Sympathoadrenergic Mechanisms in Reduced Hemodynamic Stress Responses after Exercise

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ABSTRACT


Purpose: This study examines the acute effects of moderate aerobic exercise on 1) hemodynamic and sympathetic activity during behavioral stress and 2) β-adrenergic receptor responsivity in a biracial sample of 24 sedentary adults. Methods: Before and after exercise, blood pressure (BP), impedance-derived cardiovascular measures, and plasma norepinephrine (NE) and epinephrine (EPI) were assessed during mental arithmetic and active speech tasks, and β-adrenergic receptor responsivity was assessed using a standard isoproterenol challenge procedure. Results: After exercise, BP, NE, and EPI responses to stress were reduced (0.0001 < P < 0.08), prejection period (PEP) was elongated (P < 0.0001), and β₁- and β₂-receptor responsivity (P < 0.02) was enhanced. Approximately 65% of the prepost exercise mean arterial pressure response difference could be accounted for by changes in sympathetic factors, with change in NE and PEP being the single best predictors. Conclusions: Reduced BP responses to stress after acute exercise are strongly linked to a decrease in sympathetic drive, as evidenced by reduced NE responses and elongation of the PEP. Coincident with this overall dampening of the hemodynamic response to stress, increases in cardiac and vascular β-adrenergic receptor responsivity occur. These findings may have important implications for future translational studies that seek to articulate the mechanisms through which regular aerobic exercise reduces the risks of hypertensive and coronary heart disease. Key Words: BLOOD PRESSURE, STRESS RESPONSIVITY, SYMPATHETIC NERVOUS SYSTEM, BETA-ADRENERGIC RECEPTOR, CATECHOLAMINE

It has been suggested that heightened sympathetic responses to behavioral stress may be a marker for increased cardiovascular disease risk due to other pathological processes, or perhaps even play a causal role in the etiology of hypertension (15,20). Although the precise mechanisms underlying these associations are not completely understood, it is thought that recurrent exposure to increased hemodynamic load may promote deleterious structural and/or functional adaptations in the myocardium or systemic vasculature that, in turn, depress cardiac output (CO) and elevate total peripheral resistance (TPR) in a manner predisposing to the development of established hypertension. Conversely, aerobic exercise training is strongly associated with reduced risk of hypertension and cardiovascular morbidity and mortality (13,19), and cross-sectional studies indicate a link between aerobic fitness and reduced sympathetic responses to stress (30). This collection of observations has led to the speculation that regular participation in an aerobic exercise program may lower cardiovascular risk by attenuating sympathetic responses to stress in a cumulative manner, thereby limiting exposure to the presumed pathophysiological sequelae of repeated hyper-sympathetic arousal. Although this proposition has yet to be confirmed through longitudinal investigation, a growing body of literature linking acute moderate-intensity exercise with reduced cardiovascular responses to stress is emerging.

Exercise may directly reduce autonomic and neuroendocrine responses to behavioral challenge. Several studies, including our own (3,32), have shown reduced blood pressure (BP) responsiveness to behavioral challenge after a single episode of moderate to high-intensity aerobic exercise (1,6,27). Postexercise inhibition of BP responsiveness to stress has been observed both in controlled laboratory as well as ambulatory settings—the latter findings, in particular, suggesting that acute exercise may modulate the physiological impact of everyday stress on resting BP. Despite the consistency of these findings, however, relatively less is understood about the physiological mechanisms underlying this phenomenon.

Peronnet et al. (26) reported a nearly 50% reduction in plasma epinephrine response to the Stroop test in young,
healthy male subjects after 2 h of low-intensity cycling. This study, however, did not find a significant postexercise reduction in BP response to the Stroop. Therefore, it is unclear from this study to what extent, if at all, the observed postexercise alteration in adrenomedullary activity influenced cardiovascular responsiveness during stress exposure. Previously, our research group (32) and others (6) observed marked reductions in peripheral vasoconstriction during behavioral stress tasks administered after acute exercise. However, these studies did not assess peripheral or myocardial mechanisms responsible for these effects. Therefore, the present study was designed to systematically examine alterations in cardiovascular, neuroendocrine, and β-adrenergic receptor-mediated functioning at rest and in response to behavioral challenge after a single 20-min bout of moderate-intensity aerobic bicycle exercise.

The two primary objectives of the present study were to 1) replicate earlier findings of reduced cardiovascular stress responses in sedentary individuals after acute moderate-intensity exercise, and 2) examine whether such reductions may be due to diminished sympathoadrenergic activity.

METHOD

Subjects

Twenty-four participants [12 men (6 white, 6 black), 12 women (6 white, 6 black)] were recruited by ads in newspapers and bulletin boards from the local university and surrounding communities; each provided written informed consent, as approved by the University of North Carolina Chapel Hill Committee on the Protection of the Rights of Human Subjects, before participation. Characteristics of the subjects are presented in Table 1. According to self-report and submaximal exercise testing, subjects were sedentary and low fit but otherwise healthy. Exclusionary criteria included: a) current use of antihypertensive or psychoactive medications with known cardiovascular (CV) effects or oral contraceptives; b) a history or current diagnosis of serious CV, renal, or pulmonary problems; c) chronic physical or psychological disorders; and d) average resting diastolic BP (DBP) > 95 mm Hg or systolic BP (SBP) > 160 mm Hg.

