Effects of human pregnancy on cardiac autonomic function above and below the ventilatory threshold

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Avery, N. D., L. A. Wolfe, C. E. Amara, G. A. L. Davies, and M. J. McGrath. Effects of human pregnancy on cardiac autonomic function above and below the ventilatory threshold. J Appl Physiol 90: 321–328, 2001.—This study examined the effects of human pregnancy on heart rate variability (HRV), spontaneous baroreflex (SBR) sensitivity, and plasma catecholamines at rest and during exercise. Subjects were 14 healthy, physically active pregnant women (PG; mean gestational age = 33.9 ± 1.0 wk). Results were compared with an age-matched nonpregnant control group (NPG; n = 14) with similar characteristics. The electrocardiographic R-wave-R-wave interval and systolic blood pressure (via finger plethysmograph) were measured on a beat-to-beat basis at rest and during upright cycling at 60 and 110% of the ventilatory threshold (Tvent). Parasympathetic nervous system (PNS) modulation (as reflected by HRV high-frequency/total power and SBR slope) was significantly reduced at rest in the PG vs. the NPG. During exercise, PNS modulation decreased significantly in both groups, but the magnitude of PNS withdrawal from rest to 110% Tvent was smaller in the PG vs. NPG. Sympathetic nervous system (SNS) modulation (reflected by the low-frequency power-to-high-frequency power ratio) increased above resting values at 60 and 110% Tvent in the NPG. SNS modulation at 110% Tvent was significantly lower in the PG compared with the NPG. Plasma norepinephrine and epinephrine levels were also lower at 110% Tvent in the PG. It was concluded that healthy pregnant women exhibit lower PNS modulation at rest and blunted SNS modulation during exercise above Tvent in late gestation.

spectral analysis; spontaneous baroreflex function; human gestation; exercise intensity

PREGNANCY IS CHARACTERIZED by profound changes in the function of virtually every regulatory system in the human body. These changes are initiated by ovarian and placental hormones in the first trimester but may also be modified by placental and fetal endocrine factors as gestational age advances.

Pregnancy-induced effects on cardiovascular function in the resting state are well described and include increases in heart rate (HR), stroke volume (SV), and cardiac output (28, 29). Current evidence suggests that these changes result from the interactive effects of a primary reduction in peripheral vascular resistance (12), activation of renal volume restoring mechanisms (12), estrogen-mediated increases in cardiac dimensions (17, 18), and contractility (21), as well as changes in cardiac autonomic modulation and baroreflex function that lead to a higher resting HR. As described below, the exact nature and physiological basis for these cardiac autonomic changes is poorly understood.

In recent years, the study of cardiac autonomic modulation in human subjects has been greatly facilitated by the development of computer-based methods for spectral analysis of heart rate variability (HRV) and spontaneous baroreflex (SBR) function. It is well established that high-frequency power (0.15–0.40 Hz) of HRV is mediated by parasympathetic nervous system (PNS) modulation and respiratory sinus arrhythmia (1, 2, 5), whereas low-frequency power (<0.15 Hz) reflects both sympathetic nervous system (SNS) and PNS autonomic influences (5, 26). Accordingly, the ratio of high-frequency power to total power has been employed as an index of cardiac parasympathetic modulation (PNS indicator), and the ratio of low-frequency power to high-frequency power has been used to reflect cardiac sympathetic modulation (SNS indicator) (3, 26).

Beat-to-beat PNS-mediated control of HR can also be evaluated noninvasively by the simultaneous recording of an electrocardiogram and arterial blood pressure using a finger plethysmograph. In this technique, sequences of three or more beats in which the electrocardiographic R-wave-R-wave interval (RRI) and systolic blood pressure (SBP) change in the same direction are analyzed using a linear regression analysis (6). The average slope of the RRI-SBP relationship is then used as an index of SBR sensitivity (6, 27).

