Carotid baroreflex control of arterial blood pressure at rest and during dynamic exercise in aging humans

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Fisher JP, Kim A, Young CN, Fadel PJ. Carotid baroreflex control of arterial blood pressure at rest and during dynamic exercise in aging humans. Am J Physiol Regul Integr Comp Physiol 299: R1241–R1247, 2010. First published September 8, 2010; doi:10.1152/ajpregu.00462.2010.—The carotid baroreflex is fundamental for evoking and maintaining appropriate cardiovascular adjustments to exercise. We sought to investigate how aging influences carotid baroreflex regulation of blood pressure (BP) during dynamic exercise. BP and heart rate (HR) were continuously recorded at rest and during leg cycling performed at 50% HR reserve in 15 young (22 ± 1 yr) and 11 older (61 ± 2 yr) healthy subjects. Five-second pulses of neck pressure and neck suction from +40 to −80 Torr were applied to determine the full carotid baroreflex stimulus response curve and examine baroreflex resetting during exercise. Although the maximal gain of the modeled stimulus response curve was similar in both groups at rest and during exercise, in older subjects the operating point (OP) was located further away from the centering point (CP) and toward the reflex threshold, both at rest (OP minus CP; −10 ± 3 older vs. 0 ± 2 young mmHg, P < 0.05) and during exercise (OP minus CP; −10 ± 2 older vs. 1 ± 3 young mmHg, P < 0.05). In agreement, older subjects demonstrated a reduced BP response to neck pressure (simulated carotid hypotension) and a greater BP response to neck suction (simulated carotid hypertension). In addition, the magnitude of the upward and rightward resetting of the carotid baroreflex–BP stimulus response curve with exercise was ~40% greater in older individuals. These data indicate that despite a maintained maximal gain, the ability of the carotid baroreflex to defend against a hypotensive challenge is reduced, whereas responses to hypertensive stimuli are greater with advanced age, both at rest and during exercise.

THE ARTERIAL BAROREFLEX (ABR) plays a critical role in the moment-to-moment regulation of arterial blood pressure (BP) via modulation of autonomic neural activity to the heart and vasculature. Although a wealth of data has indicated that aging is associated with impairments in resting cardiac baroreflex function (3, 14, 19, 29), studies examining ABR control of muscle sympathetic nerve activity (SNA) have reported equivocal results demonstrating impaired, preserved, or augmented responsiveness in older healthy adults (11, 14, 24, 29, 30, 46). Moreover, regarding overall ABR regulation of BP and aging, limited studies have been performed suggesting either reduced (24, 27) or unchanged (4, 41) control with advanced age. Furthermore, to date, the effect of aging on ABR control of BP during dynamic exercise has not been studied.

During exercise it has been shown in both animals (1, 8) and young healthy subjects (35, 38) that the ABR continues to regulate BP by resetting to operate around the exercise-induced elevation in BP with no change in sensitivity (i.e., gain). In young healthy individuals the resetting of the ABR during exercise occurs in direct relation to the intensity of exercise and is mediated by the activation and interaction of central signals arising from higher brain centers (central command) (21, 23, 32, 37) and by peripheral feedback arising from exercising skeletal muscle (exercise pressor reflex) (6, 20, 23, 32). Given this, one cannot simply assume that age-related alterations in ABR control noted at rest are similar during exercise, because the activation of central command and the exercise pressor reflex and their potential modulatory effects on ABR sensitivity and resetting may differ in young and older subjects (7, 28). Moreover, a properly functioning ABR appears essential for an appropriate neural cardiovascular response to exercise (25). In exercising dogs, acute baro-denervation leads to an exaggerated increase in BP (49, 50), while in humans who have surgically denervated carotid baroreceptors, not only is resting BP variability elevated but the BP response to exercise is greater (42, 47). Such observations raise the possibility that age-related impairments in ABR function may contribute to the augmented BP often observed in older individuals during exercise (9, 19, 34, 45). However, whether aging affects the resetting, sensitivity, and general parameters for the ABR control of BP during dynamic exercise is presently unknown.

