1. Regression lines for the pressor (P) and depressor (D) tests before (C) and after (E) epidural block. The slope of the pressor test after epidural block (P-E) was significantly different from the slope during control (P-C) ($P < 0.05$).

BAROREFLEX RESPONSES

There were no significant differences in the maximum change in AP resulting from nitroglycerin and phenylephrine between before and after the block (table 2). The epidural block produced a significant suppression of the slope of the pressor test in all subjects studied; the mean values of the slopes before and after the block were 29.1 ± 9.8 ms·mmHg^{-1} and 17.2 ± 6.3 ms·mmHg^{-1} ($P < 0.05$), respectively. On the other hand, the mean slope of the depressor test was 7.4 ± 2.6 ms·mmHg^{-1} before the block and 8.6 ± 3.9 ms·mmHg^{-1} after the block; the difference being insignificant (fig. 1). The correlation coefficients for any regression lines obtained were greater

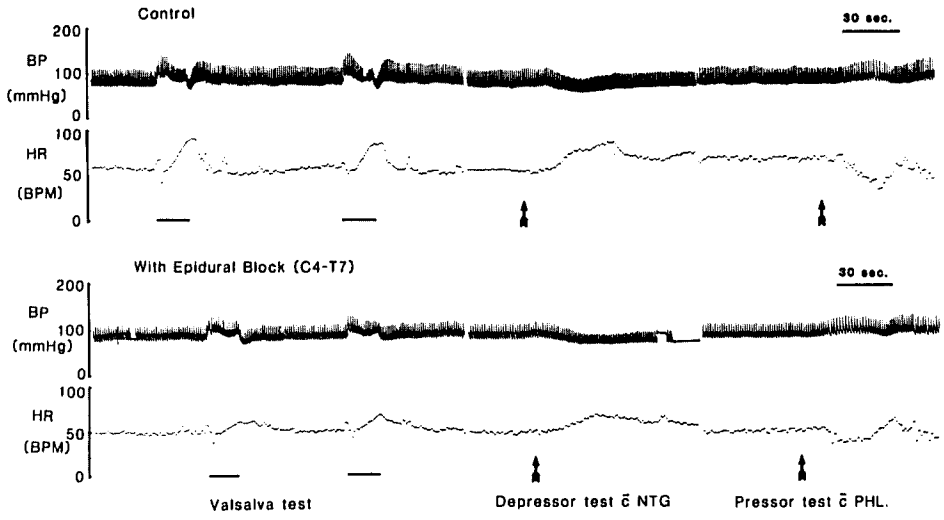

FIG. 2. Polygraph tracings of arterial blood pressure (BP) and heart rate (HR) to pressor and depressor tests and the Valsalva maneuvers before (*upper panel*) and after (*lower panel*) epidural block.

than 0.88 for both tests before and after the block in all subjects studied.

VALSALVA MANEUVER

The cervical epidural block did not produce any change in the overall responses of HR and AP to the Valsalva maneuver (fig. 2). However, the responses of HR and AP in Phases II and IV were depressed significantly after the block ($P < 0.05$) (figs. 3 and 4). There was a good correlation between the responses of HR and AP during Phase IV; the correlation coefficients of any linear regression lines were greater than 0.91 except one in which the value was 0.74. There was no significant difference in the mean values of the slope between after the block (5.48 $\pm$ 2.30 ms $\cdot$ mmHg^{-1}) and before the block (6.17 $\pm$ 3.27 ms $\cdot$ mmHg^{-1}).