Previous studies of cardiac autonomic function in human pregnancy have produced conflicting results. For example, findings of reduced total power (13, 15) and attenuated HR responses to orthostatic tests and the Valsalva maneuver (15) suggest that cardiac parasympathetic modulation is reduced in the resting state during midpregnancy (22–29 wk gestation). However, a subsequent study from the same laboratory (14) reported reduced low-frequency HRV (suggesting reduced SNS modulation) during the day and reduced
high-frequency HRV (suggesting reduced PNS modulation) at night. These studies were conducted in early to midgestation (11–27 wk). In contrast to these findings, Eneroth-Grimfors et al. (16) reported reduced high-frequency power in late gestation in women with preeclampsia but failed to detect statistically significant differences in either high- or low-frequency power in healthy pregnant women compared with nonpregnant female controls.

Studies of cardiovascular responses to strenuous exercise during pregnancy are few in number, presumably because of historical concerns about fetal well-being (34). However, some studies have reported blunted HR peak responses to maximal exercise testing in late gestation (22), and others (22, 29, 33) have reported a reduced HR reserve during exercise. In addition, Bonen et al. (7) reported lower values for both epinephrine and norepinephrine during strenuous exercise testing in the third trimester compared with midpregnancy and the nonpregnant state. Considered together, these findings suggest that sympathoadrenal responses to strenuous exercise are blunted in late gestation.

The purpose of this study was to examine the effects of human pregnancy on cardiac autonomic function in late gestation. Subjects were studied in the resting state and during exercise above Tvent in the pregnant vs. nonpregnant state. It was hypothesized that indexes of cardiac parasympathetic modulation would be reduced during exercise testing in the resting state and that indexes of cardiac parasympathetic modulation would be reduced in the pregnant vs. nonpregnant female controls.

METHODS

Subjects. Inclusion criteria for the pregnant female volunteers (pregnant group [PG]) included maternal age between 20–40 yr, physically active (minimum: brisk walking 3 days/ wk), nonsmoker, and a parity from 0 to 2. The nonpregnant female volunteers [nonpregnant group (NPG)] were physically active nonsmokers, aged 20–40 yr, and were not taking oral contraceptives. Both groups were equated for age, body height, prepregnancy body mass, and aerobic fitness. Each prospective pregnant subject was medically screened by the obstetrician monitoring her pregnancy, using a standard medical screening form, and reviewed by the study obstetrician using the Physical Activity Readiness Medical Examination for Pregnancy (10). The Physical Activity Readiness questionnaire was used to screen the nonpregnant female volunteers. All subjects provided written, informed consent before entering the study.

Subjects were recruited by posted announcements and newspaper advertisements, as well as through contact with local obstetricians, community agencies that provide services to women, and prenatal exercise classes. The study design and consent form were approved by the Queen’s University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board and by the United States Army Medical Research and Material Command, Human Subjects Protection Branch.

Each subject participated in two visits to the laboratory. The initial visit consisted of collection of demographic information, anthropometric measurements (body height and mass), and the graded exercise test described below. The final visit consisted of a two-stage submaximal exercise test that was conducted at least 3 days after the first visit.

Graded exercise test. Graded exercise tests were performed in the upright posture on a Sensor Medics (model 800) constant work rate cycle ergometer to evaluate aerobic fitness and to identify Tvent. Tvent for all subjects was determined using the V-slope method (4). This is a computerized method that involves plotting of breath-by-breath VO2 production against O2 consumption (VO2). The break point in this relationship is detected by a computer program and identifies the VO2 above which CO2 is generated by the buffering of lactic acid. The protocol involved a 4-min warm-up at 20 W, followed by a 20 W/min ramp increase in work rate, until HR = 170 beats/min (19, 34).

Respiratory responses for the graded exercise test were measured using a computerized system (First Breath) that incorporated a respiratory mass spectrometer (MGA-1100, Perkin-Elmer) with a volume turbine (VMM-110, Alpha Technologies) (20). Oxygen pulse (VO2/HR) at peak exercise was used as an index of aerobic working capacity (34).

