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CAROTID-CARDIAC BAROREFLEX INFLUENCE ON FOREARM VASCULAR RESISTANCE DURING LOW LEVEL LBNP

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I

ABSTRACT

Twelve healthy males were tested at low levels of lower body negative pressure (LBNP) with and without artificial stimulation of the carotid-cardiac baroreceptors. The carotid-cardiac baroreceptors were stimulated by applying a pressure of +10 mmHg to the carotid artery via a pressurized neck chamber. During the procedure, forearm blood flow (FBF) and forearm vascular resistance (FVR) were measured using a Whitney mercury silastic strain gauge technique. FBF decreased while FVR increased with increased intensity of LBNP. Both FBF and FVR were unaffected by carotid-cardiac baroreceptor stimulation.

II

SUMMARY

Lower body negative pressure (LBNP) at low levels is an accepted method for inducing forearm vasoconstriction (elevated peripheral vascular resistance) which in turn is used as a measure of cardiopulmonary baroreflex responsiveness. It is assumed that arterial baroreflexes are not stimulated and do not influence the cardiopulmonary baroreflex test results. As with any intact living organism, complete isolation of a physiological system is a tenuous assumption. If carotid baroreceptor unloading does exist during low levels of LBNP (-20 mmHg or less), does it alter the results in any significant way to deem the measure of cardiopulmonary baroreflex responses invalid? To address this question, 12 subjects underwent low levels of LBNP exposures (-15 and -20 mmHg) with and without additional artificial (+10 mmHg neck pressure) unloading of the carotid baroreceptors. The results indicated no measurable influence of carotid unloading on forearm vascular resistance. Forearm vascular resistance measured during cardiopulmonary baroreceptor unloading is unaffected by carotid baroreceptor unloading within the magnitude encountered during low levels of LBNP.

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TEXT

4.1 INTRODUCTION

Lower body negative pressure (LBNP) has been extensively used as a tool to create intravascular fluid shifts from the upper body into the lower extremities in order to examine cardiovascular reflex adjustments. Several investigators have suggested [9,20] that low levels of LBNP (maximum of -20 mmHg) induce reflex adjustments of vascular resistance primarily resulting from the unloading of the cardiopulmonary baroreceptors. This conclusion was based on the observations that LBNP levels down to -20 mmHg cause reductions in central venous pressure which induce forearm vasoconstriction. These alterations occur without measurable changes in determinants of arterial baroreceptor activity such as arterial blood pressure, aortic pulse pressure, arterial dp/dt (rate of change of pulse pressure), and heart rate [9,17,20]. Consequently, low levels of LBNP have been used to examine the stimulus-response characteristics of the cardiopulmonary baroreflex [6,8,10,16,18].

In recent experiments [6,16], we have observed small (two to four beats), but consistent increases in heart rate across increasing LBNP stages down to -20 mmHg, suggesting the unloading of arterial as well as cardiopulmonary baroreceptors. Data from

other investigations have confirmed these observations [12,17,18].

Unloading of carotid baroreceptor activity during low levels of LBNP may influence the response of the cardiopulmonary baroreflex. Some experiments have provided evidence that the carotid-cardiac baroreflex acts to maintain blood pressure by increasing forearm vascular resistance as well as heart rate [1,2,3,18]. If low levels of LBNP unload carotid baroreceptors and increase forearm vascular resistance, the interpretation of the cardiopulmonary baroreflex response measured by this procedure could be compromised. The purpose of our study was to determine if additional unloading of the carotid baroreceptors influences changes in forearm vascular resistance observed during low levels of LBNP.

4.2 METHODS

4.2.1 SUBJECTS. Twelve healthy, nonsmoking, normotensive men, with a mean (±SE) age of 36 ± 2 years (range 28-51), a height of 178 ± 1 cm (range 169 - 180), and a weight of 81.2 ± 2 kg (range 68 - 93), gave written informed consent to participate in this study. Selection of subjects was based on normal clinical results of a screening evaluation comprised of a detailed medical history, physical examination, complete blood count, a

panel of blood chemistry analyses, urinalysis, resting and treadmill elecrtrocardiograms, and pulmonary function tests.

4.2.2 PROTOCOL. During a preliminary visit to the laboratory, subjects were made familiar with the protocol and testing procedures. All subjects were instructed to abstain from exercise and caffeine for 12 hours prior to the testing period.

