Counteraction of aortic baroreflex to carotid sinus baroreflex in a neck suction model

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NECK SUCTION PROCEDURES have been widely used in the evaluation of carotid sinus baroreflex function in humans (6–9, 17, 18, 24). During neck suction, a negative pressure is applied around the neck to activate the carotid sinus baroreflex. In six anesthetized rabbits, a 50-mmHg pressure perturbation on the carotid sinus decreased AP by \(27.4 \pm 4.8\) mmHg when the aortic baroreflex was disabled. Enabling the aortic baroreflex significantly attenuated the AP response \((-21.5 \pm 3.8\) mmHg; \(P < 0.01\)). The observed closed-loop gain during simulated neck suction was well predicted by the open-loop gains of the carotid sinus and aortic baroreflexes using the linear model \((-0.43 \pm 0.13\) predicted vs. \(-0.41 \pm 0.10\) measured). We conclude that the linear model can be used as the first approximation to interpret AP response during neck suction.

systems analysis; closed-loop gain; open-loop gain; rabbits

MATERIALS AND METHODS

Theoretical Considerations

Were it not for the aortic baroreflex, pressure changes associated with a given neck suction procedure could be described by the block diagram shown in Fig. 1A (20). \(\Delta P\) indicates changes in AP during neck suction. \(G_{\text{CS}}\) indicates the open-loop gain of the carotid sinus baroreflex. We defined \(G_{\text{CS}}\) as a positive value for convenience and added a negative sign to \(G_{\text{CS}}\) to indicate the negative feedback through the carotid sinus baroreflex. \(\Delta X\) represents a pressure perturbation during neck suction. As an example, a neck suction of 50 mmHg corresponds to a \(\Delta X\) of 50 mmHg. Under these conditions, the closed-loop gain during neck suction \(\left(G_{\text{NS}}\right)\), defined as the ratio of \(\Delta P\) to \(\Delta X\), is

\[
G_{\text{NS}} = \frac{\Delta P}{\Delta X} = -\frac{G_{\text{CS}}}{1 + G_{\text{CS}}} \tag{1}
\]

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The intracarotid arterial pressure (CAP) was controlled by a second servo-controlled piston pump. The bilateral vagi were cut to eliminate baroreflexes from cardiopulmonary regions. The right vagal nerve was cut intrathoracically to avoid any injury to the right aortic depressor nerve. The remaining carotid sinus and aortic baroreflexes from the left side were interrupted by sinoaortic denervation. Body temperature was maintained at 38°C by using a heating pad.

Protocols

After completion of the surgical preparation, both CSP and CAP were matched to AP, and an equilibrium pressure was obtained. The study consisted of the following three protocols.

Protocol 1. We fixed CAP at the equilibrium pressure throughout the protocol, thereby disabling the aortic baroreflex in response to changes in AP. After AP reached a steady state, we increased CSP above AP by either 30 or 50 mmHg for 60 s to simulate a neck suction procedure. Because the negative pressure is attenuated to 64% from neck to perivascular tissue around the carotid sinus in humans (17), the 30- and 50-mmHg pressure perturbations corresponded to negative pressures of 47 and 78 mmHg around the neck, respectively. The magnitude of pressure perturbation, therefore, should cover the range of the neck suction procedure used in humans.

Protocol 2. To elucidate the counteraction of the aortic baroreflex to the carotid sinus baroreflex, we servo-controlled CAP to follow changes in AP, thereby enabling the aortic baroreflex. After AP reached a steady state, we increased CSP above AP by either 30 or 50 mmHg for 60 s.

Protocol 3. To estimate the aortic baroreflex function alone, we fixed CSP at the equilibrium pressure, thereby disabling the carotid sinus baroreflex in response to changes in AP. After AP reached a steady state, we increased CAP above AP by either 30 or 50 mmHg for 60 s.

The order of protocols was randomized among animals to reduce the likelihood of bias or systematic error in estimating the baroreflex gains. We recorded CSP, CAP, and AP at a sampling rate of 200 Hz using a 12-bit analog-to-digital converter. The data were stored on the hard disk of a dedicated laboratory computer system for subsequent analysis.

Data Analysis

All data are presented as means ± SD. The steady-state AP decrease in each protocol was calculated as the difference between the steady-state and baseline AP values. Baseline AP was obtained by averaging instantaneous AP for 10 s before the pressure perturbation. Steady-state AP was calculated by averaging instantaneous AP for the last 10 s of the 60-s pressure perturbation. We repeated the 60-s pressure perturbation twice in each protocol and represented the steady-state AP decrease as the mean of the two experimental runs.

We examined the differences in steady-state AP decrease between protocols 1 and 2 using a paired t-test (10). The difference was considered statistically significant when \( P < 0.05 \). All statistical analyses were performed separately on the results associated with the 30- and 50-mmHg pressure perturbations, because the number of samples would be small for a two-way analysis of variance.