All subjects were normotensive (SBP range = 92–133 mm Hg; DBP range = 58–79 mm Hg). Subjects were instructed to refrain from consuming food and caffeine for 2 h before testing; and women were tested during menstrual cycle days 3–8 to minimize potential gender differences in vascular tone during stress (10).

Instrumentation and Measures

Height and weight were measured with a DETECTO digital weight-indicating instrument (Cardinal Scale Manufacturing Co., Webb City, MO). BP was measured noninvasively using two automated devices, both of which were standardized on the basis of three throstoscopic determinations made simultaneously with the automated measurements. During stress testing, exercise, and related baseline and recovery periods, BP was measured by auscultation; during receptor responsivity testing, BP was measured by the vascular unloading technique. For auscultation, a standard inflatable occlusion cuff was positioned around the subject’s nondominant arm. The cuff was rapidly inflated and then deflated at a linear rate of 3 mm Hg s⁻¹ by a custom-designed and built device (Stan Hutchinson, Biomedical Engineer, UNC). Using this device, Korotkoff sounds were detected by a piezoelectric microphone positioned over the participant’s brachial artery under the distal end of the cuff. Cuff pressure and Korotkoff sounds were recorded in analog form and, through the use of a special output connector, displayed on adjacent channels on a Videograph II computer system (Coulbourne Instruments, Allentown, PA). Cuff pressures corresponding to onset (SBP) and disappearance (DBP) of Korotkoff sounds were recorded. Mean arterial pressure (MAP) was computed as ((SBP – DBP)/3) + DBP. During β-receptor responsivity testing, BP was measured continuously using the Finapres noninvasive BP monitor (Ohmeda, Madison, WI), which utilizes the vascular unloading technique to measure SBP, DBP, and MAP on a beat-by-beat basis. Fluctuations in cuff pressure closely follow intra-arterial pressure, and pressure pulsations are of the greatest magnitude when the cuff is at MAP. Thus, arterial blood pressure is measured continuously as a function of the external pressure applied through the cuff. Beat-by-beat data are essential for identifying the peak heart rate (HR) change due to isoproterenol challenge (i.e., the HR peak coincident with a marked decrease in BP). The HR response to isoproterenol is transient, occurring within 2 min of infusion and lasting approximately 40 s. Therefore, auscultatory methods are inadequate to capture the full dynamics of this response.

Cardiac performance was monitored with a Hutcheson Impedance Cardiograph (model HIC-1, Bioimpedance Technology, Chapel Hill, NC) using a tetrapolar band-electrode configuration. Noninvasive impedance cardiography methodology has been validated in humans using standard (dye-dilution, Fick) and two-dimensional imaging (nuclear ventriculography) methods, as well as Doppler and M-mode ultrasonography, yielding favorable correlations ranging from 0.48 to 0.97 (see 2, for review). The electrocardiogram

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**TABLE 1. Subject characteristics.**

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
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</tr>
<tr>
<td>Height (cm)</td>
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</tr>
<tr>
<td>Men</td>
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<td>6.4</td>
</tr>
<tr>
<td>Women</td>
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<td>16.9</td>
</tr>
<tr>
<td>Weight (kg)</td>
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<td>12.6</td>
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<tr>
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<td>Women</td>
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<td>11.9</td>
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<tr>
<td>Resting SBP (mm Hg)</td>
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</tr>
<tr>
<td>Resting DBP (mm Hg)</td>
<td>67.1</td>
<td>8.3</td>
</tr>
<tr>
<td>Predicted VO₂max (mL kg⁻¹ min⁻¹)</td>
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<td>7.3</td>
</tr>
<tr>
<td>Men</td>
<td>29.7</td>
<td>4.7</td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SBP and DBP, systolic and diastolic blood pressure; HR, heart rate; VO₂max, maximal oxygen consumption.
was recorded independently with disposable electrodes and processed along with basal thoracic impedance \( (Z_O) \) and the first derivative of the pulsatile impedance \( (dz/dt) \) using specialized ensemble-averaging software to filter respiratory and movement artifact (COP, BIT Inc., Chapel Hill, NC) to derive HR, CO, pre-ejection period (PEP), and stroke volume (SV) (18). TPR (dyn·s·cm\(^{-2}\)) was derived as \( \frac{MAP}{CO} \times 80 \). As recommended (28), CO, SV, and TPR were adjusted for individual differences in body surface area yielding cardiac index (CI), stroke volume index (SVI), and vascular resistance index (VRI), respectively.