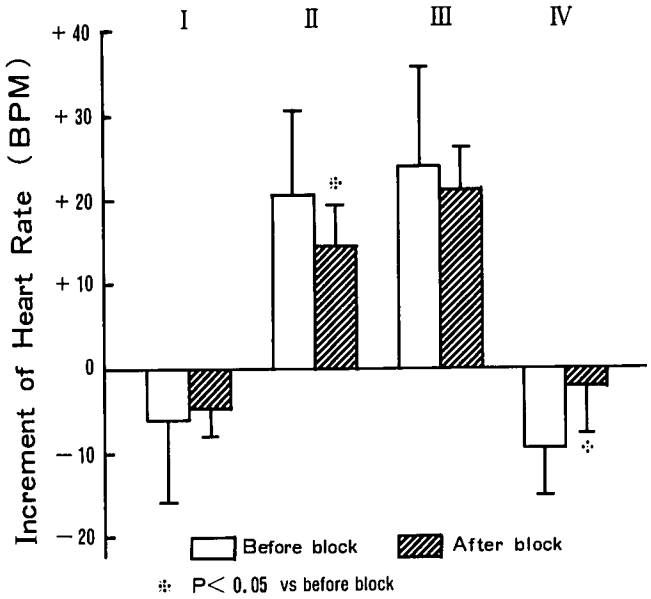

FIG. 3. Increment of heart rate in the four phases during the Valsalva maneuver before and after epidural block.

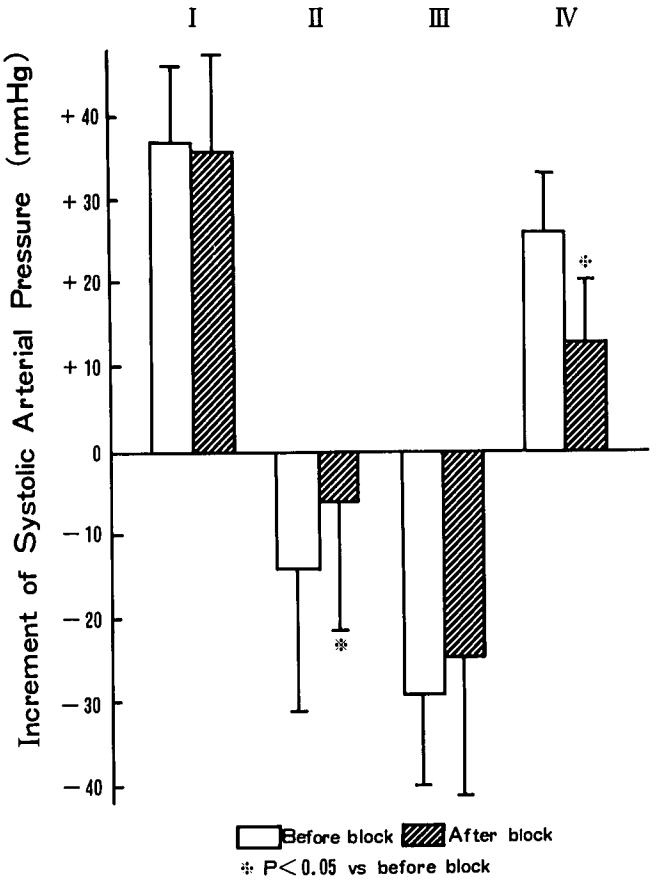

FIG. 4. Increment of systolic blood pressure in the four phases during the Valsalva maneuver before and after epidural block.

TABLE 3. Mean values (±SD) in Heart Rate (HR) and Systolic Arterial Pressure (AP) Due to Coughing, Swallowing, and Nasal Stimulation before and after Cervical Epidural Block

	Before Block		After Block	
	AP (mmHg)	HR (beats/min)	AP (mmHg)	HR (beats/min)
Coughing				
Precoughing	129 ± 12	65 ± 6	122 ± 9	57 ± 7*
Postcoughing	134 ± 11	96 ± 17	128 ± 13	74 ± 11*
Swallowing				
Preswallowing	125 ± 10	64 ± 6	114 ± 12	53 ± 4*
Postswallowing	130 ± 6	81 ± 7	120 ± 11	66 ± 11*
Nasal stimulation				
Prenasal stm.	130 ± 16	65 ± 6	123 ± 12	62 ± 10*
Postnasal stm.	140 ± 10	85 ± 5	129 ± 13	77 ± 10*

*$P < 0.05$ *versus* before block.

COUGHING, SWALLOWING, AND NASAL STIMULATION

Coughing, swallowing, and nasal stimulation with cold water always produced increases in HR and AP in all subjects studied (table 3); an example is illustrated in figure 5. The changes in AP following the block were not significantly different from those before the block. However, the magnitudes of changes in HR to all three maneuvers were depressed significantly ($P < 0.05$, fig. 6). Although significant increases in HR followed three vigorous coughings, AP remained at the level of control after the coughs. The changes in HR returned to control within 15 s after the coughs and swallowing, but the changes in HR following nasal stimulation lasted longer (30–40 s).

