Altered heart rate baroreflex during pregnancy: role of sympathetic and parasympathetic nervous systems

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Altered heart rate baroreflex during pregnancy: role of sympathetic and parasympathetic nervous systems. Am. J. Physiol. 237 (Regulatory Integrative Comp. Physiol. 42): R960–R966, 1997.—Two studies were performed to determine whether the attenuation of baroreflex control of heart rate during late pregnancy in conscious rabbits is due to changes in parasympathetic (Para) or sympathetic (Sym) control of the heart. In the first, baroreflex relationships between arterial pressure and heart rate were generated before and after treatment with propranolol (Pro) to block Sym or with methscopolamine (Meth) to block Para. Each rabbit was studied in both the pregnant and nonpregnant state. Pregnancy decreased maximum baroreflex gain from 14.9 ± 4.0 to 4.8 ± 0.9 beats·min⁻¹·mmHg⁻¹ (P < 0.01) and decreased heart rate range from 177 ± 6 to 143 ± 10 beats/min (P < 0.01), primarily by increasing minimum heart rate (14 ± 6 to 134 ± 8 beats/min; P < 0.01). The difference between pregnant and nonpregnant rabbits in baroreflex gain was not altered by Meth but was abolished by Pro, suggesting that it is due to decreased Sym control of the heart. The elevated minimum heart rate of pregnancy persisted after Pro, but was abolished by Meth, suggesting that it is mediated by decreased Para control of the heart. In the second study, isolated buffer-perfused hearts from pregnant and nonpregnant rabbits were treated with increasing doses of isoproterenol (0.3–300 mM) or acetylcholine (0.3–10,000 μM), and the heart rate responses were determined. Hearts from pregnant rabbits were more sensitive to isoproterenol (P < 0.05), but less responsive to acetylcholine (P < 0.05). In conclusion, pregnancy-induced decreases in cardiac reflex gain and range appear to be mediated by alterations in Sym and Para, respectively. The change in Sym occurs proximal to the heart, whereas the increased contribution of Para may be due, at least in part, to decreased sensitivity of the heart to acetylcholine.

Rabbits; propranolol; methscopolamine; acetylcholine; isoproterenol; Langendorff

Previous studies indicate that reflex control of renal sympathetic activity is also blunted during pregnancy (3, 9, 13). Therefore, the present studies were performed to test the hypothesis that sympathetic neural control of the heart is attenuated during gestation. This hypothesis was tested utilizing two experimental approaches. In the first, the autonomic contributions to baroreflex control of the heart were determined in pregnant and nonpregnant conscious rabbits after systemic blockade of cholinergic or β-adrenergic receptors. Second, the chronotropic responses to cholinergic and β-adrenergic receptor agonists of hearts from pregnant and nonpregnant rabbits were compared using the in vitro Langendorff preparation.

METHODS

Baroreflex Studies

Experiments were performed using six female New Zealand White rabbits weighing 3.3 ± 0.1 kg. The rabbits were fed a fixed diet (150 g/day) of high-protein rabbit chow (PMI Feeds) and were allowed free access to distilled water. A 16-h light cycle was maintained to enhance breeding.

Surgical preparation. Surgery was performed to implant nonocclusive abdominal aortic and vena caval catheters for arterial pressure measurements and drug infusions as previously described (11). The rabbits (15–16 wk of age) were anesthetized with an intramuscular injection of a 5:2:5:1 mixture of ketamine (100 mg/ml), xylazine (20 mg/ml), and acepromazine (10 mg/ml). A surgical plane of anesthetia was maintained with infusions of dilute ketamine (1:10 ketamine:0.9% saline) via a marginal ear vein. Under sterile conditions, a midline abdominal incision was made and nonocclusive Silastic tipped catheters were implanted, one into the abdominal aorta and two into the vena cava. The catheters were tunneled subcutaneously to the nape of the neck, where they were held in place with plastic washers. The rabbits were given an intramuscular injection of penicillin (60,000 U) 1 h before surgery. Buprenex was injected intramuscularly at the end of surgery and the following day. Catheters were flushed with sterile isotonic saline three times a week and filled with heparin (1,000 U/ml) when not in use. The rabbits were allowed a minimum 2-wk recovery period, during which they were trained to sit quietly in an opaque Plexiglas box.