Given the limited information regarding aging and baroreflex function during exercise, the present study was designed to provide a thorough assessment of ABR control of BP during dynamic exercise in young and older healthy subjects. The application of neck pressure (NP) and neck suction (NS) was utilized to examine responses to simulated carotid hypotension and hypertension, respectively, at rest and during moderate intensity cycling. In addition, full carotid baroreflex stimulus response curves were derived to examine exercise resetting and to determine the operating point gain and maximal gain of the carotid baroreflex BP curve. We tested the hypothesis that the carotid baroreflex control of BP would be impaired in older individuals during exercise.

METHODS

Subjects

Fifteen young (21–29 yr) and eleven older (54–71 yr) healthy subjects were recruited for voluntary participation in the study with a mean age difference between groups of 39 yr. Subject characteristics are provided in Table 1. All experimental procedures and protocols conformed to the Declaration of Helsinki and were approved by the University of Missouri Health Sciences Institutional Review Board.
Table 1. Subject characteristics

<table>
<thead>
<tr>
<th></th>
<th>Young</th>
<th>Older</th>
</tr>
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<tbody>
<tr>
<td>Men/Women</td>
<td>11/4</td>
<td>8/3</td>
</tr>
<tr>
<td>Age, yr</td>
<td>22 ± 1</td>
<td>61 ± 2*</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>73 ± 3</td>
<td>80 ± 5</td>
</tr>
<tr>
<td>Height, cm</td>
<td>173 ± 2</td>
<td>174 ± 3</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>24 ± 1</td>
<td>26 ± 1</td>
</tr>
<tr>
<td>Cholesterol, mg/dl</td>
<td>198 ± 2</td>
<td></td>
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<tr>
<td>Triglycerides, mg/dl</td>
<td>100 ± 13</td>
<td></td>
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<tr>
<td>LDL, mg/dl</td>
<td>123 ± 6</td>
<td></td>
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<tr>
<td>HDL, mg/dl</td>
<td>55 ± 5</td>
<td></td>
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<tr>
<td>Glucose, mg/dl</td>
<td>100 ± 4</td>
<td></td>
</tr>
<tr>
<td>BUN, mg/dl</td>
<td>16 ± 1</td>
<td></td>
</tr>
<tr>
<td>Na⁺, meq/l</td>
<td>140 ± 1</td>
<td></td>
</tr>
<tr>
<td>K⁺, meq/l</td>
<td>4.1 ± 0.1</td>
<td></td>
</tr>
<tr>
<td>Exercise workload, W</td>
<td>104 ± 7</td>
<td>95 ± 8</td>
</tr>
<tr>
<td>Peak HR, beats/min</td>
<td>186 ± 3</td>
<td>159 ± 2*</td>
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Values are means ± SE. BMI, body mass index; LDL, low-density lipoprotein; HDL, high-density lipoprotein; BUN, blood urea nitrogen; HR, heart rate. *P < 0.05 vs. young.

Following a full verbal explanation of the experimental procedures and measurement techniques, subjects provided written informed consent.

Each subject completed a medical health history questionnaire, underwent a physical exam by a physician investigator, and in older subjects a 12-h fasting blood chemistry screening was performed (Table 1). Notably, no subject had a history or symptoms of cardiovascular, pulmonary, metabolic, or neurological disease. Subjects were nonsmokers and none were using prescribed or over-the-counter medications. Older subjects underwent Duplex ultrasound imaging within the University Radiology Department to screen for significant carotid artery plaques prior to performing NP and NS (see below). Both young and older subjects were moderately active and typically engaged in low (e.g., walking)-to-moderate (e.g., jogging, stationary bike) intensity aerobic activities (2–3 days/wk), but none competed in endurance events.

Prior to any experimental sessions, subjects were requested to abstain from eating for 2 h, caffeinated beverages for 12 h, and strenuous physical activity and alcohol for at least 24 h. All subjects were familiarized with the equipment and procedures prior to the experimental session.