Blood sampling and drug infusions were achieved through a flexible cannula inserted into a forearm vein, and attached polyethylene tubing, kept patent via continuous slow-rate normal saline (NS, 0.9% NaCl) drip. Blood sample for catecholamines was collected in EDTA-treated tubes, immediately cold centrifuged, pipetted for plasma extraction, stored in triplicate, and frozen \((\sim -80^\circ \text{C})\). Plasma epinephrine (EPI) and norepinephrine (NE) were assayed using high-performance liquid chromatography (University of North Carolina Clinical Research Center). Drug (0.2 mg·mL\(^{-1}\) Isuprel, Sanofi Winthrop, NY) was prepared (0.4 mL·9.6 mL\(^{-1}\) NS) and serially diluted into bolus doses (4, 2, 1, 0.5, 0.25, and 0.125 \( \mu \)g) and refrigerated until 30 min before administration. Blood samples were successfully obtained during rest and behavioral stress testing from all subjects on both test days and during steady-state exercise from all subjects on day 2 and from 22 subjects on day 1.

**Mental arithmetic (math).** The Paced Auditory Serial Addition Task (PASAT) consists of four series of tape-recorded single-digit numbers in which each series has a slightly faster presentation rate. Subjects add each number presented on the tape to the immediately preceding number and state the sum out loud before the next number is presented. Subjects completed series 1, 2, and 3 before exercise and series 2, 3, and 4 after exercise and were awarded a monetary bonus (up to $5.00) based upon performance. The duration of each three-series task was 5 min. The use of series no. 4, with its slightly increased rate of delivery (1.2 vs 1.6 s for series no. 3) and potential for greater bonus ($0.045 vs $0.035 per correct answer for series no. 3), was intended to promote subject engagement. Subjects were aware of the bonus by virtue of informed consent and were reminded of the association of this bonus to their performance before completing the task.

**Speech.** Subjects engaged in a 3-min active speaking task in which they described how they would handle a hypothetical conflict situation. Each speech was preceded by a 2-min preparation period and was recorded by the experimenter using a hand-held taping device. Before exercise, subjects spoke about confrontations with a close friend who borrowed a prized possession and returned it damaged without any explanation; after exercise, the hypothetical confrontation involved a family member houseguest whose discourteous behavior was becoming an emotional and financial burden. Novel topics were used at these different intervals in an effort to minimize habituation to the task.

**Exercise testing and challenge.** Subjects completed 25 min of submaximal cycle ergometry. The 25-min challenge began with a submaximal cycle ergometer test used to predict maximal oxygen uptake \( (pV_{O2max}) \). Following the standard YMCA protocol (11), resistance was initially set at 150 kg·m·min\(^{-1}\) (0.5 kp) for women and 300 kg·m·min\(^{-1}\) (1.0 kp) for men. Subjects pedaled a Monark cycle ergometer (model 818, Varberg, Sweden) at a rate of 50 rpm and resistance was increased in 3-min stages according to individual HR response at each stage. A mechanical metronome signaled the correct cadence. The goal was to obtain a HR of approximately 150–160 beats per minute (bpm) at the end of the third stage. This goal was met for 23 of the 24 subjects; one subject required a fourth stage to reach the desired HR range. HR was monitored minute-by-minute throughout the test. Immediately at the end of this exercise test, \( pV_{O2max} \) was determined as recommended (11). To accomplish this task, a predrawn grid with HR ranging from 80 to 200 bpm on the Y-axis and power output ranging from 150 to 2100 kg·m·min\(^{-1}\) and maximum \( O_2 \) uptake ranging from 0.6 to 5.0 L·min\(^{-1}\) on the X-axis was used (11). At the conclusion of stage 3 (e.g., min 9 of exercise), the HR from stages 2 and 3 was quickly plotted on the grid, the resulting line was extended to the subject’s individual age-adjusted maximum HR, and \( pV_{O2max} \) was estimated by drawing a vertical line from the point corresponding to maximum HR down to the X-axis; 70% of the \( pV_{O2max} \) was computed, and the power output corresponding to this value was then determined. This process took approximately 30–45 s, during which time the subject continued to pedal at the power output level used during stage 3. The power output was then adjusted to the level corresponding to 70% \( pV_{O2max} \) and subjects pedaled at this level for the remainder of the 25-min exercise challenge (approximately 16 min). HR was monitored continuously throughout the procedure to ensure safety. Age-adjusted maximum HR in this sample ranged from 185 to 201 bpm. Average HR measured at the conclusion of stage 3 was 157.3 \( \pm 10.3 \) bpm, and steady-state HR at 70% \( pV_{O2max} \) was 140.4 \( \pm 6.0 \) bpm, which represents 70–76% maximum HR for this sample. When exercise was repeated on day 2, this same protocol was followed, including the incremental submaximal test, with power output being set and maintained at the conclusion of stage 3 at the same level specified on day 1.