Baroreflex function curves. On the day of the experiment, the rabbits were placed in the box and allowed 30–45 min to stabilize. Arterial pressure and heart rate were measured continuously (Spectramed pressure transducer, Grass tachometer) and were recorded on a polygraph (Grass model 7D). To determine the baroreflex relationship between arterial pressure and heart rate, arterial pressure was first lowered by infusing increasing doses of nitroprusside [3, 6, 12, 24, and 48 μg·kg⁻¹·min⁻¹ for nonpregnant (NP) rabbits; 1.5, 3, 6, 12, 24, and 48 μg·kg⁻¹·min⁻¹ for pregnant (P) rabbits]. After a 30-min rest period, arterial pressure was raised by infusing...
increasing doses of phenylephrine (0.5, 1, 2, 4, and 8 µg·kg⁻¹·min⁻¹). Some rabbits also received a higher dose of phenylephrine (~10.5 µg·kg⁻¹·min⁻¹) and/or a higher dose of nitroprusside (~63 µg·kg⁻¹·min⁻¹) to more accurately estimate maximum and minimum heart rates. Each dose was infused until blood pressure and heart rate stabilized, ~3–5 min. After the control baroreflex relationship was established, the rabbits were treated on different days with either propranolol (Pro) or methscopolamine (Meth) to block sympathetic or parasympathetic efferents, respectively. Pro was injected in a bolus dose (1 mg/kg) 15 min after the first phenylephrine infusion to investigate the function of parasympathetic control of the heart. A booster injection of 0.5 mg/kg was given 15 min after the second nitroprusside infusion. An infusion of Meth at 1 µg·kg⁻¹·min⁻¹ was begun immediately after the first phenylephrine infusion to investigate the function of the sympathetic nervous system, and rabbits were given ~30 min to stabilize. These experiments were performed before pregnancy (NP) and at 27–30 days of gestation (P). Each rabbit was studied in both the P and NP state.

The efficacy of Meth and Pro to block the parasympathetic and sympathetic efferents was tested in other experiments. Isoproterenol (0.4 µg) was given before and after Pro (1 mg/kg). Acetylcholine (0.1 mg/kg) was injected before and after Meth infusion. The doses of Pro and Meth totally eliminated the cardiovascular effects of isoproterenol and acetylcholine in both NP and P rabbits (n = 3).

Langendorff Studies

NP and P (~28 days gestation) female New Zealand White rabbits (2.5–3.0 kg) were anesthetized with 30 mg/kg pentobarbital sodium via a marginal car vein. A left thoracotomy was performed in the fourth intercostal space, and the heart was suspended in a pericardial cradle. The heart was then rapidly excised, placed in iced saline for transport, and mounted on a nonrecirculating Langendorff apparatus. Excision, mounting, and restoration of perfusion was accomplished within 45–60 s. Hearts were gravity perfused with a modified Krebs-Henseleit buffer at 100 cmH₂O. Buffer composition was as follows (in mM, pH = 7.4): 118.48 NaCl, 24.76 NaHCO₃, 10.00 dextrose, 4.74 KCl, 2.50 CaCl₂, 1.19 KH₂PO₄, and 1.19 MgSO₄. The buffer was prefiltered using a 0.45-µm filter (Super-450, 90 mm; Gelman Sciences, Ann Arbor, MI) and filtered in-line with a 50-µm filter (MicronSep, 47 mm; MSI, Westboro, MA). Buffer was bubbled with 95% oxygen and 5% carbon dioxide. Perfusate temperature was maintained between 35–38°C with water-jacketed chambers and tubing; a pediatric temperature probe was introduced into the right atrium. Perfusion pressure was monitored and charted with a fluid-filled latex balloon, which was introduced into the right atrium through the pericardial cradle. The heart was then suspended in the Langendorff apparatus and heart rate was determined using analysis of covariance (30). The results of the Langendorff experiments were statistically assessed in two ways. First, between-group differences in the heart rate responses to increasing doses of cholinergic or β-adrenergic agonists were determined using two-way ANOVA for repeated measures. Because the variances were not homogeneous among doses, the data were subjected to logarithmic transformation before ANOVA, again using GB Stat (Dynamic Microsystems, Silver Spring, MD) (30).