Subject instrumentation for the test procedures occurred simultaneously with a supine stabilization period which lasted approximately 30 minutes. Subjects were positioned in the LBNP device with both the right and left arms extended outward at heart level. The right arm was used for measurement of forearm blood flow and the left was used for beat-to-beat finger blood pressure measurements.

The experimental protocol consisted of six different combinations of LBNP and neck chamber pressure administered to each subject in a random order. LBNP was either off (0mmHg), decompressed to -15 mmHg, or decompressed to -20 mmHg. The neck chamber device [15] was either off (0 mmHg) or on at a pressure of +10 mmHg, i.e., baroreceptor unloading. Each treatment was applied over a 2-min period with a 5-min rest interval separating each of the six treatments. Lower body negative pressure was used to unload cardiopulmonary baroreceptors whereas the neck chamber was used to provide additional unloading of carotid baroreceptors. A neck cuff pressure of +10 mmHg was chosen since

this pressure has previously been shown to be within the responsive range of the baroreflex to cause a shortening of the R-R interval in most normotensive subjects [6,15,16]. A between treatment interval of five minutes was chosen to ensure that heart rate and blood pressure returned to pre-LBNP baseline values. Electrocardiograph measurements, using standard leads I, II, III, and beat-to-beat blood pressures, measured with the Finapress finger blood pressure technique [4] were recorded continuously throughout the protocol on a strip chart. Mean arterial pressure was calculated by dividing the sum of systolic blood pressure and twice diastolic pressure by three. At alternate 10-sec intervals during the 2-min test periods, forearm blood flow was measured by venous occlusion plethysmography, using a Whitney mercury-in-silastic strain gauge placed around the left forearm with circulation to the hand occluded [10,16,19]. An index of forearm vascular resistance was calculated by dividing mean arterial pressure by forearm blood flow and expressed in peripheral resistance units (PRU). Although data were collected continuously throughout the two minutes of testing, only measurements made in the last minute of testing were retained for statistical analysis. This was done to allow subjects to stabilized once the treatment was applied.

4.2.3 STATISTICAL METHODS. Data analysis was based on a 2 (barocuff status) x 3 (LBNP stage) factorial analysis of variance run in 12 randomized blocks (subjects). This was in keeping with

the experimental design in which each of the 12 subjects received each of the six treatment combinations in random order. When appropriate, orthogonal polynomials were fit and tested across LBNP stage to further describe observed treatment differences. Barocuff by LBNP pressure stage means are graphically presented since the interactive effects of these two treatments were of primary interest. Measures of variability are presented graphically as standard errors both adjusted and unadjusted for subject variation. Probabilities associated with tests of statistical inference reflect the chances of falsely concluding that the observed differences were attributable to the experimental manipulation and not random variability associated with the experimental methods or selection of the subjects for the given sample size of this experiment.

4.3 RESULTS

Figure 1 graghically presents the barocuff by LBNP stage interaction means for heart rate. Heart rate tended to increase with increasing levels of negative lower body pressure when the barocuff was at ambient pressure. Conversely, heart rate was elevated and tended to remain unchanged across LBNP stage when the barocuff was pressurized. However, the large TYPE I error rate generated from the analysis of variance for the barocuff by LBNP stage interaction indicated that this observed difference could be accounted for by random variation ($F(2,55) = 1.06$, $p = 0.3535$).

The results of a polynomial (linear) trend analysis across LBNP stages when the cuff was at ambient pressure indicated that the observed heart rate change of 3 beats from ambient LBNP to -20 mmHg was large enough to be detected within a TYPE I error rate of 10 percent ($F(1,55) = 2.81$, $p = 0.0994$). A comparison of heart rate between the pressurized and unpressurized barocuff at ambient lower body pressure yielded a moderately high TYPE I error rate ($F(1,55) = 2.27$, $p = 0.1379$). Overall, the results tend to indicate small differences in heart rate (one to three beats) as a result of the two types of stress with little or no interaction existing between the two procedures. Since the overall statistical model explained 89 percent of the total variation in heart rate, the results indicate that the observed differences were probably real but difficult to detect due to the small effect size.