**\( \beta \)-adrenergic receptor responsivity testing.** A standardized isoproterenol sensitivity test was administered to evaluate \( \beta \)-adrenergic receptor responsivity (5). Progressively increasing bolus doses of isoproterenol were infused, and HR responses were computed after each dose as the shortest three successive ECG R-R intervals after drug infusion compared with the shortest three R-R intervals recorded during preinfusion rest. Beat-by-beat HR and BP data were collected and displayed using custom-designed software (Richard Lutz and Stan Hutchinson, UNC). Data were edited on-line to immediately assess the peak HR response to the initial dose, and after HR and MAP had restabilized (approximately 5 min), the procedure was repeated until a dose was administered that increased HR at
least 25 bpm. $\beta_1$-receptor responsiveness was determined as the dose of isoproterenol needed to increase HR 25 bpm (chronotropic dose: $CD_{25}$), based on interpolation of the linear regression model of log dose/HR response. In addition, BP, HR, and SV data were saved in 7-s epochs and later used to compute mean MAP, CO, and TPR values for each epoch using previously stated formulae. Vascular $\beta_2$-receptor responsiveness was determined as the dose of isoproterenol needed to decrease TPR by 50% (vasodilatory dose: $VD_{50}$) relative to each predose baseline, based on interpolation of the log dose/TPR response.

### Design and Procedures

Each subject was studied on three occasions, including a preliminary screening session and two separate test days. The two test days occurred within a 72-h period, with time of testing held constant to minimize the effects of diurnal variations in catecholamine levels. On the first day of testing (day 1), subjects underwent behavioral stress testing before and after completing 25 min of moderate-intensity bicycle exercise followed by a 30-min exercise recovery period to evaluate the impact of the acute exercise bout on CV and catecholamine reactivity. On the second day of testing (day 2), subjects underwent $\beta$-adrenergic receptor responsivity testing before and after completing 25 min of moderate-intensity exercise followed by a 30-min exercise recovery period (identical to day 1) to evaluate $\beta$-adrenergic adaptations to acute exercise.

### Preliminary Screening

Each volunteer’s resting BP status was confirmed on the basis of three stethoscopic BP measurements. Next, each volunteer completed series 1 of the PASAT during which MAP was recorded at 10-s intervals using the Finapres. Because one aim of this study was to examine sympathetic mechanisms underlying hypothesized exercise-induced reductions in reactivity, the sample was intentionally biased toward ensuring the requisite stress response. Thus, this brief stress exposure session was used to identify individuals who were at least modest stress reactors. Based on our previous studies involving similar groups of subjects (3,32), we defined a modest reactor as exhibiting at least an 8 mm Hg increase in MAP during this task. Subsequently, two low responders (i.e., $< 8$ mm Hg MAP increase) were excluded from further participation.

### Day 1: Behavioral Stress before and after Exercise

Subjects were seated upright for 20 min. Impedance-derived cardiac measurements and BP were obtained at 3-min intervals through minute 19, and blood samples were drawn during minute 20 of this prestress rest period (Rest$_1$). The subject then completed preexercise stress testing (Set$_1$). The math task was completed first, followed by a 5-min rest period, and then the speech task. BP and impedance-derived measures were obtained at minutes 1, 3, and 5 of the math task, and minutes 1 and 3 of the speech. Blood samples were obtained during the final 30 s of each task. After completing the speech task, subjects then rested again quietly alone for 5 min.

Subjects next completed the 25-min exercise test and challenge. HR and BP were recorded at 3-min intervals through minute 24 and blood samples were drawn during the final 30 s of min 25. After exercise, subjects returned to the testing chair, were given water (3 mL·kg$^{-1}$ body weight) to drink, and remained seated upright for 30 min after the exercise in an attempt to reestablish resting CV values. CV measurements were obtained at 3-min intervals through the 30-min postexercise rest period, and a blood sample was obtained during the final minute. At the conclusion of the postexercise rest period (Rest$_2$), subjects completed postexercise stress testing (Set$_2$; math, 5-min rest, and speech). All CV measures were obtained at the same time intervals as mentioned above for the preexercise stress exposure period.

### Day 2: $\beta$-Adrenergic Receptor Responsivity Assessment before and after Exercise

Subjects rested for 20 min in the reclined position; impedance-derived measurements were obtained at 3-min intervals through minute 19, and MAP was monitored continuously to establish stability of Finapres measurements. A blood sample was drawn during minute 20. At the conclusion of this rest period, the isoproterenol responsivity test was completed. HR, BP, and impedance-derived measures were obtained beat-by-beat, as described above. Subjects were returned to the upright-seated position and sat quietly for approximately 5 min while the ergometer was brought into the testing room and positioned in front of the testing chair. Subjects then completed the identical exercise protocol described for day 1, including the 25-min exercise test and challenge and the 30-min postexercise rest period. At the conclusion of the postexercise rest period, the subject returned to the testing chair, was reclined, and isoproterenol responsivity testing was repeated using the same procedures as before the exercise challenge.

### Data Reduction and Analyses

Before data reduction, the experimenter (KB) manually edited all impedance-derived CV and corresponding BP data to improve accuracy by detecting extreme outliers due to movement artifact, poor signal quality, or data entry error in the case of BP that, in turn, affected TPR calculations. If an obvious source of error was not identifiable, individual values were left as missing and task means were computed from the remaining within-task values. To ensure stability and accuracy of resting measures, BP and impedance-derived variables were calculated as the mean of minutes 12, 15, and 18 of the prestress rest period (Rest$_1$), and of minutes 23, 26, and 29 of the postexercise rest period (Rest$_2$). Cardiovascular measures during the stressor tasks (Set$_1$ and Set$_2$) were calculated as the mean of minutes 1, 3, and 5 for the math task and as the mean of minutes 1 and 3 of the active speaking component of the speech task. Next,
reactivity variables for both tasks were computed as the average task value minus the mean rest value (preexercise: Set$_1$ – Rest$_1$; postexercise: Set$_2$ – Rest$_2$). Finally, to capture prepost exercise changes in cardiovascular reactivity, delta (Δ) scores were computed as: preexercise reactivity (Set$_1$ – Rest$_1$) minus postexercise reactivity (Set$_2$ – Rest$_2$). Similar delta scores were computed for CD$_{25}$ and VD$_{50}$ by subtracting preexercise values from postexercise values.