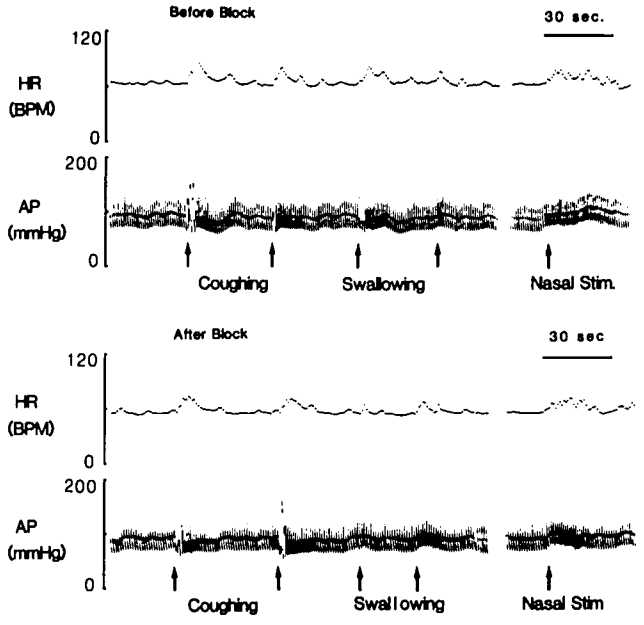

FIG. 5. Polygraph tracings of arterial blood pressure (AP) and heart rate (HR) to coughing, swallowing, and nasal stimulation before (*upper panel*) and after epidural block (*lower panel*).

PLASMA CONCENTRATIONS OF EPINEPHRINE AND NOREPINEPHRINE

There was no significant difference in plasma concentrations of both epinephrine and norepinephrine between before and after the block (table 1). Neither the pressor test nor the depressor test caused any significant changes in those concentrations both before and after the block (fig. 7).

There was no difference in analgesic levels between at 15 min and 40 min after the epidural injection.‡

Discussion

The purpose of the present study was to examine the manner in which sympathetic denervation of the heart by epidural anesthesia modifies reflex circulatory responses. We tested circulatory responses to five different maneuvers, increasing or decreasing AP, the Valsalva maneuver, coughing, swallowing, and nasal stimulation. The results obtained indicate that high-level sympathectomy induced by epidural anesthesia does not greatly impair reflex circulatory responses, though the responses in HR to the maneuvers were suppressed partially, probably by the sympathetic efferent block of the heart. In addition to the heart, cervical epidural anesthesia should also block sympathetic innervation of the lungs and the great vessels at the spinal cord level,[21,22] because we obtained complete sensory analgesia of C4–T7 with a potent local anesthetic. In such central organs, there are many important peripheral receptors such as arterial baroreceptors, cardiopulmonary receptors, lung irritant and stretch receptors, *etc.* These are usually tonically active through the balance of both sympathetic and parasympathetic tone and could modulate the reflex responses of each other.[1,3,7,23] Regarding autonomic functions, each of the five maneuvers is complicated[3] and does not involve only one reflex arc. Therefore, the results are discussed either separately or in combination.

BAROREFLEX RESPONSES

The arterial baroreceptors normally respond more actively to a decrease in pressure than to an increase, *i.e.*, are more effective in compensating for acute hypotension than acute hypertension.[7,26] We thus expected that sympathectomy of the heart should cause serious impairment of reflex circulatory control as suggested in the case of

‡ In the other series of eight persons under the same experimental conditions, plasma concentration of lidocaine measured by fluorescence polarization immunoassay (FPIA) were 2.6 ± 0.8 μg/ml (range 1.6–3.7 μg/ml) and 2.4 ± 1.0 μg/ml (range 1.6–4.3 μg/ml) at 20 and 30 min after the epidural injection of lidocaine, respectively, during which most of the tests were performed.