Figure 2, Panel A presents the interaction means for forearm blood flow. The graph indicates a strong linear main effect of LBNP stage with a slight interaction with barocuff status. The low TYPE I error rate for the overall LBNP linear component ($F(1,55) = 23.64$, $p = 0.0001$) and the moderately high Type I error rate for the barocuff by LBNP linear interaction ($F(1,55) = 1.75$, $p = 0.1914$) support the idea that forearm blood flow decreases with increasing LBNP and that this decrease was unaffected to any significant extent by barocuff pressurization, i.e., carotid baroreceptor unloading, at +10 mmHg. The overall

statistical model explained 78 percent of the total variation in forearm blood flow.

Figure 2, Panel B presents the interaction means for forearm vascular resistance. Except for a change in direction, the results are similar to those for forearm blood flow. The strong overall linear component across LBNP stage ($F(1,55) = 15.84$, $p = 0.0002$) does not seem to interact (change) with barocuff pressurization ($F(1,55) = 0.07$, $p = 0.7923$). The overall statistical model explained 68 percent of the total variation in forearm vascular resistance. This lower percentage of explained variation as compared to forearm blood flow probably reflects the fact that true forearm vascular resistance is not actually measured but calculated from mean arterial pressure.

4.4 DISCUSSION

Although it is generally accepted that low levels of LBNP (20 mmHg or less) exclusively unload the cardiopulmonary baroreceptors [8,9,10,12,20], our data from the present study suggest that carotid baroreceptors may also be unloaded since small but consistent linear increases in heart rate were observed during LBNP levels of -15 and -20 mmHg, and that unloading of carotid baroreceptors at rest produced similar elevation in heart rate as that observed during LBNP. These findings are supported by the data of other investigators [12,17,18] and are consistent with unpublished observations from our previous investigations in

which mean (±SE) heart rate increased from 62 ± 3 to 67 ± 3 bpm ($F(1,23) = 17.23$, $P = 0.0004$) in 24 subjects [6] and from 58 ± 4 to 62 ± 4 bpm ($F(1,7) = 12.75$, $P = 0.0091$) in 8 subjects [16] when exposed from zero to -20 mmHg LBNP, respectively. The consistent observation that heart rate is elevated during low levels of LBNP suggests the possibility of carotid baroreceptor unloading and refutes the assumption that this technique isolates the cardiopulmonary baroreflex [8,10]. These data raise the concern that carotid baroreceptor unloading may accentuate the reduction in forearm vascular resistance during LBNP levels of 20 mmHg or less [5,7] and thus influence the measured response of the cardiopulmonary baroreflex.

There is some discrepancy in the literature as to the contribution of the carotid baroreceptors in controlling forearm vascular resistance responses. Loading of the carotid baroreceptors by neck suction or manual compression of the carotid arteries has been shown in some investigations to have negligible effects on vasomotor tone [1,11,13,14]. In contrast, Epstein et al. [7] found a 16 percent reduction in forearm vascular resistance when directly stimulating the carotid nerves of patients undergoing implantation of carotid sinus nerve stimulators. This finding supported the work of Carlsten et al. [5] who also demonstrated a reduction in vascular resistance with direct stimulation to the carotid sinus nerve. Significant alterations in vasomotor tone have also been observed by several

investigators during baroreceptor loading induced by neck suction [2,3] and unloading induced by neck pressure [18]. In our study, carotid baroreceptor unloading with +10 mmHg neck cuff pressure caused increases in heart rate compared to control values indicating that we successfully induced a reflex response. We observed no effect of carotid unloading on forearm vascular resistance. Our results suggest that a carotid baroreceptor stimulus equivalent to slight hypotension (-10 mmHg) does not influence forearm vascular resistance either directly or through an interaction with cardiopulmonary baroreceptor responses.

Victor and Mark [18] performed an experiment very similar to ours using neck cuff pressures of +20 mmHg and +30mmHg during -10 mmHg LBNP. Neck cuff pressure at +20 mmHg caused no alteration in forearm vascular resistance while +30 mmHg neck pressure resulted in increases in FVR with and without LBNP. The forearm vascular resistance response to +30 mmHg neck pressure during LBNP was greater than the sum of the separate responses to LBNP and neck pressure alone. These investigators concluded that not only do the carotid baroreceptors have a direct effect on forearm vascular resistance, but they also have a potentiating effect on the cardiopulmonary baroreceptor FVR responses to LBNP.