Two-stage submaximal exercise test. Subjects performed a two-stage submaximal exercise test on a separate day, which involved data collection in the resting state and during upright cycling at 60 and 110% of measured Tvent. The 60% Tvent work rate was chosen because it is a steady-state exercise intensity that should reflect the initial period of vagal withdrawal that occurs in nonpregnant subjects in response to a low-level exercise stimulus. The 110% Tvent exercise intensity was selected because previous studies have shown that the sympathoadrenal stimuli required to increase HR become important just above Tvent (35, 36). Immediately before the two-stage test, HRV was evaluated at rest in both the left lateral decubitus and sitting postures, at a breathing frequency of 16 breaths/min (0.267 Hz), to ensure that respiration-mediated oscillations occurred above 0.15 Hz for proper interpretation of the PNS-mediated activity. A metronome with a speaker and a light indicator were used to regulate R. The test in the left lateral posture preceded the seated posture test, so that we could study the autonomic response to a change from recumbent to upright posture in late gestation. Subjects rested in the left lateral and sitting positions for at least 5 min before data collection began.

After the resting data collection, the exercise testing protocol involved a 3-min warm-up at 20 W, followed by a 20 W/min ramp increase in work rate, within a 30-s period, to a level corresponding to 60% of the work rate at Tvent. After 20 min of rest and a 3-min warm-up, the subjects performed a second exercise bout at 110% of Tvent. On the basis of respiratory and acid-base data from an earlier study of exercise responses in pregnant women, which used a similar protocol (19), the 20-min rest period was considered to provide an adequate recovery between exercise levels. Respiratory measurements, including f, tidal volume (VT), minute ventilation (VE), and VO2, were studied on a breath-by-breath basis during both postures at rest and during both submaximal exercise bouts.

HRV spectral analysis. RRI output from a Marquette Max-1 exercise electrocardiograph was recorded continuously from standard bipolar leads in the resting state (left lateral and sitting postures) and during the two-stage submaximal exercise test protocol. Analog output from the electrocardiograph was stored to a personal computer via an analog-to-digital converter (Teemar Lab Master) and then stored to diskette for later analyses. Both resting measures and the stable portion of the two-stage submaximal test included data collection of ~600 heart cycles for HRV general
spectral analysis (GSA). Before spectral analysis, all signals were inspected visually in the time domain for artifacts (30). The best window of \( \pm 512 \) heart cycles was selected, with artifacts omitted by the computer software filtering program (Data Collection and Analysis of Beat-by-Beat Heart Rate and Blood Pressure software, Hughson RL and Yamamoto Y). GSA was based on the fast Fourier transform that quantified total power spectra (\( \pm 0.5 \) Hz), low-frequency power (0–0.15 Hz), and high-frequency power (0.15–0.5 Hz). The calculated high-frequency power-to-total power ratio was utilized as the PNS indicator, and the SNS indicator was calculated as the low-frequency power-to-high-frequency power ratio (3, 26).

**SBR function.** Analysis of SBR function involved the simultaneous collection of HR (Max-1 ECG) and SBP (Ohmeda 2300 Finapres) data on a beat-to-beat basis during both postures at rest and during both submaximal exercise intensities. During data collection, the servo-reset mechanism of the Finapres was turned off so that continuous blood pressure could be recorded (27). Also, the pulse rate and pressure alarms were turned off to avoid sudden disturbances that might influence test results. Analog output from both the Finapres and electrocardiograph were stored to a personal computer via an analog-to-digital converter (Tecmar Lab Master). Indexes of SBR function, including mean slope, mean RRI, and SBP, were calculated and recorded for each test by a computer software package (SBRX; Ref. 6). SBR sequences were determined by matching SBP with the corresponding RRI for each beat of data collected. Matched RRI that changed in the same direction as SBP (increased or decreased in value) at the same time (lag 0), during the next beat (lag 1), or the next following beat (lag 2) were used as SBR sequences (6).

**Blood biochemistry.** A registered nurse drew venous blood samples from the antecubital vein by using an indwelling catheter that was placed 20 min before taking the first sample. The samples were used to determine either plasma lactate or catecholamine concentrations. During the progressive cycle exercise test, blood was drawn at rest, and at 1, 3, 5, 7, 10, and 15 min postexercise. During the two-stage submaximal protocol, samples were obtained during the last minute at rest (sitting posture) and during the last minute of exercise at both 60 and 110% \( T_{\text{vent}} \). Samples for plasma lactate concentrations were treated with an anticoagulant (potassium oxalate) and an antiglycolytic agent (sodium fluoride). Samples collected for plasma catecholamine concentrations were treated with EGTA and glutathione. All samples were centrifuged (IEC Centra-MP4R) at 4°C and frozen for later analyses. Lactate samples were analyzed using an automated analyzer (Yellow Springs Instruments, Model 2300 STATPLUS), and catecholamine concentrations were analyzed in duplicate for epinephrine and norepinephrine concentrations by HPLC (Waters), as described by Weiker et al. (31).

