Spontaneous baroreflex sensitivity in young and older people during voluntary and electrically evoked isometric exercise

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Abstract

Background: in young people, cardiovagal baroreflex sensitivity alters during isometric exercise. We investigated whether the reduced resting baroreflex sensitivity seen with increasing age is similarly altered during exercise.

Methods: cardiovagal baroreflex sensitivity was examined in 8 young (age ± SEM, 25 ± 1.7 years) and 9 older (61 ± 3.0 years) subjects, using sequence analysis during voluntary and electrically evoked isometric exercise (at 30% maximum voluntary strength) and during subsequent post-exercise circulatory occlusion.

Results: in all phases of both conditions, baroreflex sensitivity was significantly reduced in the older group compared with the young group. (Median (interquartile range), voluntary 7.0 (4.4) vs 3.6 (3.8) ms . mmHg⁻¹, post-exercise circulatory occlusion 9.0 (8.2) vs 4.6 (4.0) ms . mmHg⁻¹; electrically evoked 6.6 (10.6) vs 3.2 (3.6) ms . mmHg⁻¹, post-exercise circulatory occlusion 8.3 (7.7) vs 2.9 (2.2) ms . mmHg⁻¹, young vs older respectively; P<0.05.) There was a marked rightward shift (resetting) of the baroreflex during exercise with the exception of electrically evoked in the older group.

Conclusion: our data demonstrate that the reduction in baroreflex sensitivity in older people is maintained during exercise and during post-exercise circulatory occlusion. Resetting of the baroreflex in the older subjects during moderate voluntary isometric calf exercise is largely the result of central command.

Keywords: autonomic nervous function, blood pressure, cardiovagal baroreflex, heart rate

Introduction

Cardiovagal baroreflex sensitivity (BRS) is the arterial baroreflex-mediated change in the R-R interval per unit change in systolic blood pressure (SBP). As well as its involvement with blood pressure control [1], cardiovagal BRS is thought to influence cardiac electrical stability especially during ischaemia [2]. Reduced BRS is also associated with various pathophysiological states, such as hypertension [3].

It is well documented that resting cardiovagal BRS decreases with age in men [4–7], however, whether an age-related difference in baroreflex persists during isometric exercise is not known. If, as some investigators believe, the decrease in resting BRS with age is due mainly to reduced aortic and carotid artery compliance [8–10], then it is likely that a reduced BRS would persist during isometric exercise. However, others believe that changes in the neural components of the baroreflex influence the age-related decline in BRS [11, 12]. Therefore in exercise, where neural inputs to the baroreflex are increased, elderly BRS may be expected to change. Furthermore, alterations in BRS observed during voluntary isometric exercise, where central command is present, may differ from those seen during electrically evoked exercise, where central command is absent. Voluntary isometric exercise causes a pressor response which is mediated by central drive and peripheral reflex activity [13]. During electrically evoked (STIM) isometric exercise, however, central command is by-passed and the pressor response is produced by mechanoreceptive and chemoreceptive muscle afferent activity alone. We, and others, have shown distinctly different roles of muscle chemoreceptors and mechanoreceptors in altering BRS in young subjects [14, 15].

The aims of the present study were: (i) to determine whether the age-related decrease in resting BRS is maintained during isometric exercise; (ii) to identify the
contribution to any such change made by metabolically sensitive muscle afferents; (iii) to examine possible central command involvement in any BRS change by comparison of responses to voluntary and evoked exercise.

Methods

Data were collected from 8 young and 9 older subjects whose physical characteristics are given in Table 1. All subjects, who were recruited from the University or from the local population of Birmingham, were healthy, normotensive, non-smokers, non-obese and were not taking any medication. Written, informed consent was given by all subjects before their participation in the study, which had local ethical committee approval.

The methods used to measure maximum voluntary contraction (MVC) and voluntary (VOL) and STIM pressor responses at 30% MVC are well established [16, 17].

After thorough prior habituation, subjects performed two experimental protocols on the same visit; one VOL and one STIM isometric plantar flexion. Subjects rested for 10 minutes positioned in the dynamometer to attain a stable basal circulatory state then began an 8 minute protocol, consisting of four phases. A 2 minute control rest period was followed immediately by 2 minute VOL or STIM (20 Hz, 50 ms pulse width) contraction. Circulatory occlusion was maintained during exercise and post-exercise circulatory occlusion (PECO) phases by inflation of a thigh cuff to above 200 mmHg. The cuff was then released for a 2 minute recovery phase. Subjects rested out of the dynamometer for at least 20 minutes before the second protocol was performed. The order in which the STIM and VOL protocols were carried out was randomized.