Experimental Measurements

Arterial BP was measured on a beat-to-beat basis using photoplethysmography obtained from a finger of the left hand, while it rested on an adjustable bedside table at the level of the right atrium (Finometer; Finapres Medical Systems, Amsterdam, Netherlands). Beat-to-beat BP recordings were verified using an automated sphygmomanometer (Angio V2; Lode, Groningen, The Netherlands), while HR (12-lead ECG) and BP (automated sphygmomanometer) were measured. Following a 3-min warm-up period of cycling at 60 rpm, the workload was increased by 25 Watts every minute. Peak responses were determined at the power output where the subject could no longer maintain a pedal frequency of 60 rpm despite strong verbal encouragement. All subjects gave a maximal rating of perceived exertion (i.e., 19–20) at exhaustion.

Cardiopulmonary baroreflex control of BP. Full cardiac baroreflex stimulus-response curves for the control of BP were derived at rest and during moderate intensity cycling (16, 35) at least 48 h following the incremental maximal exercise test. Following instrumentation, subjects were fitted with a malleable lead collar that encircled the anterior two-thirds of the neck for the application of NP and NS. Appropriate neck chamber placement was assured by identifying the location of the carotid sinus bifurcation with ultrasound imaging and then fitting the subjects based on observed neck size. In a subset of subjects, the two trials of NP and NS were always performed during a screening session to determine directionally appropriate and consistent mean BP responses. Carotid baroreflex function was determined by applying random-ordered, single 5-s pulses of NP and NS ranging from +40 to −80 Torr (i.e., +40, +20, −20, −40, −60, −80 Torr).

To minimize respiratory-related modulation of HR and BP the 5-s pulses of pressure and suction were delivered to the carotid sinus during a 10- to 15-s breath hold at end expiration under resting conditions. During exercise the breath hold was eliminated to avoid any potential for straining maneuvers and inadvertent activation of the ABR and/or chemoreflex (38). In addition, no differences have been identified between the responses to neck collar stimuli during inspiration and expiration at a breathing frequency of > 24 breaths/min as occurs with dynamic exercise (15). Four to five trials of NP and NS at each chamber pressure were performed at rest. However, during exercise, to allow subjects to be at steady state before carotid baroreflex testing began and to minimize any potential confounding effects of cardiovascular drift on carotid baroreflex function, only two to three perturbations at each chamber pressure were performed (33). A minimum of 45 and 30 s of recovery was allotted between NP and NS trials at rest and during exercise, respectively, to allow all physiological variables to return to prestimulus values. The exercise bout began with a low workload (~30 Watts), which was then adjusted to elicit a target HR corresponding to 50% HR reserve, while pedal frequency was maintained at 60 rpm. Once the target HR was achieved, subjects exercised for ~5 min to assure steady-state conditions, after which carotid baroreflex function was assessed.

Derivation of carotid baroreflex stimulus response curves. At rest and during steady-state exercise, carotid-BP responses were evaluated by plotting the peak and nadir changes in mean BP evoked by NP and NS, respectively, against the estimated carotid sinus pressure (ECSP), which was calculated as mean BP minus neck chamber pressure. Beat-to-beat changes in mean BP measured by photoplethysmography were uniformly corrected to the absolute BP recorded via automated sphygmomanometry to provide accurate estimates of ECSP and mean BP. The carotid baroreflex stimulus response data were fitted to the logistic model described by Kent et al. (26) using the following equation: mean BP = A₀ [1 + exp[A₁ (ECSP − A₂)]⁻¹] + A₃, where mean BP is the dependent variable, ECSP is the ECSP, A₀ is the mean BP range of response (minimum–maximum), A₁ is the gain coefficient, A₂ is the carotid sinus pressure required to elicit an equal pressor and depressor response (centering point), and A₃ is the minimum mean BP response. The data were fit to this model by nonlinear least-squares regression (using a Marquardt-Levenberg algorithm), which minimized the sum of squares error term to predict a curve of best fit for each set of raw data. The overall fit of the curves was similar in the young and older subjects with r² values of 0.989 ±
We calculated the sum of the changes in NP and curves and associated parameters, individual responses to function. In addition to the derivation of carotid-BP stimulus response (BP) is within 5% of the upper or lower plateau of the sigmoid sinus pressures at which the reflexly controlled variable (i.e., mean BP) becomes important during exercise as the operating point may move away from the centering point to a locus of reduced responsiveness (39). Thus, a reduction in the operating point gain can occur independently of a change in maximal gain (i.e., the gain at the centering point).