**Statistical analyses.** The physical characteristics and peak responses to the graded exercise test of the PG and NPG were compared using an independent Student’s \( t \) statistic. Postural effects were analyzed by a two-way analysis of variance (group \( \times \) posture). Cardiac autonomic, metabolic, and respiratory responses to exercise were analyzed using a two-way analysis of variance (group \( \times \) work rate) for repeated measures. When significant \( F \) ratios were obtained Tukey’s honestly significant difference tests were used to compare paired means. Results of all statistical tests are considered significant if \( P \leq 0.05 \).

## RESULTS

**Subjects.** The PG was composed of 14 healthy, non-smoking, physically active, pregnant female volunteers. The mean age of the PG was 30.9 ± 0.9 yr (range 28–39 yr), with a mean gestational age of 33.9 ± 1.0 wk (26–39 wk). NPG was also composed of 14 healthy, nonsmoking and physically active but nonpregnant female volunteers with similar ages (28.4 ± 1.8 yr; range 21–42 yr) and acted as a control group (Table 1). The NPG was studied at varying stages of the menstrual cycle. As expected, PG had significantly higher body mass and body mass index than NPG. However, the self-reported prepregnancy body mass and body mass index were similar between the two groups. Oxygen pulse at 170 beats/min and \( V_{\text{O}}_{2} \) at \( T_{\text{vent}} \) did not differ significantly between groups.

**Metabolic and respiratory data.** Metabolic and respiratory data were collected during the two-stage exercise tests (Table 2). There were no significant differences in exercise \( V_{\text{O}}_{2} \), \( f \), \( V_{\text{t}} \), and \( V_{\text{s}} \) between the two groups. Values for plasma lactate at 60% \( T_{\text{vent}} \) were <4.0 mmol/l. Exercise at 110% \( T_{\text{vent}} \) elicited values >4.0 mmol/l for both groups. There was no difference between groups for plasma lactate concentration. The values for plasma lactate indicated that the exercise work rates used were, in fact, above and below \( T_{\text{vent}} \).

**Cardiac autonomic control.** At rest, in the left lateral and sitting postures, the mean RRI was shorter and SBP was lower in the PG compared with the NPG. Mean RRI decreased and SBP increased with a change in posture from left lateral decubitus to sitting in the NPG but not the PG (Table 3). HRV total power spectra and the PNS indicator were significantly lower in the PG than NPG at rest in both postures (Table 3). SBR slope was significantly lower in the PG in both postures. There was an interaction in SBR slope with a change in posture, with the NPG showing a larger
decrease in SBR slope during sitting than the PG. The SNS indicator was significantly higher in both postures in the PG vs. NPG and was not altered with a change in posture.

Both groups had a significant decrease in RRI as a function of exercise. RRI values were similar at 60 and 110% $T_{vent}$ for the two groups. However, the decrease in RRI from sitting to exercise (significant interaction) at both 60 and 110% $T_{vent}$ was smaller in the PG compared with the NPG (Fig. 1A).

In the PG, there was significantly lower HRV total, low-frequency, and high-frequency power at sitting rest compared with the NPG. During exercise at 60% $T_{vent}$, the PG had significantly reduced low-frequency power compared with the NPG. Total, low-frequency, and high-frequency power all decreased from sitting to exercise at 60 and 110% $T_{vent}$ (Fig. 2).

Both the PNS indicator and SBR slope were decreased in the PG at sitting rest compared with the NPG (Fig. 3). SBR slope decreased from sitting to 60% $T_{vent}$ and from sitting to 110% $T_{vent}$ in both groups. The PNS indicator also decreased in the transition from sitting to exercise at 60 to 110% $T_{vent}$ in both groups.