ECG (Cardiorater CR7, Cardiac Records Ltd, London, UK) and blood pressure (2300 Finapres, Ohmeda, Louisville, CA, USA) were recorded continuously. Analogue signals were transmitted to an analogue to digital converter (Cambridge Electronic Design 1401 plus, Cambridge, UK) sampled at a frequency of 1000 Hz. Blood pressure and ECG data were displayed and analysed on a personal computer (Vale Platinum TX, Evesham Micros, Evesham, UK).

Calculation of BRS by the spontaneous sequence technique

Beat-to-beat SBP and R-R intervals were searched, using purpose-written software, for sequences of 3 or more consecutive beats in which SBP progressively increased and the subsequent R-R interval lengthened (up sequence), or SBP progressively decreased and the subsequent R-R interval shortened (down sequence). The minimum required change was 1 mmHg for SBP and 1 ms for R-R interval and a lag of one beat was used. Linear regressions relating SBP to R-R interval were plotted for each sequence and only those with linear $r$ values $>0.92$ were used. Slopes derived from all up and down sequences within 2 minute phases were pooled for each subject.

Statistics

Data are reported either as group means ($\pm$SEM) or as median (interquartile range) for non-parametric data. The Wilcoxon Signed Ranks Test was used to compare data within groups and the Mann–Whitney $U$ test was used to compare data between young and older subject groups. For comparisons of cardiovascular data during the exercise and PECO phases of the experiment, summary measures were calculated [18]. These are given as average values (analogous to area under the curve) of the four measurements made in each phase for changes in blood pressure and heart rate, relative to the four control resting levels (between 0 and 90 seconds). The criterion for statistical significance was $P<0.05$.

Results

Cardiovascular responses

Resting SBP, diastolic DBP and heart rate prior to VOL and STIM were not significantly different between the groups (Table 2). The group mean changes in SBP and HR during VOL are shown in Figures 1a and b, respectively. The cardiovascular response followed the same pattern during STIM.

Table 1. Physical characteristics of the subjects

<table>
<thead>
<tr>
<th></th>
<th>Younger subjects</th>
<th>Older subjects</th>
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<tr>
<td>$n$</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>Sex M/F</td>
<td>7/1</td>
<td>7/2</td>
</tr>
<tr>
<td>Age (y)</td>
<td>25.5 ± 1.7</td>
<td>60.7 ± 3.0</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>77.4 ± 3.1</td>
<td>80.7 ± 5.8</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>177.6 ± 1.9</td>
<td>170.2 ± 3.2</td>
</tr>
</tbody>
</table>

Values are mean ± SEM.

<table>
<thead>
<tr>
<th></th>
<th>Electrically evoked</th>
<th>Voluntary</th>
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<tbody>
<tr>
<td></td>
<td>Older</td>
<td>Young</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>131 (20)</td>
<td>135 (28.6)</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>71 (11.5)</td>
<td>75 (13)</td>
</tr>
<tr>
<td>HR (b. min$^{-1}$)</td>
<td>76 (6)</td>
<td>73 (14.7)</td>
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Values are median (interquartile range); SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate.
None of the blood pressure or heart rate changes were significantly different between young and older groups during any phase of the VOL or STIM protocols. However, the older group tended to have a decreased SBP response during PECO following STIM (summary measures 6 (7.1) vs 13 (11.2) mmHg older vs young, respectively).

Within group comparisons showed that the blood pressure response at end of VOL exercise was significantly greater (P<0.05) than STIM in both young and older groups (Table 3). Furthermore, in the older group, during PECO following STIM the change in SBP (summary measures 7±1.7 mmHg) was significantly smaller (P=0.011) than that during VOL (13±2.4 mmHg).

**Baroreflex analysis**

In all phases of both the VOL and STIM protocols (Table 4) the mean BRS was significantly reduced (P<0.05) in the older group compared with the young group. Group mean regression lines for voluntary and electrically evoked protocols are shown in Figures 2 and 3, respectively.

In the older group BRS was not significantly altered during VOL, STIM or subsequent PECO. In the young group, there was a trend to increase BRS during PECO following STIM and VOL but this did not reach statistical significance.