The movement of the operating point away from the centering point was directly assessed using the equation: operating point – centering point. The threshold (THR; point where no further increase in mean BP occurred, despite reductions in ECSP) and the saturation (SAT; point where no further decrease in mean BP occurred, despite reductions in ECSP) were calculated by applying equations described by McDowall and Dampney (31): THR = \(-2.944/A_3 + A_1 + A_2\exp[A_2(ECSP_{op} - A_2)]/(1 + \exp[ECSP_{op} - A_1])^2\), whereas the GOP was calculated as the gain at the operating point and used as an index of overall carotid baroreflex responsiveness, whereas the GOP was calculated as the gain at the operating point and used to provide a measure of responsiveness at the operating point of the carotid-BP stimulus response curve. The latter measure becomes important during exercise as the operating point may move away from the centering point to a locus of reduced responsiveness (39). Thus, a reduction in the operating point gain can occur independently of a change in maximal gain (i.e., the gain at the centering point).

Table 2. Selected cardiovascular parameters at rest and during moderate-intensity cycling in young and older subjects

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Rest</th>
<th>Exercise</th>
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<tbody>
<tr>
<td>Systolic BP, mmHg†</td>
<td>116 ± 3</td>
<td>116 ± 4</td>
</tr>
<tr>
<td>Diastolic BP, mmHg†</td>
<td>65 ± 2</td>
<td>75 ± 2</td>
</tr>
<tr>
<td>Mean BP, mmHg‡</td>
<td>81 ± 2</td>
<td>89 ± 3</td>
</tr>
<tr>
<td>Pulse pressure, mmHg+++</td>
<td>51 ± 2</td>
<td>40 ± 2</td>
</tr>
<tr>
<td>HR, beats/min+++</td>
<td>59 ± 2</td>
<td>61 ± 3</td>
</tr>
</tbody>
</table>

Values are means ± SE. BP, blood pressure; †P < 0.05, main effect of condition; ‡P < 0.05, main effect of group; ††P < 0.05, interaction between condition and group.

0.001 vs. 0.980 ± 0.006, respectively, at rest and 0.983 ± 0.004 vs. 0.978 ± 0.005, respectively, during exercise. The coefficient of variation for the overall fit of this model to the individual responses was 18% for the younger subjects and 19% for the older subjects. The carotid-BP maximal gain and operating point gain were calculated using the following equations: $G_{\text{MAX}} = -A_1A_2/A_4$ and $G_{\text{OP}} = A_1A_2\exp[A_2(ECSP_{op} - A_2)]/(1 + \exp[ECSP_{op} - A_1])^2$, where $G_{\text{MAX}}$ is the maximal gain of carotid-BP stimulus response curve, $G_{\text{OP}}$ is the gain of carotid baroreflex stimulus response curve at the operating point, and ECSP_{op} is the ECSP at the operating point (i.e., prestimulus mean BP). The $G_{\text{MAX}}$ was calculated as the gain at the centering point and used as an index of overall carotid baroreflex responsiveness, whereas the $G_{\text{OP}}$ was calculated as the gain at the operating point and used to provide a measure of responsiveness at the operating point of the carotid-BP stimulus response curve. The latter measure becomes important during exercise as the operating point may move away from the centering point to a locus of reduced responsiveness (39). Thus, a reduction in the operating point gain can occur independently of a change in maximal gain (i.e., the gain at the centering point).