There was no significant difference in the SNS indicator at rest between the groups (Fig. 4A). There was a decrease in SBR slope during sitting than the PG. The SNS indicator was significantly higher in both postures in the PG vs. NPG and was not altered with a change in posture.

### Table 2. Metabolic and respiratory responses during submaximal exercise

<table>
<thead>
<tr>
<th>Metabolic and respiratory responses during submaximal exercise</th>
<th>Pregnant Group</th>
<th>Nonpregnant Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>$V\dot{O}_2$, ml/min</td>
<td>1,114 ± 37</td>
<td>1,163 ± 54</td>
</tr>
<tr>
<td>60% $T_{vent}$</td>
<td>1,780 ± 67</td>
<td>1,868 ± 90</td>
</tr>
<tr>
<td>110% $T_{vent}$</td>
<td>24.8 ± 1.9</td>
<td>24.6 ± 1.0</td>
</tr>
<tr>
<td>$f$, breaths/min</td>
<td>30.6 ± 2.3</td>
<td>30.2 ± 1.5</td>
</tr>
<tr>
<td>$Vr$, ml</td>
<td>1,407 ± 63</td>
<td>1,202 ± 62</td>
</tr>
<tr>
<td>60% $T_{vent}$</td>
<td>2,059 ± 83</td>
<td>1,877 ± 73</td>
</tr>
<tr>
<td>$Vt$, l/min</td>
<td>33.1 ± 1.6</td>
<td>28.2 ± 1.1</td>
</tr>
<tr>
<td>60% $T_{vent}$</td>
<td>61.4 ± 3.7</td>
<td>55.6 ± 3.1</td>
</tr>
<tr>
<td>Work rate, W</td>
<td>59 ± 3</td>
<td>63 ± 4</td>
</tr>
<tr>
<td>60% $T_{vent}$</td>
<td>126 ± 4</td>
<td>137 ± 7</td>
</tr>
<tr>
<td>Plasma lactate, mmol/l</td>
<td>2.1 ± 0.3</td>
<td>1.5 ± 0.2</td>
</tr>
<tr>
<td>60% $T_{vent}$</td>
<td>5.2 ± 0.5</td>
<td>5.6 ± 0.7</td>
</tr>
</tbody>
</table>

Values are means ± SE; $n = 14$ for both groups. No significant between-group effects were observed during exercise at 60 or 110% $T_{vent}$. $V\dot{O}_2$, $O_2$ consumption; $f$, breathing frequency; $Vr$, tidal volume; $Vt$, minute ventilation.

### Table 3. Cardiac autonomic function at rest in the left lateral and sitting postures

<table>
<thead>
<tr>
<th>Cardiac autonomic function at rest in the left lateral and sitting postures</th>
<th>Pregnant Group</th>
<th>Nonpregnant Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>RRI, ms</td>
<td>760 ± 19†</td>
<td>1,075 ± 54*</td>
</tr>
<tr>
<td>Sitting</td>
<td>721 ± 20†</td>
<td>996 ± 50</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>104 ± 5†</td>
<td>115 ± 6*</td>
</tr>
<tr>
<td>Left lateral</td>
<td>112 ± 4†</td>
<td>128 ± 3</td>
</tr>
<tr>
<td>Sitting</td>
<td>6.9 ± 2.0†</td>
<td>1.8 ± 0.4</td>
</tr>
<tr>
<td>SNS indicator</td>
<td>7.1 ± 2.6†</td>
<td>1.8 ± 0.3</td>
</tr>
<tr>
<td>Left lateral</td>
<td>0.23 ± 0.04†</td>
<td>0.46 ± 0.06</td>
</tr>
<tr>
<td>Sitting</td>
<td>0.26 ± 0.06†</td>
<td>0.41 ± 0.05</td>
</tr>
<tr>
<td>Total power, ms²/Hz</td>
<td>617 ± 122†</td>
<td>5,386 ± 1,754</td>
</tr>
<tr>
<td>Left lateral</td>
<td>715 ± 109†</td>
<td>4,174 ± 1,226</td>
</tr>
<tr>
<td>Sitting</td>
<td>9.0 ± 1.1†</td>
<td>26.3 ± 4.1*</td>
</tr>
<tr>
<td>SBR slope, mmHg/ms</td>
<td>8.5 ± 1.1†</td>
<td>18.8 ± 3.4*</td>
</tr>
</tbody>
</table>