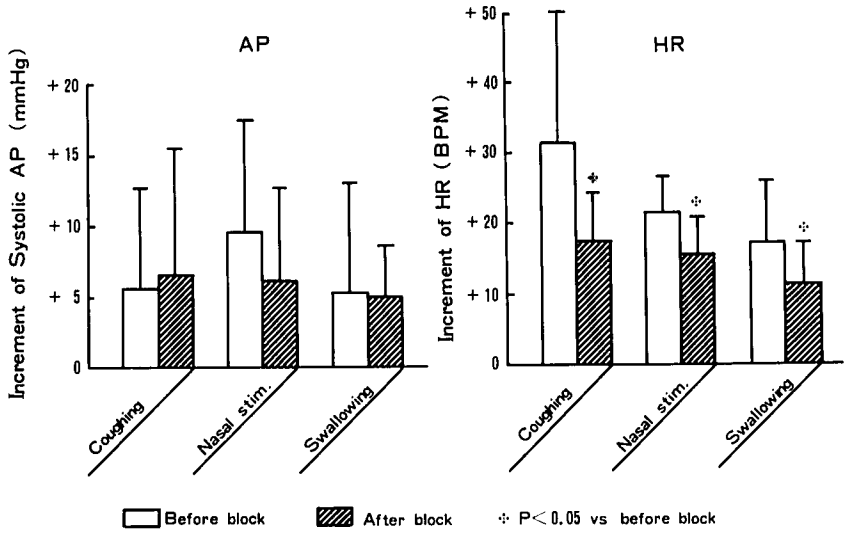

FIG. 6. Increment of AP (*left*) and HR (*right*) to coughing, nasal stimulation, and swallowing before and after epidural block.

the anesthetized dog treated with β-adrenergic blocking agent.[2] However, the results demonstrated that cervical epidural block only partially suppressed the baroreflex sensitivity to the pressor test and did not produce any change whatsoever in the sensitivity to the depressor test.

There are considerable differences in baroreflex sensitivity among the methods used to test for it such as the pressor test, depressor test, Valsalva maneuver, and neck suction.[15,27-29] and the values of the slopes of the regression lines to the pressor test are always greater than those to the depressor test both in humans[1,3,15,27,28] and animals.[29] Phenylephrine[1-3,15,22,27] and nitroglycerin[1,3,15] have been used extensively for the measurement of the sensitivity of the baroreflexes because of no demonstrable intrinsic effect on HR. A recent report in dogs indicates that phenylephrine has an enhancing effect on the baroreflex response, possibly resulting from a modification of baroreceptor output by direct reduction of the radius of the carotid sinus.[30] This may account for the greater slope of the pressor test in the present study as well as in the others.[15,27,28] In addition, even though we observed similar changes in AP by the same dose of each agent before and after the block, (table 2) the absence of direct efferent sympathetic modulation of baroreceptor discharges might have affected baroreceptor sensitivity. It is reported that an increase in cardiac sympathetic activity produced by decreasing AP elicits smaller changes in HR relative to the increase in parasympathetic tone produced by increasing AP.[31]

Cardiopulmonary baroreceptors could be affected by increasing or decreasing the central blood volume secondary to peripheral vasoconstriction or vasodilation.[3,32-34] Presumably, afferent impulses originating in the cardiopulmonary area relayed centrally in the vagi