To evaluate the effects of exercise on cardiovascular and catecholamine responses to stress, and on β-adrenergic receptor responsivity, an initial series of mixed model multivariate repeated measures ANOVA with three within-subject repeated factors (Time: pre- and postexercise; Task: baseline, math, speech; Variable) were conducting clustering blood pressure (SBP, DBP, MAP), cardiac (SVI, CI), and β-adrenergic receptor measures (CD$_{25}$, VD$_{50}$) into three separate models. This multivariate approach limits overall Type I error rate associated with multiple univariate tests and is reasonably robust against violations of sphericity and normality (31). The remaining dependent variables (VRI, NEP, HR, EPI, and NE) were subsequently treated separately in identical mixed model repeated measures ANOVA. Statistical power calculations for these models (N = 24) indicated power was high for BP and HR (>0.92), and low to moderate for other hemodynamic measures (0.29–0.58). Power was generally high for β-adrenergic receptor measures (VD$_{50}$ at 60 min = 0.40; all others >0.84) and for the catecholamine responses to the speech task (>0.83) but very low for the catecholamine responses to the Math task (<0.13). Significant Time × Task interactions were followed by separate tests of the within-task Time effect. When these follow-up tests yielded significant Time effects for stress but not rest periods, it became of interest to see whether exercise also reduced reactivity per se. Thus, reactivity variables were subsequently analyzed using 2 (Time: pre-, postexercise) × 2 (Task: math reactivity, speech reactivity) repeated measures ANOVA, followed by separate tests of the within-task Time effect, when indicated.

The next analytical step was designed to evaluate whether prepost exercise changes in cardiovascular responses were related to prepost exercise changes in catecholamine responses, β-receptor responsivity, or cardiac sympathetic activation (PEP). These relations were assessed using stepwise multiple regression, with the criterion significance level for entry into the predictive model set at 0.15. Regression analyses were conducted separately by task (math and speech). Dependent measures included ΔSBP, ΔDBP, ΔMAP, ΔCI, and ΔVRI. Predictors included ΔPEP, ΔEPI, ΔNEP, and ΔCD$_{25}$ and ΔVD$_{50}$ measured 60 min postexercise.

To quantify the magnitude of selected effects of interest, eta-squared was calculated for analysis of variance results, and the squared multiple correlation was calculated for multiple regression analyses. For simplicity, both are denoted as $\eta^2$. Alpha was set at 0.05 for primary analyses, with trends noted at $P < 0.10$ for follow-up tests consistent with significant omnibus effects. Multivariate analyses were performed using SAS Proc Mixed (V. 8.0) and regression analyses were performed using SAS Proc REG (V. 8.0), SAS Institute, Cary, NC.

### RESULTS

#### Evidence of Exercise Equivalence on the Two Test Days

Mean (± SD) catecholamine levels (pg·mL$^{-1}$) during exercise and the postexercise rest period on the 2 days were as follows: Peak NE: day 1 = 581.5 ± 205.9, day 2 = 570.2 ± 171.7; Peak EPI: day 1 = 86.3 ± 33.8, day 2 = 84.3 ± 30.8; Recovery NE: day 1 = 204.4 ± 87.2, day 2 = 161.4 ± 59.2; Recovery EPI: day 1 = 40.8 ± 15.5, day 2: 40.0 ± 21.4. These data suggest equivalence in the magnitude of the exercise challenge on the two days.

#### Exercise Effects on Hemodynamic and Cardiovascular Responses to Stress

Results of the mixed-model multivariate ANOVA revealed a significant Time × Task interaction for BP (P(2,46) = 15.86, $P < 0.0001$), indicating differential Time effects by Task across the three BP measures. Postexercise resting BP levels were not different from preexercise levels ($P > 0.72$); however, average BP levels during both the math (−4.6 ± 1.0 mm Hg; $t = −4.5$) and speech (−7.7 ± 1.0 mm Hg; $t = −7.5$) tasks were significantly lower after exercise ($\eta^2 = 0.33–0.51$, $P < 0.001$). As can be seen in Table 2, these effects were largely consistent across all three BP measures (e.g., SBP, DBP, and MAP). As a result of