Values are means ± SE; $n = 14$, except for left lateral posture in the nonpregnant group, where $n = 13$. RRI, R-wave-R-wave interval; SBP, systolic blood pressure; SNS, sympathetic nervous system; PNS, parasympathetic nervous system; SBR, spontaneous baroreflex. *Significant difference ($P \leq 0.05$) between left lateral and sitting postures within group; †significant difference ($P \leq 0.05$) between groups in left lateral or sitting.
significant increase in the SNS indicator in the transition from sitting to exercise at both 60 and 110% $T_{vent}$ and from 60 to 110% $T_{vent}$ in the NPG. There was no significant effect of intensity on the SNS indicator in the PG. The SNS indicator was significantly decreased at 110% $T_{vent}$ in the PG.

Plasma catecholamines. There was no significant difference in plasma norepinephrine levels at rest or at 60% $T_{vent}$ between groups; however, the PG had significantly lower levels at 110% $T_{vent}$ compared with the NPG (Fig. 4B). Plasma epinephrine levels were significantly lower in the PG at rest and at 60 and 110% $T_{vent}$ than the NPG (Fig. 4C). Both plasma norepinephrine and epinephrine levels increased significantly from rest to 60% $T_{vent}$ and from 60 to 110% $T_{vent}$.

**DISCUSSION**

This study is the first to examine the effects of healthy human pregnancy on cardiac autonomic function both at rest and at exercise intensities above and below $T_{vent}$. An important strength of this study is the combined use of HRV spectral analysis, noninvasive evaluation of SBR sensitivity, and measurement of plasma catecholamines to study the effects of pregnancy and exercise on cardiac autonomic control. The overall results supported our original hypotheses that parasympathetic modulation (as reflected by reductions in HRV high-frequency power/total power and SBR slope) would be blunted in the resting state and that sympathetic modulation (as reflected by reductions in HRV low-frequency power/high-frequency power and plasma catecholamines) would be attenuated in late gestation.
ated during exercise above $T_{vent}$. These results provided a logical and mechanistic explanation for earlier findings that resting HR is increased (8, 11), that HR responses to strenuous exercise are blunted (22), and that maximal HR reserve is reduced (23, 28, 29, 33) in healthy pregnant women.

Our findings are also consistent with the hypothesis of Duvekot et al. (12) that cardiovascular changes in human pregnancy are initiated by a reduction in peripheral vascular resistance that is mediated by elevated circulating estrogen levels. The decrease in peripheral vascular resistance becomes more pronounced as the fetoplacental shunt develops and a greater percentage of the total cardiac output is diverted toward the fetus. A reduction in blood pressure would then be prevented by activation of renal “volume-restoring mechanisms” (i.e., renin-angiotensin system, arginine vasopressin release) activated by baroreceptors. At the same time, an estrogen-mediated increase in heart volume occurs that helps to accommodate augmented venous return without an increase in left ventricular preload (17, 18). Finally, an increase in resting HR, mediated by the lower level of parasympathetic/vagal mediation observed in the present study, along with an augmented SV, would explain the so-called “hyperkinetic” cardiac output that has been documented in pregnant women and would help to maintain a normal resting blood pressure, even though peripheral vascular resistance is reduced.

Our results confirmed that the higher resting HR in late gestation is primarily the result of less parasympathetic modulation in both the left lateral and the sitting posture. This finding is consistent with the earlier study of Brooks et al. (8), which reported that the higher minimal HR observed during pregnancy compared with the nonpregnant state is abolished in conscious rabbits by parasympathetic pharmacological blockade. Because the SNS indicator was increased in the PG in both resting postures (but not plasma catecholamines measured in the sitting posture), some evidence was also provided in the present study for increased sympathetic modulation at rest in late gestation.

After the transition from the left lateral position to the sitting posture, RRI increased significantly in the NPG but not the PG. No significant change was observed in the PNS or SNS indicators in either group, but SBR slope, an index of vagally mediated HR control, decreased significantly in both groups and a significant group $\times$ posture interaction was observed. Thus it appears that both the degree of PNS modulation and the degree of vagal withdrawal with this change in posture were attenuated in the PG vs. NPG. As discussed previously by Brooks et al. (8, 9), evidence also exists for attenuation of sympathetic responses to more intensive forms of orthostatic stress and during challenges, such as hemorrhage, in late gestation.