The stimulus response curves relating mean BP to ECSP at rest and during exercise in young and older subjects are shown in Fig. 1. Table 3 and Fig. 2 present the logistic model parameters and derived variables describing carotid baroreflex control of BP in the young and older individuals at rest and during exercise. The $A_1$ was similar between young and older groups at rest ($P > 0.05$), and this persisted during exercise. However, the $A_3$, $A_4$, THR, and SAT were all significantly greater in older individuals both at rest and during exercise ($P < 0.05$ vs. young). An upward and rightward resetting of the carotid-BP stimulus response curve was observed in both young and older subjects as demonstrated by the significant increase in $A_3$, $A_4$, THR, and SAT from rest to exercise (all $P < 0.05$ vs. rest in young and older). Notably, the magnitude of carotid sinus pressure thresholds, and inverted triangles represent the carotid sinus pressure saturations. Values are means ± SE.

Statistical Analysis

Statistical comparisons of physiological variables were made using a two-way repeated-measures ANOVA test, and a Student-Newman-Keuls test was employed post hoc to investigate significant main effects and interactions. Statistical significance was set at $P < 0.05$. Results are presented as means ± SE. Analyses were conducted using SigmaStat (Jandel Scientific Software; SPSS, Chicago, IL) for Windows.
Table 3. Logistic model parameters and derived variables describing carotid baroreflex control of BP at rest and during moderate-intensity cycling in young and older subjects

<table>
<thead>
<tr>
<th>Rest</th>
<th>Exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Young</td>
</tr>
<tr>
<td>A1, mmHg</td>
<td>22 ± 2</td>
</tr>
<tr>
<td>A2, au†</td>
<td>0.10 ± 0.01</td>
</tr>
<tr>
<td>A3, mmHg†‡</td>
<td>79 ± 3</td>
</tr>
<tr>
<td>A4, mmHg†‡</td>
<td>72 ± 2</td>
</tr>
<tr>
<td>Threshold, mmHg†‡</td>
<td>46 ± 4</td>
</tr>
<tr>
<td>Saturation, mmHg*†</td>
<td>112 ± 4</td>
</tr>
</tbody>
</table>

Values are means ± SE. A1, response range; A2, gain coefficient; A3, centering point; A4, minimum response; au, arbitrary units. † P < 0.05, main effect of condition (rest vs. exercise); ‡ P < 0.05, main effect of group (young vs. older).

baroreflex resetting (i.e., the sum of the changes in A3, A4, THR, and SAT from rest to exercise for each subject) was ~40% greater in the older group compared with the younger group (65 ± 9 vs. 90 ± 11 mmHg, young vs. older; P < 0.05).

The GMAX for the carotid baroreflex BP stimulus response curve was similar in young and older subjects both at rest and during exercise, whereas the gain at GOP tended to be lower in the older group (Fig. 2, A and B). Of note, this tendency for a difference in GGP became significant (P = 0.004) with the omission of one older individual with an exceptionally high gain (~1.11 mmHg/mmHg). Compared with the young group, the operating point of the modeled stimulus response curve was located further away from the centering point and toward the reflex THR both at rest and during exercise in the older subjects (Fig. 2C), indicating a reduced ability to respond to hypotension with an augmented capacity to defend against hypertension. In line with this, compared with the younger group, the change in mean BP with +40 Torr NP was significantly attenuated, while the change in mean BP with −80 Torr NS was significantly greater in the older subjects, both at rest and during exercise (Fig. 3). Notably, in a subset analysis of seven young and seven older subjects with a similar resting mean BP (84 ± 1 vs. 86 ± 1 mmHg, young vs. older, P > 0.05), the changes in mean BP with +40 Torr NP (Δ9 ± 1 vs. 4 ± 1 mmHg, young vs. older, P < 0.05) and −80 Torr NS (Δ−9 ± 1 vs. −15 ± 1 mmHg, young vs. older, P < 0.05) were similar to the larger cohort.