### TABLE 2. Mean (±SD) cardiovascular and neuroendocrine measures before and after exercise.

<table>
<thead>
<tr>
<th></th>
<th>Preexercise</th>
<th>Postexercise</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rest</td>
<td>Math</td>
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<tr>
<td>SBP (mm Hg)</td>
<td>113.7 ± 11.8</td>
<td>133.1 ± 15.9</td>
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<tr>
<td>DBP (mm Hg)</td>
<td>67.7 ± 5.9</td>
<td>82.8 ± 7.5</td>
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<tr>
<td>MAP (mm Hg)</td>
<td>82.8 ± 5.1</td>
<td>102.4 ± 9.4</td>
</tr>
<tr>
<td>VRI (dys·cm$^{-5}$·m$^{-2}$)</td>
<td>1913.3 ± 565.5</td>
<td>2217.4 ± 753.3</td>
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<tr>
<td>CI (L·min$^{-1}$·m$^{-2}$)</td>
<td>3.74 ± 1.04</td>
<td>3.99 ± 1.33</td>
</tr>
<tr>
<td>SVI (mL·kg$^{-1}$)</td>
<td>56.4 ± 15.6</td>
<td>47.9 ± 15.5</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>67.1 ± 8.3</td>
<td>84.2 ± 16.2</td>
</tr>
<tr>
<td>PEP (ms)</td>
<td>111.4 ± 14.2</td>
<td>102.8 ± 19.9</td>
</tr>
<tr>
<td>Noradrenaline (pg·mL$^{-1}$)</td>
<td>196.9 ± 70.3</td>
<td>241.7 ± 107.2</td>
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<tr>
<td>Epinephrine (pg·mL$^{-1}$)</td>
<td>40.2 ± 20.3</td>
<td>62.1 ± 38.5</td>
</tr>
</tbody>
</table>

MAP, mean arterial blood pressure; VRI, SVI, vascular resistance, cardiac, and stroke volume indexes; PEP, preexercise period; see Table 1 for other abbreviations.

† $P < 0.03$: different than preexercise mean value.

‡ $P < 0.02$: different than preexercise mean value.

Note: With the exception of CI, all task levels differed from rest both before ($P < 0.04$) and after exercise ($P < 0.06$). CI was not affected by exercise or task ($P > 0.09$).
resting BP levels being unchanged and stress BP levels being reduced after exercise, SBP, DBP, and MAP reactivity during both stressors was significantly reduced after exercise (F(1,23)/H11005 35.45, 16.36, and 28.48, respectively, P < 0.001; see Fig. 1).

A significant Time × Task interaction was also observed for HR (F(2,22) = 47.81, P < 0.0001). In contrast to exercise effects on BP, HR levels were higher at rest (F(1,23) = 82.41, η² = 0.78, P < 0.0001) but not during either task (η² = 0.04 and 0.14, P > 0.07) after exercise. A significant main Time effect emerged for SVI (F(2,21) = 41.41, η² = 0.65, P < 0.0001), with SVI being lower after exercise. However, after adjusting for preexercise resting SVI, pre- and postexercise SVI reactivity did not differ (P > 0.28). All main effects and interactions involving CI and VRI failed to reach statistical significance (η² = 0.02–0.43, P > 0.08).

Exercise Effects on Measures of Sympathetic and Adrenergic Activity

Significant Time × Task interactions were obtained for NE and EPI (F(2,17) = 7.23 and 3.79, η² = 0.27 and 0.17, P < 0.04). Compared with preexercise, postexercise resting levels of NE and EPI were similar (P > 0.36) but task levels were lower (Table 2). Specifically, after exercise, NE levels were lower during speech with a similar trend during math (F(1,19) = 6.67 and 3.37, η² = 0.22 and 0.26, P < 0.02 and 0.08, respectively); EPI levels were lower during speech (F(1,19) = 5.73, η² = 0.22, P < 0.03). As a result, NE and EPI reactivity to the speech task were smaller after exercise (F(1,19) = 7.54 and 7.54, η² = 0.28, P < 0.01; Fig. 2). Significant main effects of Task and Time emerged for PEP. PEP decreased during stress (F(2,22) = 3.75, P < 0.04), indicating an increase in sympathetic activation during speech and math. Sustained elevations in PEP and the PEP/LVET ratio (a HR-sensitive measure of changes in cardiac sympathetic drive) were observed in the postexercise period.
A significant overall effect of Time was observed for CD25 ($F(2,21) = 7.38$, $\eta^2 = 0.31$, $P < 0.004$) and for VD50 ($F(1.19) = 4.66$, $\eta^2 = 0.22$, $P < 0.02$). Increases in $\beta_1$ and $\beta_2$-receptor responsiveness—evidenced by reductions in CD25 and VD50, respectively—occurred throughout the 2-h postexercise period (Fig. 3). Specifically, CD25 was decreased by 20% at 60 min and by 26% at 120 min postexercise, and VD50 was decreased by 5% and 22% at 60 and 120 min postexercise.