During VOL, a rightward shift of the regression line along the pressure axis was apparent in both subject groups (Figure 2, lines B). For example, at an R-R interval of 750 ms (80 b. min⁻¹) mean SBP increased from 138 mmHg to 155 mmHg in the young subjects and from 112 mmHg to 143 mmHg in the older men. During STIM (Figure 3, lines B) the young group showed a marked rightward shift from a mean SBP of 127 mmHg to 153 mmHg but in the older group the shift was smaller, from 123 mmHg to 137 mmHg.

**Discussion**

The main new findings of the present study are threefold. First, the age-related decrease in human cardiovagal BRS at rest is maintained during isometric exercise and during subsequent PECO. Second the reduced BRS of the older group was observed during both VOL and STIM. Finally, the resetting of the baroreflex during moderate intensity voluntary isometric exercise in the older group appears to depend largely on central command.

In agreement with many previous studies [4–7, 19] we observed a reduction in cardiovagal BRS in a...
resting older men. The precise mechanisms underlying the reduction in resting BRS with age are not known. Possibilities include increased arterial stiffness [8, 9], defects in central mediation of the baroreflex, ineffective coupling of afferent baroreceptor activity to efferent autonomic outflow [11] and decreased efficacy of cardiac parasympathetic activity [20].

Recently, Hunt et al. [12] provided evidence that reduced arterial compliance only partially accounts for the reduction in baroreflex gain with age. They reported
that BRS was not significantly different between young and older trained men, but that untrained men had gains of only half that of their trained, age-matched peers. Increases in both mechanical and neural components of the baroreflex contributed to the preservation of BRS in the older trained men but neural components accounted for 53% of the variance and was the greater predictor of BRS.

During the present study, we found that there was no change from rest in BRS during either VOL or STIM in the young or older men. However, although BRS was unchanged, the regression line tended to shift rightward along the pressure axis on exercise (Figures 2 and 3). This rightward shift is consistent with a resetting of the baroreflex and has been reported previously, in young subjects [14, 15, 21–23]. To our knowledge it has not been reported in older subjects.

Recently, we have reported not only a resetting of the baroreflex during STIM isometric contraction but also an increase in BRS during subsequent PECO [14] in young subjects. The model we used to explain our findings [14] may be extended to the present study. The level of autonomic outflow during evoked isometric exercise may be influenced by 3 components: (i) mechanoreflex activation; (ii) chemoreflex activation and; (iii) baroreflex activation. Mechanoreflex activation inhibits cardiac vagal motoneurone activity and elevates HR [24, 25]. Progressive chemoreflex activation causes sympatoexcitation and BP increase [26, 27] activating the baroreflex and further increasing the excitation of cardiac vagal motoneurones [28]. During STIM the baroreflex excitation offsets the inhibitory effect of muscle mechanoreflex activation [29] resulting in unchanged BRS about a higher arterial pressure. During PECO following STIM, muscle mechanoreceptor activation ceases at the end of exercise whilst muscle chemoreceptor activation continues. This sustains the pressor response during PECO [26, 27] and the elevated baroreflex-mediated excitatory input of the cardiac vagal neurones.

In older subjects, it seems that low BRS at rest is little altered by weak muscle chemoreflex activation during STIM and PECO [30–32], and the right shift appears small. This suggests that the pressor response to STIM depended largely on mechanoreflex activation. However, heart rate change during STIM was very small in the older subjects. With reference to our model, there are two possible explanations for this. (i) The mechanoreceptor input is weak in the older subjects and does not cause significant inhibition of vagal motoneurones. On the basis of the blood pressure response, this seems unlikely; (ii) the mechanoreceptor input is adequate but central integration is impaired in the older subjects [12].

During VOL, central command is an additional influence. Clearly, in VOL there is resetting of the baroreflex in both young and older subjects. In older subjects the rightward shift of BRS must indicate a greater influence of central command as muscle afferent input should be of the same magnitude as in STIM where a much smaller rightward shift was seen. The result is a greater increase in heart rate and SBP during VOL without a change in BRS.

In conclusion, we have reported that low BRS is maintained during VOL and STIM isometric exercise and subsequent PECO in older subjects. In addition, we have found that in older subjects, during moderate VOL isometric exercise of the calf muscles, the resetting of the baroreflex appears to be heavily influenced by central command.

Key points
- The age-related decrease in human cardiovagal BRS at rest is maintained during isometric exercise and during subsequent post exercise circulatory occlusion.
- The reduced BRS of the older group was observed during both voluntary and electrically evoked isometric exercise.
- The apparent resetting of the baroreflex during voluntary isometric exercise would seem to depend largely on central command.

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References


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