RESULTS

Baroreflex Studies

Basal levels of arterial blood pressure and heart rate before and after administration of Meth or Pro are summarized in Table 1. Before drug administration, blood pressure tended to be lower and heart rate tended to be higher when the rabbits were pregnant. The lower

<table>
<thead>
<tr>
<th>Blood pressure, mmHg</th>
<th>NP Control</th>
<th>NP Pro</th>
<th>P Control</th>
<th>P Pro</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate, beats/min</td>
<td>176 ± 4</td>
<td>174 ± 4</td>
<td>202 ± 12*</td>
<td>185 ± 11†</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Blood pressure, mmHg</th>
<th>NP Control</th>
<th>NP Meth</th>
<th>P Control</th>
<th>P Meth</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate, beats/min</td>
<td>171 ± 6</td>
<td>218 ± 9†</td>
<td>188 ± 10</td>
<td>228 ± 14†</td>
</tr>
</tbody>
</table>

Values are means ± SE; n = 6 rabbits for propranolol (Pro) administration, n = 4 rabbits for methscopolamine (Meth). NP, nonpregnant; P, pregnant. *P < 0.05, NP vs. P; †P < 0.05, control vs. Pro or Meth within groups.
Pregnancy and baroreflex control of heart rate

Fig. 1. Baroreflex relationships between arterial pressure and heart rate in rabbits (n = 6) before (■) and at the end of pregnancy (○). Basal values of heart rate and pressure are indicated for nonpregnant (△) and pregnant (▲) rabbits. bpm, Beats/min.

Pregnancy reached significance in the Meth group, and the elevated heart rate was significant in the Pro group. Because neither drug affected arterial pressure, the reduced blood pressure of pregnancy persisted after drug administration (P < 0.05). Heart rate increased (P < 0.05) after Meth in both groups. Pro decreased basal heart rate only in P rabbits (P < 0.05), but not to the level of NP rabbits.

Effect of pregnancy on baroreflex control of heart rate. Pregnancy exerted two major effects on baroreflex control of heart rate (Fig. 1, Table 2). Maximal baroreflex gain, or the slope of the baroreflex curve, was reduced (P < 0.05), and reflex heart rate range was decreased (P < 0.05), primarily because of an increase in the minimum heart rate (P < 0.05).

Sympathetic and parasympathetic components of baroreflex heart rate range in NP rabbits. In NP rabbits before drug administration, resting heart rate was closer to the lower plateau (34 ± 2% of the heart rate range) than the upper plateau (Figs. 1–3). After Meth, resting heart rate increased (Fig. 2, Table 1) and heart rate range was reduced (Fig. 2, Table 3). The ability to suppress heart rate with increases in pressure above normal was abolished (Fig. 2). Indeed, resting heart rate was 0.1 ± 8% of the heart rate range after Meth. Maximal heart rate was enhanced (Fig. 2, Table 3), suggesting that zero vagal tone was not achieved during maximal hypotension-induced increases in heart rate before Meth.

In contrast to the effects of Meth, Pro did not alter resting heart rate or the lower heart rate plateau. However, Pro markedly reduced the tachycardic response to decreases in pressure, thereby decreasing heart rate range (Fig. 3, Table 4). These data indicate that resting heart rate is defined mainly by vagal tone, with little or no influence from the sympathetic nervous system. In addition, the bradycardic response is medi-

Table 2. Effect of pregnancy on logistic parameters

<table>
<thead>
<tr>
<th></th>
<th>Nonpregnant</th>
<th>Pregnant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum gain,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>beats·min⁻¹·mmHg⁻¹</td>
<td>14.9 ± 4.0</td>
<td>4.8 ± 0.9*</td>
</tr>
<tr>
<td>HR range, beats/min</td>
<td>177 ± 6</td>
<td>143 ± 10*</td>
</tr>
<tr>
<td>BP midpoint, mmHg</td>
<td>63.0 ± 0.7</td>
<td>61.3 ± 4.2</td>
</tr>
<tr>
<td>Minimum HR, beats/min</td>
<td>114 ± 6</td>
<td>134 ± 8*</td>
</tr>
<tr>
<td>Maximum HR, beats/min</td>
<td>291 ± 9</td>
<td>277 ± 6</td>
</tr>
</tbody>
</table>

Values are means ± SE; n = 6. HR, heart rate; BP, blood pressure. *P < 0.05, pregnant vs. nonpregnant.