**DISCUSSION**

In the present study, we have for the first time assessed the carotid baroreflex control of BP in young and older subjects during dynamic exercise. The major novel findings are that the upward and rightward resetting of carotid baroreflex-BP stimulus response curve with exercise is augmented in older individuals and that compared with the younger group the reflex operating point is located further away from the centering point and toward the THR. This age-related relocation of the operating point was also present at rest and indicates that despite a maintained maximal gain, the ability of the carotid baroreflex to defend against a hypotensive challenge is reduced, whereas responses to hypertensive stimuli are greater with advanced age. Given the latter, these data indicate that impairments in the maximal gain of the carotid baroreflex control of BP do not appear to underlie the augmented pressor response to exercise in older adults.

There is convincing evidence that a properly functioning ABR is requisite for an appropriate neural cardiovascular response to exercise. Indeed, previous studies in both dogs (49, 50) and humans (42, 47) have demonstrated that baroreceptor denervation can lead to exaggerated BP responses to exercise. It has been suggested that the ABR acts to partially restrain the BP response to exercise by buffering increases in vasomotor tone (25). Thus, reductions in ABR gain (i.e., sensitivity) during exercise could lead to inappropriate increases in vascular tone and elevations in BP (25). In the present study, we...
hypothesized that older individuals would have reductions in ABR control of BP during exercise. Our rationale was that impairments in ABR function with increased age may contribute to the augmented BP often observed in older individuals during exercise (9, 19, 34, 45). However, the results suggest that although the carotid baroreflex BP function curve was reset further upward and rightward during exercise in the older group, no age-related differences in the maximal gain were observed. As such, reports of exaggerated BP responses to exercise in older individuals do not appear to be related to impaired ABR gain and may be attributable to dysregulation in other mechanisms implicated in the control of the vasculature and BP during exercise [e.g., impaired metabolic vasodilatation (40) and exaggerated sympathetic vasoconstriction (13, 17)].

Interestingly, our results show that although the maximal gain of the carotid baroreflex BP stimulus response curve was similar in young and older subjects, the operating point was located further away from the centering point and toward the reflex THR of the baroreflex curve in older individuals. Shi et al. (41) also reported that the resting sensitivity of the carotid-BP stimulus response curves were similar in young and older subjects; however, the location of the operating point on the reflex function curve was not examined. Moreover, Studinger et al. (46) demonstrated that age-related differences in ABR-mediated responses of SNA to rises and falls in BP were not evident when the responses were combined; that is, the gain of the integrated ABR control of SNA was not different between the young and older groups. However, sympathetic responses to reductions in BP were clearly attenuated in older subjects, while greater sympathetic inhibition to pharmacologically induced hypertension was also present. Taken together, these findings highlight the importance of examining the ability of the ABR to respond to rises and falls in BP separately. Indeed, although overall carotid baroreflex gain was similar between groups in the present study, older subjects had a reduced response to simulated carotid hypotension and a greater response to hypertensive stimuli both at rest and during exercise.

The finding that the BP responses to NS (i.e., simulated carotid hypertension) were greater in the older group during exercise suggests that the ability to inhibit sympathetic outflow to the peripheral vasculature was greater in the older group than in the younger individuals during exercise. This possibility is in accordance with recent work demonstrating greater ABR-mediated sympatho-inhibition in older subjects in response to pharmacological increases in BP at rest (46). However, whether an enhanced ability to inhibit sympathetic outflow persists during dynamic exercise in older subjects remains to be determined. In addition, alterations in vascular responsiveness cannot be excluded. In contrast to the augmented responses to carotid hypertension, the BP responses to simulated carotid hypotension (i.e., NP) were attenuated in older individuals. This observation concurs with the findings of Studinger et al., (46) who reported that the sympatho-excitative responses to a pharmacologically induced reduction in systemic BP was attenuated in older compared with younger individuals. This blunted response in older individuals was attributed to a decrement in the mechanical transduction of the fall in BP to barosensitive vessels due to increased arterial stiffening. While this may explain our observations, decreased α-adrenergic receptor sensitivity has also been reported in healthy older subjects (12, 22, 43), suggesting that NP-induced increases in sympathetic outflow may be less effective in increasing BP due to impaired neural vascular transduction. However, previous studies examining the influence of age on vascular responses to sympathetic activation have reported both blunted (10) and preserved (14) responses in older individuals. In addition, the reduced BP response to carotid baroreceptor unloading may also be related to an attenuated tachycardic response (18, 19). Further work is required to examine the influence of aging on the ABR-regulation of vascular conductance and the relative contribution of central hemodynamics to overall ABR control of BP.