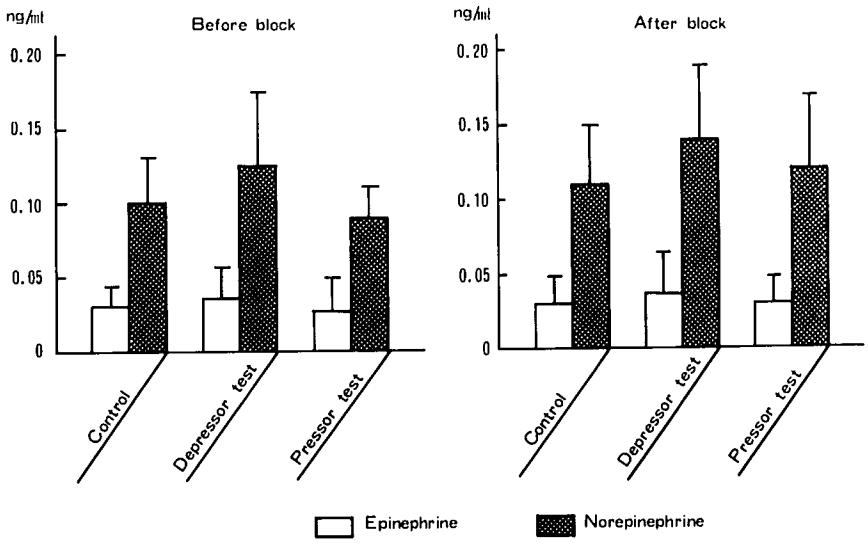

FIG. 7. Changes in plasma concentrations of epinephrine and norepinephrine to depressor and pressor tests before (*left*) and after epidural block (*right*).

could modulate HR responses to phenylephrine or nitroglycerin. Circulating catecholamines also can affect the baroreceptors directly or indirectly via alteration in the tone of the carotid sinus vascular smooth muscle,[34,35] thus a difference in the plasma concentrations of circulating catecholamines between the pressor and the depressor test should be considered.[35] The absence of significant differences in plasma levels of epinephrine and norepinephrine before and after the block precludes this possibility from the present results. At present we are unable to explain the discrepancy in the effects of cardiac sympathectomy on the baroreflex sensitivities between that of decreasing and increasing AP. A similar discrepancy also has been observed in the effects of 1.5 MAC isoflurane in humans.[27]

Valsalva Maneuver

The valsalva maneuver is a widely used test for human autonomic functions.[3,12,15] In the present results the overall responses in HR and AP to the maneuver were not markedly different following the epidural block. In subjects with intact autonomic effectors, the cardiac output response to the Valsalva maneuver has a large mechanical and a relatively small reflex component,[5] whereas the increase in total peripheral resistance is almost entirely reflex and is mediated through sympathetic-mediated constrictor mechanisms.[5] The responses during Phases I and III, which are chiefly determined by the mechanical effects of forced expiration,[2,3] were not affected; this could indicate the absence of an important effect of motor blockade after the epidural block in the present study. Thus, the suppression of the responses in Phases II and IV could be due to the sympathectomy induced by the cervical epidural. It has also been reported in humans that sympathetic blockade by propranolol suppresses the responses in HR of Phases II and IV.[2,3]

It has been suggested that during the Valsalva maneuver, several groups of the low-pressure receptors including cardiopulmonary baroreceptors can be stimulated[2,7,25,28,31] and the role of the different receptor groups may vary at different levels of pressure (2.5 to 35 mmHg).[5] Therefore, without measuring the pressure of intrathoracic great vessels, we can not exclude the possibility that such receptor activity could modify the responses, even though a similar pressure of 40 mmHg at the mouth was observed before and after the block in the present study.

Coughing

The heart rate response to cough recently was demonstrated to be a reliable index of integrity of the capacity for cardiac accelerator.[6,36] The increase of about 30 beats/min in HR in the present study is quite similar to that observed in subjects aged 20–29 yr in the study done by Wei *et al.*[36] It is thought that the tachycardic response following cough represents, at least in part, a baroreceptor-mediated response to the post-cough-reduction in arterial and pulse pressure.[6] However, we did not find this in the present study; arterial and pulse pressure remained stable following three coughs in all subjects studied (fig. 5).

The tachycardic response to cough was reduced significantly following the cervical epidural block. The reduction in peak HR to cough could be due to cardiac sympathetic block of the heart and probably less likely to the differences in baseline heart rate or blood pressure, reflex sensitivities, or cough-induced physical dynamics.[6] Since intrathoracic pressure was not measured in the present study, it is also possible that the block might cause a less forceful cough because of a decrease in both the ability to expand the chest wall and to exhale gases secondary to a possible slight motor blockade of expiratory muscles.[37] However, previous measurements in human subjects have demonstrated that cough-generated transient intrathoracic pressure elevations normally range from 25 to 250 mmHg[6] and HR responses are not correlated with the magnitude of the intrathoracic pressure elevation.[6]

Vigorous coughs also can affect the pressure of intrathoracic great vessels and cardiopulmonary baroreceptors, and lung irritant and stretch receptors in a manner similar to that of the Valsalva maneuver. However, since such receptors mediate a bradycardiac response when stimulated by increasing the pressure,[4,7,23,25] contributions of such receptors in reflex circulatory responses to coughing could not be involved in any important way.