Table 3. Effect of methscopolamine on logistic parameters

<table>
<thead>
<tr>
<th></th>
<th>NP Control</th>
<th>NP Meth</th>
<th>P Control</th>
<th>P Meth</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum gain,</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>beats·min⁻¹·mmHg⁻¹</td>
<td>12.7 ± 2.3</td>
<td>12.7 ± 1.0</td>
<td>5.7 ± 0.7*</td>
<td>5.3 ± 1.0*</td>
</tr>
<tr>
<td>HR range, beats/min</td>
<td>178 ± 12</td>
<td>94 ± 11†</td>
<td>142 ± 10*</td>
<td>68 ± 11†</td>
</tr>
<tr>
<td>BP midpoint, mmHg</td>
<td>62.7 ± 1.7</td>
<td>64.1 ± 2.6</td>
<td>57.1 ± 1.4*</td>
<td>57.3 ± 1.3*</td>
</tr>
<tr>
<td>Minimum HR,</td>
<td>111 ± 2.7</td>
<td>217 ± 2.4†</td>
<td>137 ± 6.9*</td>
<td>213 ± 12.6†</td>
</tr>
<tr>
<td>Maximum HR, beats/min</td>
<td>299 ± 13</td>
<td>311 ± 8†</td>
<td>279 ± 7</td>
<td>281 ± 11*</td>
</tr>
</tbody>
</table>

Values are means ± SE; n = 4. *P < 0.01, P vs. NP. †P < 0.01, before (control) vs. after Meth within groups.
Effect of pregnancy on sympathetic and parasympathetic components of baroreflex heart rate range. As in NP rabbits, resting heart rate was closer to minimum rather than maximum heart rate (35 ± 5% of heart rate range). Meth also reduced heart rate range in P rabbits, by increasing minimum heart rate (P < 0.05), and abolished the between-group difference in minimum heart rate (Fig. 2, Table 3). However, heart rate range remained smaller in P rabbits after Meth, primarily due to increased maximum heart rate after Meth only in NP rabbits (Fig. 2, Table 3). Interestingly, in P rabbits after Meth, resting heart rate was significantly higher than minimum heart rate (23 ± 17% of heart rate range; P < 0.05). In other words, increases in pressure decreased heart rate after Meth only in P rabbits. These data suggest that basal sympathetic activity to the heart is elevated during pregnancy.

As in NP rabbits, the major effect of Pro in P rabbits was to decrease heart rate range primarily by decreasing maximum heart rate (P < 0.01; Fig. 3, Table 4). However, heart rate range was still smaller and minimum heart rate was still higher in P compared with NP rabbits after Pro (P < 0.05; Table 4). In summary, the elevated minimum heart rate of P rabbits was still present after blockade of β-adrenergic receptors, but was eliminated after blockade of cholinergic receptors.

Effect of pregnancy on the sympathetic and parasympathetic components of baroreflex gain. Meth did not affect gain in either P or NP rabbits, and the between-group difference persisted (Fig. 2, Table 3). Pro also did not significantly alter gain during pregnancy (Fig. 3, Table 4), in contrast to the decrease in gain produced by Pro in NP rabbits. After Pro, there was no difference in gain between NP and P rabbits (Table 4). Thus elimination of sympathetic control of the heart with Pro eliminated the between-group difference in gain, whereas this difference remained after blockade of the parasympathetic nervous system, when only sympathetics were functional.

Langendorff Studies

Responsiveness to the cholinergic agonist acetylcholine. Average basal heart rate before acetylcholine administration was not different in hearts from P (171 ± 5 beats/min) and NP (158 ± 8 beats/min) rabbits. Acetylcholine produced dose-dependent decreases in heart rate in both groups (P < 0.0001) (Fig. 4). However, P hearts were less sensitive to the drug, as indicated by a reduced bradycardia at two doses of acetylcholine (P < 0.05). The slopes of the linear relationship between dose of acetylcholine and decrease in heart rate were not different (P > 0.5) between P and NP rabbits.

Responsiveness to the β adrenergic agonist isoproterenol. Basal heart rate was similar in hearts from P (202 ± 5 beats/min) and NP (194 ± 17 beats/min) rabbits. Isoproterenol produced dose-dependent increases in heart rate in both groups (P < 0.0001), but P hearts were more sensitive, as indicated by the greater increase in heart rate in response to three doses of isoproterenol (P < 0.05) (Fig. 5). However, there was no
Fig. 4. Effect of increasing doses of acetylcholine on heart rate in isolated, buffer-perfused hearts from nonpregnant (●) and pregnant (○) rabbits. *P < 0.05, pregnant vs. nonpregnant; **P < 0.01, pregnant vs. nonpregnant.

between-group difference in the slopes of the linear relationship between dose of isoproterenol and increase in heart rate (P > 0.10).