Relation of Sympathetic/Adrenergic Changes to Reduced Cardiovascular Reactivity After Exercise

**Speech task.** Overall, 68% of the prepost exercise change in MAP reactivity could be accounted for by prepost exercise changes in sympathetic reactivity ($F(5,19) = 5.97$, $P < 0.004$, full model $\eta^2 = 0.41$). Reduced NE reactivity emerged as the best single predictor of reduced BP reactivity after exercise, accounting for 46%, 31%, and 24% of the variance in $\Delta$MAP, $\Delta$SBP, and $\Delta$DBP ($F(1,18) = 15.18$, 8.04, and 5.57, respectively; $\beta = 0.53–0.81$, $P < 0.02$). An additional 18% of the variance in $\Delta$MAP and 17% of the variance in $\Delta$DBP were accounted for by an inverse association with $\Delta$EPI ($\beta = -0.45$ and $-0.46$, respectively, full model $\eta^2 = 0.39$ and 0.29, $P < 0.03$). Prepost exercise differences in CI reactivity were inversely related to $\Delta$PEP and $\Delta$CD25 at 60 min; $\Delta$PEP and $\Delta$CD25 accounted for 39% and an additional 19% of the variance in $\Delta$CI ($F(1,18) = 12.36$ and 7.57, $\beta = -0.56$ and $-0.44$, respectively, full model $\eta^2 = 0.37$, $P < 0.02$). Reductions in VRI reactivity were most closely related to changes in PEP; however, this model was nonsignificant ($\eta^2 = 0.13$, $P > 0.12$).

**Math task.** Overall, 64% of the prepost exercise change in MAP reactivity could be accounted for by prepost exercise changes in sympathetic reactivity ($F(4,19) = 6.82$, $P < 0.003$, full model $\eta^2 = 0.39$). The change in PEP reactivity was the best overall predictor of change in BP reactivity during this task, accounting for 24%, 14%, and 26% of the prepost exercise change in $\Delta$SBP, $\Delta$DBP, and $\Delta$MAP ($\beta = 0.54$, 0.42, and 0.60, respectively, $P < 0.05$). $\Delta$NE further accounted for 16% and 14% of the change in $\Delta$DBP and $\Delta$MAP ($\beta = 0.40$ and 0.30, respectively, $P < 0.05$). In addition, $\Delta$CD25 and $\Delta$VD50 each accounted for 13% of the variance in $\Delta$SBP ($\beta = 0.84$ and $-0.60$, $P < 0.05$) and 12% of the variance in $\Delta$MAP ($\beta = 0.82$ and $-0.63$, $P < 0.04$). No predictors met criteria for model entry for $\Delta$VRI.

**DISCUSSION**

In this sample of healthy, sedentary young adults, we found evidence of reduced BP responses to stress after a single episode of moderate-intensity bicycle exercise. These BP reductions were accompanied by corresponding reductions in neuroendocrine responses to stress and by sustained increases in $\beta_2$-adrenergic receptor responsivity. Thus, the cardiovascular stress-buffering benefits observed in this study were associated with reductions in sympathetic tone and with enhanced peripheral vasodilatation. Additional analyses showed a highly significant correlation between reductions in norepinephrine (and to a lesser degree epinephrine) responses and BP responses after exercise. These converging lines of evidence indicate that acute aerobic exercise reduces stress-related hemodynamic load by damping sympathetic activity and enhancing $\beta_2$-mediated vasodilatation.

These findings are consistent with previous studies showing reduced BP but not HR responses to behavioral stress after a single bout of aerobic exercise in normotensive (27,32) and borderline hypertensive adults (1,21). Previous investigations that failed to find evidence of postexercise stress-buffering in normotensive subjects differed methodologically from the present study in three primary ways: 1) a lower exercise intensity was often utilized, 2) changes in HR rather than BP served as the primary index of cardiovascular stress-buffering, and 3) a passive physical cold pressor task rather than an active cognitive or speaking task was used (7). The tasks used in the present study (math, speech) are considered “myocardial tasks.” That is, in the presence of a fixed stroke volume, they primarily elicit increases in HR and, thus cardiac output, which in turn elevate BP. In contrast, the cold pressor task used in other studies is generally considered a “vascular task” because it tends to elicit large increases in vascular resistance and, thus, BP. These different tasks have been shown to have high test-retest reliability (24,29) and to be predictive of BP status as long as 10 yr later (9). However, the extent to which the underlying hemodynamic pattern of a given stressor influences the extent to which exercise reduces BP reactivity during that stressor remains a question for future research.

In the present study, resting BP was not reduced after exercise. The absence of resting postexercise hypotension in our normotensive subjects is entirely consistent with earlier studies in which stress exposure occurred within 1 h of aerobic exercise (27,32). One possible explanation for the lack of postexercise hypotension might be that the introduction of the stress
challenge prevented BP from dipping below prestress resting levels during the recovery process. Alternatively, postexercise hypotension may be dependent upon preexercise BP level, such that only individuals with elevations in resting pressure subsequently exhibit resting BP reductions after exercise. Consistent with this idea, we previously found a correlation between preexercise resting BP level and the magnitude of postexercise reductions in ambulatory BP (3). Nonetheless, a follow-up study that includes a longer postexercise recovery period in normotensive subjects may be needed to resolve this question. Meanwhile, the present study is consistent with current literature in suggesting that the short-term antipressor effect of acute exercise (i.e., its lowering effect on resting BP) is limited to individuals with preexercise elevations in BP, whereas postexercise reduction in BP responsiveness to stress is independent of preexercise BP status. If this distinction holds true, it would have important implications for future planning of primary versus secondary exercise prevention models of hypertensive heart disease.