Although our data and those of others [1,11,13,14] may appear contradictory to the findings of several investigations [2,3,5,7], the magnitude of stimulation may provide an

explanation for all findings. Taken together, the results of our experiment and those of Victor and Mark [18] suggest that a hypotensive stimulus of 20 to 30 mmHg may be required to elicit a threshold response for initiating a vasoconstriction from carotid baroreceptor unloading. The degree to which we unloaded the carotids was greater than that expected by the small blood pressure reductions of 2 to 4 mmHg reported during 20 mmHg of LBNP [10,17,20]. Further, concommitant application of LBNP and neck cuff pressure in our experiment assured greater unloading of the carotid baroreceptors than that experienced by LBNP alone. Therefore, it is unlikely that the small degree of carotid baroreceptor unloading that occurs in most human subjects during LBNP of 20 mmHg or less influences forearm vascular resistance. Consequently, protocols of low levels of LBNP (-20 mmHg or less) can be employed to measure the stimulus-response relationship of the cardiopulmonary baroreflex with the confidence that carotid baroreceptor unloading is not affecting the response.

V

CONCLUSIONS

Artificial stimulation of the carotid-cardiac baroreceptors (to approximate a +10 mmHg drop in pressure) does not effect the measurement of FBF or FVR during exposure to low levels of LBNP. Limited levels of stimulation and undescribed mechanisms of heart rate alterations suggest areas for future research.

VI

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VII

FIGURES AND LEGENDS

Figure 1. Mean (±SE) heart rates by barocuff status (neck pressure) and LBNP stage. The pooled SE is calculated from the analysis of variance and is adjusted for between subject variation.

Figure 2. Mean (±SE) forearm blood flows (Panel A) and forearm vascular resistance (Panel B) by barocuff status and LBNP stage. The pooled SE is calculated from the analysis of variance and is adjusted for between subject variation.