Cardiac compliance. The relationship between cardiac volume and pressure was assessed in P and NP rabbits to determine whether pregnancy alters cardiac compliance and, therefore, potentially the relationship between cardiac pressure and the degree of activation of cardiac afferents. Figure 6 illustrates that the relationships between left ventricular balloon volume and left ventricular end-diastolic pressure were not different between P and NP rabbits.

DISCUSSION

Baroreflex control of heart rate is changed at the end of pregnancy in conscious rabbits. In particular, baroreflex gain is reduced, and minimum heart rate is elevated, thereby reducing heart rate range (Fig. 1). The purpose of the present study was to determine whether pregnancy alters cardiac compliance and, therefore, potentially the relationship between cardiac pressure and the degree of activation of cardiac afferents. Figure 6 illustrates that the relationships between left ventricular balloon volume and left ventricular end-diastolic pressure were not different between P and NP rabbits.

Fig. 5. Effect of increasing doses of isoproterenol on heart rate in isolated, buffer-perfused hearts from nonpregnant (●) and pregnant (○) rabbits. *P < 0.05, pregnant vs. nonpregnant; **P < 0.01, pregnant vs. nonpregnant.

Fig. 6. Relationship between balloon volume and left ventricular end-diastolic pressure (LVEDP) in hearts from nonpregnant (●) and pregnant (○) rabbits. gain in NP rabbits to P levels, but blockade of the parasympathetic nervous system with Meth did not alter gain in either group. These data suggest that the decreased gain present in P rabbits is due to a change in sympathetic control of the heart. 2) The difference in minimum heart rate between P and NP rabbits was still evident after Pro, but was abolished by Meth. These data suggest that the increased minimum heart rate observed in P rabbits is due to a decrease in parasympathetic control of the heart. 3) Two findings suggest that basal sympathetic activity to the heart is increased during pregnancy: basal heart rate was decreased by Pro only in P rabbits, and increases in pressure decreased heart rate after Meth only in P rabbits. 4) Hearts from P rabbits are more sensitive to the chronotropic effects of the β-agonist isoproterenol, but are less sensitive to the cholinergic agonist acetylcholine. These data suggest that the reduced effectiveness of the parasympathetic nervous system on the heart (increased minimum heart rate, 2 above) can be due in part to reduced cardiac responsiveness to acetylcholine. The reduced role of the sympathetic nervous system in control of reflex gain during pregnancy (1 above) cannot be explained by reduced cardiac responsiveness to adrenergic agonists, but increased myocardial sensitivity to β-adrenergic agonists could contribute to the apparent increased basal sympathetic tone during pregnancy.

A number of studies have evaluated the effect of pregnancy on reflex control of heart rate. In most studies, only the pressor or the depressor limb of the baroreflex was studied. The results have been variable, although most investigators report that hypotension-induced reflex increases in heart rate are attenuated during pregnancy, whereas reflex bradycardia is potentiated (for reviews, see Refs. 3, 13, and 19). The latter finding appears to be due to the fact that basal heart rate is increased during gestation, which provides a greater potential for suppression of heart rate (3). Few studies have investigated both the tachycardic and bradycardic segments of the baroreflex concurrently. Conrad and Russ (8) found no change in the overall baroreflex during pregnancy in the rat, although, when
examined alone, reflex bradycardia was potentiated. Pregnancy has been reported to be without effect on baroreflex control of heart rate in other rat studies (14, 26). On the other hand, we have found that pregnancy produces a profound decrease in overall baroreflex function in conscious rabbits.

The results of the present study support the hypothesis that the decrease in baroreflex gain is due to a decrease in the rate of change of sympathetic activity to the heart for a given change in arterial pressure. Meth had no effect on gain in either group, suggesting that, if the vagus contributes to gain, its loss can be compensated for by the sympathetic nervous system. On the other hand, Pro decreased gain in NP rabbits to the level of P rabbits and did not affect gain in P rabbits. These data indicate that the reduced gain is due to reduced influence of the sympathetic nervous system and is consistent with reports that baroreflex control of renal sympathetic activity is also reduced during pregnancy (3, 9, 13).