We also found evidence of sustained elongation of the prejection period and the PEP/LVET ratio at rest and during stress in the postexercise period; similar effects have been demonstrated in hypertensive rats (4). Increased afterload (i.e., impedance or resistance to ventricular emptying) can elongate the prejection period (see 28). However, diastolic BP and vascular resistance were actually reduced after exercise. Thus, it is likely that lowered sympathetic nervous system activation, and not an increase in afterload, was responsible for the decrease in PEP.

Results of the regression analyses emphasized the role of sympathetic and adrenergic contributions to the attenuated reactivity seen after exercise. Together, changes in peripheral catecholamine concentrations and peripheral and myocardial (as indexed by PEP) β-adrenergic receptor responsivity accounted for approximately 65% of the variance in MAP. Although these findings are provocative, it is clear that factors other than those examined in this study also contributed to the postexercise reductions in BP reactivity. β-endorphins are a likely candidate, given their stress-modulatory (23) and exercise-responsive attributes. Other potential neuropeptide substrates might include substance P, adrenocorticotropin hormone (which is co-released with β-endorphin), or oxytocin—all of which are responsive both to physical and psychological challenge and which have downstream effects that could influence cardiovascular responses to stress. The psychogenic effects of exercise might also moderate or mediate postexercise stress responses. And, down-regulation of vascular α-adrenergic receptors may also play a role in exercise-induced reductions in cardiovascular stress responses (14). Future studies addressing these particular factors are warranted.

Up-regulation of myocardial (β₁) receptor responsivity was evident throughout the 2-h postexercise period. In contrast, up-regulation of vascular (β₂) receptor responsivity occurred on a more delayed time course, with significant reductions in VD₅₀ only being achieved 2 h postexercise. These two may produce offsetting effects: increased vascular β₂-receptor responsivity would contribute to reduced BP reactivity by enhancing vasodilatation, and enhanced myocardial β₁-receptor responsivity would serve to maintain cardiac output in the face of systemic vasodilatation. Changes in β₂-receptor responsivity, in particular, may reflect increased receptor density and intracellular cAMP production and/or translocation of receptors from intracellular sites to the cell surface, which have been shown to occur in lymphocytes after acute exercise in humans (8,12). It is not clear to what extent long-term changes in adrenergic receptor responsivity contribute to the long-term cardio-protective effects of endurance training. For example, training-induced reductions in adrenergic receptor density are reversible within weeks (25) and improvement in cardiopulmonary fitness does not appear to alter β-receptor responsivity (8).

There were several limitations of the present study. First, subjects in this study were at least moderate BP reactors and thus were presumably physiologically vulnerable to the effects of exercise on cardiovascular stress responses. Whether less stress-reactive individuals would similarly benefit is uncertain. Nonetheless, this aspect of the study design raises the possibility that other populations with specific psychophysiological vulnerabilities (e.g., highly hostile individuals who are high sympathetic reactors) would likewise demonstrate the BP dampening effect of acute exercise. Second, the order of task presentation and speech content were not counterbalanced across subjects or across time (pre- vs postexercise). Thus, it is difficult to establish whether the postexercise reductions in sympathetic activity—which appeared to be somewhat more consistent and robust in magnitude during the speech task—were influenced by task habituation, task order, or individual differences. It is also possible that the evaluative component of the speech stressor may have rendered it less susceptible to habituation—and, thus, more likely to show an exercise effect—particularly with respect to cardiac adaptation to repeated testing (16,17). These remain important issues for future studies to address. Third, isoproterenol infusions were not conducted in the presence of vagal blockade; thus, it is not clear to what degree agonist-induced compensatory parasympathetic withdrawal and adrenergic stimulation were superimposed upon and subsequently accentuated exercise-induced chronotropic and receptor adaptations. Fourth, submaximal HR as an estimation of VO₂max is subject to numerous sources of error, including nonlinearity of the HR-VO₂ relationship at high intensities of exercise, between- and within-individual variability in maximum HR, and mechanical efficiency. Given these limitations of this method, predicting VO₂max from submaximal HR is typically accurate within 10–20% of an individual’s actual value, as determined by metabolic measures (22). The impact of such individual variability would be most problematic in between-subjects designs; our use of within-subjects design should have served to minimize these sources of error. Nonetheless, future studies would benefit from the use of respiratory measures to determine VO₂max more directly and, thus, insure validity of the exercise challenge both within and across subjects.

POSTEXERCISE STRESS RESPONSE MECHANISMS
In summary, our findings indicate that BP reactivity to behavioral stress is attenuated after a single bout of moderate-intensity exercise due to decreases in circulating norepinephrine and sympathetic tone, and to increases in β-adrenergic receptor-mediated peripheral vasodilatation. These findings add to the growing literature regarding postexercise stress buffering and may provide an additional building block toward better understanding of the psychophysiological mechanisms linking regular aerobic exercise with decreased hypertensive and cardiovascular disease risk.

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