FIGURE 1

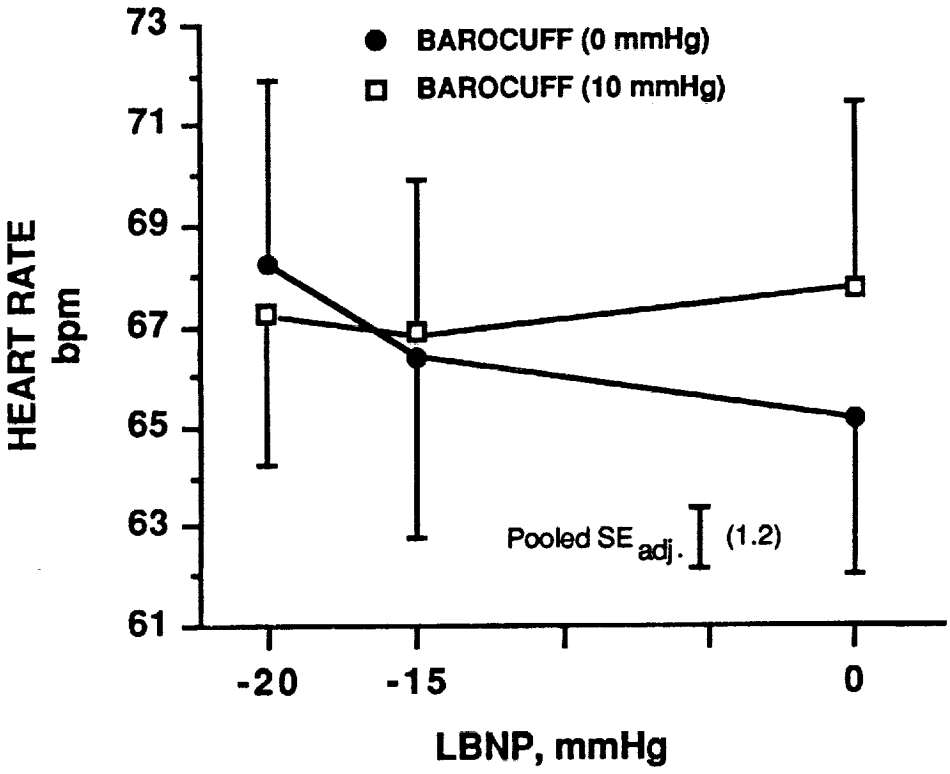
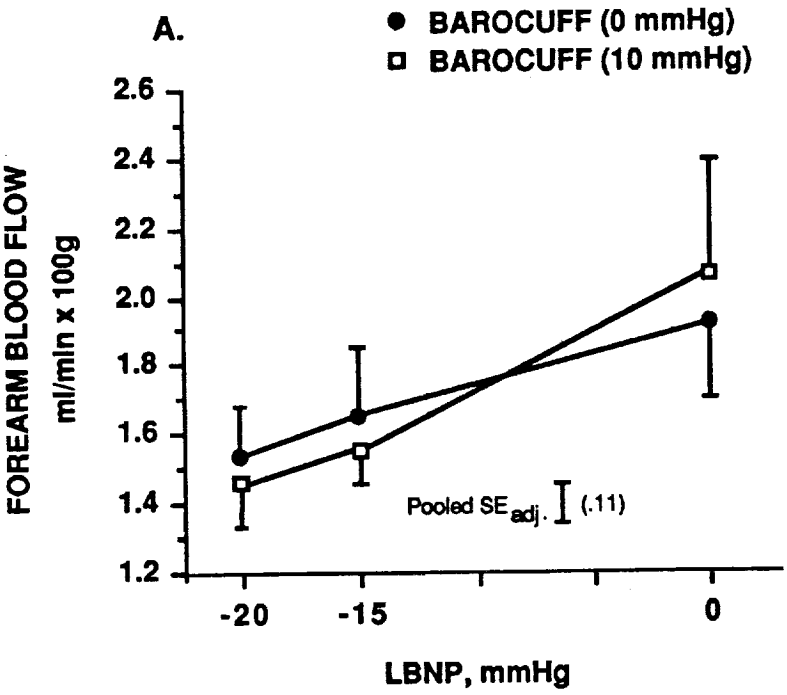
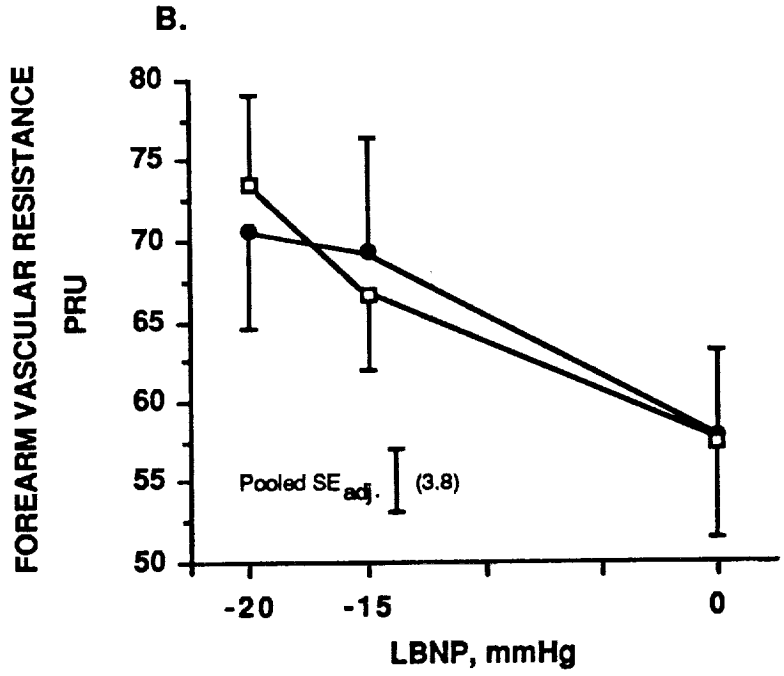

73
71
69
67
65
63
61
HEART RATE
bpm
BAROCUFF (0 mmHg)
BAROCUFF (10 mmHg)
Pooled SE adj.
(1.2)
-20
-15
0
LBNP, mmHg

FIGURE 2


A.
BAROCUFF (0 mmHg)
BAROCUFF (10 mmHg)
FOREARM BLOOD FLOW
ml/mln x 100g
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
Pooled SE adj. (.11)
-20
-15
0
LBNP, mmHg


B.
FOREARM VASCULAR RESISTANCE
PRU
80
75
70
65
60
55
50
Pooled SE adj. (3.8)
-20
-15
0
LBNP, mmHg