To determine whether Eq. 3 can account for the results of protocol 2, we first calculated \( G_{CS} \) from the results of protocol 1 using Eq. 2. We also estimated \( G_{AO} \) from the results of protocol 3 by substituting \( G_{AO} \) for \( G_{CS} \) in Eq. 2. After obtaining \( G_{CS} \) and \( G_{AO} \) values, we predicted \( G_{NS} \) according to the right term of Eq. 3. Finally, we compared the predicted \( G_{NS} \) with the measured value.
with actual, measured $G_{NS}$ in protocol 2 by using a paired $t$-test (10).

**RESULTS**

Figure 2A shows typical recordings of CSP, CAP, and AP obtained from protocol 1 with a 50-mmHg pressure perturbation. CSP was matched to mean AP in the first 40 s. We then elevated CSP above mean AP by 50 mmHg in the following 60 s. AP decreased in response to the pressure perturbation. Because the pressure difference between CSP and mean AP was kept at 50 mmHg to simulate the neck suction procedure, the decrease in AP caused an overshoot-like change in the CSP tracing. When the 60-s pressure perturbation was discontinued, CSP was again matched to mean AP. The increase in AP upon cessation of pressure perturbation caused a negative overshoot-like change in the CSP tracing. Throughout the protocol, CAP was maintained at the equilibrium pressure to disable the aortic baroreflex in response to any change in AP.

Figure 2B shows typical recordings of CSP, CAP, and AP obtained from protocol 2 with a 50-mmHg pressure perturbation. CSP was controlled in the same manner as in protocol 1. The pressure difference between CSP and mean AP was maintained at 50 mmHg during the 60-s simulated neck suction. In contrast to protocol 1, however, CAP was servo-controlled to follow changes in mean AP, thereby enabling the aortic baroreflex. The steady-state AP decrease was attenuated compared with that in Fig. 2A.

Table 1 summarizes the steady-state AP decreases during the simulated neck suction obtained from protocols 1 and 2. The steady-state AP decrease in protocol 2 was significantly attenuated compared with that in protocol 1 under conditions of either 30- or 50-mmHg pressure perturbation.

Figure 3 shows typical recordings of CSP, CAP, and AP obtained from protocol 3 with a 50-mmHg pressure perturbation. CSP was maintained at the equilibrium pressure throughout the protocol. Thus the carotid sinus baroreflex was not operative in response to any change in AP. We matched CAP to mean AP in the first 40 s and then elevated CAP above mean AP by 50 mmHg in the following 60 s. AP decreased in response to the pressure perturbation.

Table 2 summarizes gain values obtained from the three protocols. The predicted and measured $G_{NS}$ values did not differ significantly under conditions of either 30- or 50-mmHg pressure perturbation ($P = 0.59$ and $P = 0.83$, respectively).

**DISCUSSION**

We have shown that the steady-state AP decrease during a simulated neck suction procedure is attenuated by the aortic baroreflex (Table 1). $G_{NS}$ measured in protocol 2 could be predicted from $G_{CS}$ and $G_{AO}$ by using the right term of Eq. 3 (Table 2), suggesting that the AP response during simulated neck suction can be described by the linear model shown in Fig. 1B.

![Fig. 2. Representative recordings of carotid sinus pressure (CSP), carotid arterial pressure (CAP), and systemic arterial pressure (AP) during a 50-mmHg pressure perturbation on CSP. The aortic baroreflex was disabled (A) and enabled (B).](image)
The amplitude of pressure perturbation is known to affect $G_{CS}$ due to the sigmoidal input-output relationship of the arterial baroreflex system (3, 16, 21, 22, 27). Although a 50-mmHg pressure perturbation seems to be sufficiently large to fall within the range of sigmoidal nonlinearity, $G_{NS}$ predicted from $G_{CS}$ and $G_{AO}$ using Eq. 3 conformed to the measured $G_{NS}$, suggesting a linearity in the steady-state AP response during the simulated neck suction. Attenuation of pressure perturbation through the closed-loop feedback may account for the observed linearity as follows. The steady-state input to CSP during the simulated neck suction was not $\Delta X$ itself but $\Delta X + \Delta AP$, as in Fig. 1. For instance, the steady-state input to CSP in protocol 1 was 22.6 mmHg, on average, when a 50-mmHg pressure perturbation was applied. Therefore, the steady-state input during the simulated neck suction might have been within the linear operating range of the AP regulation.