The cardiac autonomic response to exercise in both groups was qualitatively similar to that reported previously by Yamamoto et al. (35) in healthy, nonpregnant subjects. In this regard, both groups displayed progressive vagal withdrawal in the transition from rest to exercise and enhanced sympathetic modulation at work rates above $T_{vent}$. However, owing to lower baseline levels of PNS modulation, the magnitude of withdrawal was less in the pregnant vs. nonpregnant state. Similarly, plasma catecholamines increased significantly in the transition from rest to strenuous exercise in both groups, but this effect was quantitatively greater in the NPG, and the exercise-induced changes
in the SNS indicator within the PG did not reach statistical significance.

The present study also provides strong evidence for blunted cardiac autonomic (HRV-SNS indicator) and sympathoadrenal (plasma epinephrine and norepinephrine) responses to exercise above T_{vent} in the pregnant vs. nonpregnant state. Although no significant between-group difference was observed for RRI at 110% T_{vent} in the present study, blunted cardiac autonomic responses would provide a logical mechanistic explanation for the attenuated peak HR responses to maximal exercise testing that have been reported in earlier studies (22). This viewpoint is consistent with two earlier studies of cardiac autonomic function in laboratory animals (8, 23), which reported a reduced cardiac baroreflex gain in the pregnant vs. nonpregnant state.

Reduced epinephrine and norepinephrine responses to strenuous exercise in late gestation were also reported in healthy human subjects by Bonen et al. (7). As postulated in a recent review from this laboratory (33), the reduced epinephrine response could also contribute to a lower rate of catecholamine-mediated liver glycogenolysis, an exercise-induced reduction in maternal blood glucose concentration (7), and reduced carbohydrate utilization and lactate production during maximal or near maximal exercise (34).

The integrated HR response to graded exercise testing in healthy pregnant women has also been described using linear regression analysis of HR expressed as a function of VO_2. Earlier studies have consistently reported a reduced slope and increased y-intercept of the HR vs. VO_2 regression (22, 29, 33). The pattern of exercise-induced changes in RRI in this study is consistent with the earlier findings and further suggests that the reduced HR vs. VO_2 slope in late gestation is the combined result of reduced PNS modulation during mild exertion and blunted SNS modulation during strenuous exercise.

Although the present results provide clear evidence for attenuated parasympathetic cardiac modulation in the resting state and blunted sympathoadrenal responses to strenuous exertion in late gestation, it is important to recognize the limitations of the noninvasive methodologies employed in this study. In this regard, data obtained from HRV spectral analyses reflect changes within the normal cardiac autonomic operating range of individual subjects and do not constitute quantitative measures of cardiac autonomic activity (24). Similar limitations exist for SBR sensitivity data obtained by linear regression analyses of HR and SBP sequences, as this method provides information on beat-to-beat vagal control of HR rather than the full operating range of the baroreflex (27).

Another potential limitation of the use of HRV spectral analysis is the contribution of exercise-induced increases in f and VT to the estimate of high-frequency power (25). There were no significant differences in f or VT between groups for this study; however, the PG had slightly higher values for both respiratory measures in all conditions. This may increase the HRV high-frequency power and, therefore, increase the estimates of PNS modulation. In the present study, we were able to confirm the finding that sympathoadrenal responses to strenuous exercise are blunted in late gestation by the plasma epinephrine and norepinephrine values.

In conclusion, the findings of this study support our original hypothesis that cardiac parasympathetic-vagal modulation is reduced in the resting state and that sympathoadrenal responses to strenuous exercise above T_{vent} are blunted in healthy women in late gestation. Evidence also exists for a reciprocal increase in SNS modulation in the resting state. These findings have important practical implications for the use of HR to monitor and prescribe exercise intensity in prenatal physical conditioning programs (10). Future research is recommended to examine the effects of advancing gestational age, physical conditioning, and maternal-fetal disease states (e.g., preeclampsia).

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