Because hearts from P rabbits were more, rather than less, sensitive to the β-adrenergic agonist isoproterenol and because there was no between-group difference in the increase in heart rate for a given increase in isoproterenol in vitro, this decrease in gain may originate from a defect proximal to the heart. One possible site is cardiac or arterial baroreceptors. The results of the present study that cardiac compliance is not changed by pregnancy, in agreement with earlier studies in the rat (17, 18), suggests that the responsiveness of cardiac stretch receptors may be normal. Furthermore, pregnancy increases arterial distensibility (12, 25), suggesting that, if anything, the change in activity of arterial baroreceptors for a given change in pressure would be greater rather than lesser. However, direct measurements of cardiac and arterial afferent activity during changes in pressure are required to confirm these suggestions. Nevertheless, it appears likely that the reduced baroreflex responsiveness of the sympathetic nervous system may be due to a change in the central or ganglionic control of sympathetic outflow rather than at baroreceptor afferents.

The mechanism by which central nervous system control of sympathetic outflow could change during pregnancy is not known. However, our recent finding that the change does not occur until the end of pregnancy (4, 5) and the baroreflex is not altered until later, estrogen is not a likely candidate. This conclusion is supported by other studies demonstrating that chronic infusion of estrogen does not decrease baroreflex gain (3). Other possible mediators include hormones that increase late in pregnancy and that affect the cardiovascular system, such as angiotensin II (27) or oxytocin (31). Alternatively, a derivative of the blood volume expansion may be involved, because blood volume increases progressively during pregnancy to reach a peak just before delivery (21, 22).

In addition to effects on gain, the present study also demonstrated that heart rate range is reduced during pregnancy, due to an increase in minimum heart rate. In these normal rabbits, reflex bradycardia appears to be largely due to vagal activation. Therefore, it is not surprising that blockade of the parasympathetic nervous system abolished the between-group difference in range and minimum heart rate, whereas blockade of the sympathetics did not. The results of the Langendorff experiments revealed a possible mechanism for this effect. Because the hearts from P rabbits were less sensitive to acetylcholine, it may be that the elevated minimum heart rate is due to a change in the heart, rather than in central nervous system regulation of parasympathetic activity.

Basal heart rate is increased during pregnancy in the rabbit as in many species. Part of this increase may be due to increased basal cardiac sympathetic activity and/or augmented myocardial responsiveness to adrenergic activation, because Pro decreased heart rate only in P rabbits. Moreover, when the sympathetic nervous system was functioning alone after administration of Meth, increases in pressure decreased heart rate only in P rabbits. However, decreased parasympathetic activity, perhaps via decreased cardiac responsiveness to acetylcholine, may also contribute to the elevated heart rate of pregnancy, because Pro did not normalize the between group difference in basal cardiac rate.

In conclusion, the alterations in baroreflex control of heart rate observed in P rabbits are mediated via changes in both sympathetic and parasympathetic control of the heart. A central defect in the regulation of sympathetic outflow appears to explain the pregnancy-induced decrease in baroreflex gain. In addition, reduced parasympathetic nervous activity mediates the reduced ability to suppress heart rate when arterial pressure is high. This latter change may be due, at least in part, to a decrease in the sensitivity of the heart to acetylcholine.

**Perspectives**

We and others have found that pregnant animals are less able to maintain arterial pressure during hemorrhage (2, 3, 15, 24, 29). Whether pregnant women also experience this difficulty has not been directly quantitated; however, several studies have documented that women in late pregnancy respond to orthostatic stress with smaller increases in systemic vascular resistance or in plasma norepinephrine levels (1, 7, 10, 23). Because these changes in cardiovascular homeostasis are associated with reduced baroreflex gain, we have speculated that the change in the baroreflex mediates the altered response to hemorrhage (3). Hemorrhage is a common result of normal delivery (6); therefore, an understanding of the mechanism of the blunted baroreflex regulation during pregnancy is clearly essential for effective patient care. The results of the present study suggest that the mechanism that mediates the change in baroreflex control of heart rate is multifactorial, involving changes not only in the heart but also in sites proximal to the heart, possibly the central nervous system. A possible rule for the brain is also supported by previous studies demonstrating that control of a num-
ber of baroreflex efferents is altered during pregnancy (for reviews, see Refs. 3, 13, 16, and 19). However, further experiments are required to identify the site and mode of action of pregnancy on the baroreflex.

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