Clinical Implications

As indicated in Eq. 3, we must specify $G_{AO}$ to determine $G_{CS}$ from observed $G_{NS}$. The $G_{AO}$-to-$G_{CS}$ ratio was $-0.6$ in the present study. Hosomi et al. (11) reported the $G_{AO}$-to-$G_{CS}$ ratio of $-0.9$ using a quick hemorrhage method in anesthetized rabbits. The $G_{AO}$-to-$G_{CS}$ ratio has been reported as $-0.5$ in anesthetized dogs (2, 3, 5). On the basis of these findings, we specified the $G_{AO}$-to-$G_{CS}$ ratio variously at 0 (aortic baroreflex disabled), 0.5, 1, and 2, then calculated the relationship between $G_{CS}$ and $G_{NS}$ (Fig. 4A). We also calculated $(G_{CS} + G_{AO})$ vs. $G_{NS}$ (Fig. 4B). In the simulation, $G_{CS}$ or $(G_{CS} + G_{AO})$ monotonously increased as $G_{NS}$ approached $-1$, regardless of the $G_{AO}$-to-$G_{CS}$ ra-

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**Table 2. Gain values obtained from the three protocols**

<table>
<thead>
<tr>
<th>$\Delta X$</th>
<th>$G_{CS}$</th>
<th>$G_{AO}$</th>
<th>Predicted $G_{NS}$</th>
<th>Measured $G_{NS}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 mmHg</td>
<td>1.37 ± 0.77</td>
<td>0.59 ± 0.20</td>
<td>-0.43 ± 0.13</td>
<td>-0.41 ± 0.10</td>
</tr>
<tr>
<td>50 mmHg</td>
<td>1.35 ± 0.66</td>
<td>0.69 ± 0.19</td>
<td>-0.43 ± 0.09</td>
<td>-0.43 ± 0.08</td>
</tr>
</tbody>
</table>

Values are means ± SD. $G_{CS}$, open-loop gain of the carotid sinus baroreflex (protocol 1); $G_{AO}$, open-loop gain of the aortic baroreflex (protocol 3); predicted $G_{NS}$, closed-loop gain during neck suction predicted from $G_{CS}$ and $G_{AO}$ values (Eq. 3); measured $G_{NS}$, measured closed-loop gain during neck suction (protocol 2). The predicted and measured $G_{NS}$ values did not differ significantly.
tio. Therefore, if we repeat the neck suction procedure in the same subject before and after some environmental stress and observe an increase in the negative value of G_{NS}, we can at least conclude that the arterial baroreflex gain has also increased.

According to the human study in normal subjects by Mancia et al. (18), the regression coefficient of steady-state changes in mean AP on changes in neck tissue pressure is \(-0.41\). Using this value, we can estimate G_{CS} to be 2.3 when G_{CS} equals G_{AO} on the basis of Fig. 4A. However, these estimations vary depending on the specified ratio of G_{AO} to G_{CS}. Figure 4 would represent the utility as well as the limitation of the neck suction procedure to estimate the open-loop gain of the arterial baroreflex from the steady-state AP response during neck suction.

**Limitations**

There are several limitations to this study. First, we investigated the carotid sinus and aortic baroreflexes in anesthetized rabbits. Although we chose an anesthetic agent that is minimally suppressive to circulatory regulation, the absolute values of G_{CS} and G_{AO} might have been affected by the anesthesia to some degree. However, we compared the predicted G_{NS} and measured G_{NS} under the same anesthetic conditions, and we believe that the linear model shown in Fig. 1B would explain the steady-state AP response to neck suction, even in the absence of anesthesia.

Second, CSP and CAP were exposed to nonpulsatile pressure. The absolute gain values might have been different had CSP and CAP been exposed to pulsatile pressure (2, 4). Furthermore, we denervated the left carotid sinus nerve while preserving the left internal carotid artery to maintain the blood flow to the brain. Therefore, the possible interaction between the left and right carotid sinus baroreflexes during neck suction (26) was not assessed in the present study.

Third, we cut the vagi to eliminate the possible baroreflex from the cardiopulmonary regions. Consequently, we were unable to evaluate the vagal control of heart rate during the simulated neck suction procedure. Several investigators suggest the advantage of using the heart rate response over the AP response (6–9, 24) to evaluate carotid sinus baroreflex function by neck suction. Future studies with intact vagi are required to examine the counteracting effects of the aortic baroreflex on the heart rate response during neck suction.

Finally, we filled the isolated baroreceptor regions with warmed physiological saline (13, 14, 21, 22). Because ion content affects the sensitivity of baroreceptors (1), the absolute values of G_{CS} and G_{AO} might have been different had we used other solutions, such as Ringers solution. However, because we did not change the intravascular content of the isolated baroreceptor regions among protocols, the sensitivity of baroreceptors to pressure input would have remained unchanged.

In conclusion, the aortic baroreflex counteracted the carotid sinus baroreflex during simulated neck suction and attenuated the steady-state AP response. The linear model shown in Fig. 1B was able to account for the AP response during the simulated neck suction. Therefore, we can estimate the arterial baroreflex gain from the observed AP response during neck suction by assuming the G_{AO}-to-G_{CS} ratio. Although the G_{AO}-to-G_{CS} ratio in humans is unknown, according to animal experiments, it most likely falls within the range of 0.5–1.0.

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