Swallowing and Nasal Stimulation

It has been observed that swallowing evokes transient tachycardia (increases of 10–30 beats/min for a few minutes and nasopharyngeal stimulation with water evokes reflex transient bradycardia in anesthetized dogs.[25] In the present study both swallowing and nasal stimulation produced transient tachycardia, which was partially reduced by the epidural block. These responses in HR seem to be modified by respiration[4,25] when they are timed to occur in the expiratory phase of the respiratory cycle.[4,24,25] Since neither cardiopulmonary receptors, nor lung irritant and stretch receptors are likely to be stimulated by both maneuvers, we may consider the partial suppression observed to be due purely to sympathetic denervation of the heart.

Epidural anesthesia-induced circulatory changes related to the neural blockade might be modulated by the autonomic nervous system, depending on the level of circulating local anesthetic.[38] Also, systemic lidocaine can suppress the cough reflex[39] and probably reflex circulatory

responses. Dohi *et al.*[22] have suggested that following its epidural injection circulating local anesthetic (mepivacaine) is unlikely to affect the baroreflex control of HR in anesthetized, mechanically ventilated humans. A recent abstract, however, demonstrated that in awake dogs plasma concentrations of lidocaine of 3–4 μg/ml altered the baroreflex control of HR to phenylephrine, probably by increasing the efferent vagal tone, but a concentration of 1–2 μg/ml did not.[40] Because of a 1.6–4.3 μg/ml of plasma lidocaine level conjectured in the present study, we cannot disregard a possibility that systemic pharmacologic effects of lidocaine might affect the results. However, no evidence of increased vagal tone in the present results should preclude such a possibility. This suggests that the partial suppression of reflex circulatory responses were attributable to sympathectomy by cervical epidural block *per se*.

Exercise cardiac acceleration results from release of parasympathetic inhibition at low exercise intensities and from both parasympathetic inhibition and sympathetic action at moderate intensities.[41,42] Furthermore, there is ample evidence that the vagal effect actually overwhelms the sympathetic influence.[1–3,8,31] With respect to overall stimulation, an increase in the sympathetic stimulation evokes vagal activity; however, when vagal activity prevails, the same change in sympathetic activity evokes a very weak positive chronotropic response.[8] The present results in humans with acute cardiac sympathectomy appear to be explained by such parasympathetic and sympathetic interactions. It is also suggested that sympathetic activity of HR control appears to function as an inhibitor of the vagus rather than as an active cardiac accelerator in awake, healthy humans.

Good preservation of reflex autonomic function during high-level sympathectomy may provide an advantage in some clinical situations. First, it might be suggested that better preserved baroreflex function to decreasing blood pressure is advantageous in the presence of hypovolemia. Second, it is possible that in certain clinical situations depressed reflex responses to physical maneuvers such as coughing or swallowing would be preferable. For example, absence of reflex tachycardia in patients with coronary artery disease and myocardial ischemia reduces myocardial oxygen demands. Indeed, it has been reported that cardiac sympathectomy *per se* by epidural anesthesia provides relatively small increases in myocardial oxygen demands when systemic oxygen requirements increased in humans[20] and redistributed coronary blood flow favoring the endocardium in both the normal and the infarcted heart in dogs.[43] However, since autonomic function appears to decrease with an increase in age,[36] the present results in 22 or 23 yr old healthy humans may not apply to older patients with ischemic heart disease, which could itself involve an impaired function of autonomic nervous system.[17] In such patients, the partial suppression may have significant implications in hemodynamic adjustments following high-level epidural anesthesia.[44]

We thus conclude that high-level sympathectomy by epidural block depresses reflex circulatory responses only partly in young healthy humans. Good preservation of autonomic reflex functions during cardiac sympathetic denervation may be attributable to the opposing side of the autonomic nervous system being intact, but further studies are necessary before establishing a physiologic explanation for our present observations.

The authors thank Dr. H. Naito, Professor of Anesthesiology, Institute of Clinical Medicine, University of Tsukuba, for his review of the manuscript.

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