Age-related impairments in ABR-mediated sympatho-excitation have previously been suggested to be linked with im-

**Fig. 3.** Summary data showing changes in mean BP to neck pressure (+40 Torr; A) and neck suction (−80 Torr; B) at rest and during moderate intensity cycling in young and older subjects. Values are means ± SE. P values indicate ANOVA results.
pairments in neural vascular transduction (13, 43) and/or increases in barosensory vessel stiffness (46). It may be reasonable to expect that these factors are modulated by dynamic exercise. Indeed, while resting α-adrenergic sensitivity appears to be reduced in older individuals (12, 22), the normal metabolic modulation of sympathetic vascular regulation (i.e., functional sympatholysis) is blunted (13, 17), and as such, sympathetic vasoconstrictor tone may be enhanced during exercise. Furthermore, exercise-induced changes in carotid artery distensibility may alter SNA responses to NP in older individuals. However, despite the potential for exercise to modulate the BP response to NP, we observed similarly attenuated BP responses to carotid baroreceptor unloading in the older subjects both at rest and during exercise. An alternative explanation for the impaired ability of the older subjects to increase BP in response to NP during exercise may be related to increased central blood volume and the subsequent influence of cardiopulmonary baroreceptor loading (39). Indeed, cardiopulmonary baroreceptor loading may exert a central inhibitory effect during sympatho-excitatory maneuvers, such as carotid baroreceptor unloading or exercise. However, as cardiopulmonary baroreceptor loading during exercise is strongly associated with an attenuated carotid baroreflex resetting (36, 48), it is unlikely that this would explain the age-related relocation of the operating point observed in the present study, as we observed an augmented carotid baroreflex resetting in older individuals. Further studies are needed to determine the mechanisms underlying the age-related attenuation in the BP responses to carotid baroreflex unloading during exercise.

In the present study, the variable-pressure neck chamber was utilized, as it has the advantages of being noninvasive and nonpharmacological and permits the derivation of full carotid baroreflex stimulus response curves and its associated parameters during dynamic exercise, unlike alternative methodologies (e.g., modified Oxford technique, sequence technique). Importantly, this allows statistical comparisons of baroreflex function to be made between young and older subjects as rest and during exercise. However, there are limitations that should be considered. As we did not perform the required invasive procedure of placing a pressure transducer at the carotid artery during NP and NS, we cannot definitively know whether the transmission of pressure to the carotid sinus differs between young and older groups. Nevertheless, if one assumes that the older adults have less mechanical deformation for a given level of NS or NP, this would further support our main finding that the gain of the carotid baroreflex is not impaired during exercise in older individuals. Furthermore, as the variable-pressure neck chamber technique is selective for the carotid baroreflex, no measure of aortic baroreflex control is presented. However, because of the parallel activity of the carotid and aortic baroreceptors (44), the assumption is made that a selective modeling of the carotid baroreflex would be characteristic of the overall ABR. Finally, we recognize that the results of the present study are specific to steady-state dynamic exercise at moderate, relative intensities and thus, the potential for age-related differences at higher exercise intensities or when comparing at absolute workloads cannot be dismissed.

In summary, our findings suggest that the magnitude of resetting of the carotid baroreflex-BP stimulus response curve during exercise is augmented in older individuals, and although maximal gain was similar in young and older subjects, the operating point of the modeled curve was located further away from the centering point and toward the reflex THR in older individuals. This age-related relocation of the operating point was also present at rest and indicates that despite a maintained maximal gain, the ability of the carotid baroreflex to defend against a hypertensive challenge is reduced, whereas responses to hypertensive stimuli are greater with advanced age. Given the latter, these data suggest that impairments in the maximal gain of the carotid baroreflex control of BP do not appear to underlie the augmented pressor response to exercise in older adults.

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GRANTS

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

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