The following is the abstract of the article discussed in the subsequent letter:

**Gender differences in autonomic functions associated with blood pressure regulation.** Am. J. Physiol. 275 (Regulatory Integrative Comp. Physiol. 44): R1246–R1247, 1998.—Functions of carotid and aortic baroreflex control of heart rate (HR), cardiopulmonary baroreflex control of vascular resistance, adrenoceptor responsiveness, indexes of baseline vagal and sympathetic tone, circulating blood volume, and venous compliance were compared in men and women to test the hypothesis that lower orthostatic tolerance in women would be associated with lower responsiveness of specific mechanisms of blood pressure regulation. HR, stroke volume (SV), cardiac output (Q̇), mean arterial blood pressure (MAP), central venous pressure, forearm (FVR) and leg (LVR) vascular resistance, catecholamines, and changes in leg volume (%ΔLV) were measured during various protocols of lower body negative pressure (LBNP), carotid stimulation, and infusions of adrenoceptor agonists in 7 females and 10 males matched for age and fitness. LBNP tolerance for the women (797 ± 63 mmHg/min) was 35% lower (P = 0.002) than 1,235 ± 101 mmHg/min for the men. At presyncope, SV, Q̇, MAP, and %ΔLV were lower (P < 0.05) in females compared with males, whereas HR, FVR, and total peripheral resistance were similar in both groups. Lower LBNP tolerance in females was associated with reduced HR response to carotid baroreceptor stimulation, lower baseline cardiovascular activity, greater decline in Q̇ induced by LBNP, increased β₁-adrenoceptor responsiveness, greater vasoconstriction under equal LBNP, lower levels of circulating NE at presyncope, and lower relative blood volume. The results of this investigation support the hypothesis that women have less responsiveness in mechanisms that underlie blood pressure regulation under orthostatic challenge.

**Gender and Heart Rate Regulation**

To the Editor: We write in reference to the recent article “Gender differences in autonomic functions associated with blood pressure regulation” by Dr. Convertino (1). We would first like to congratulate the author on his comprehensive treatment of gender differences in blood pressure regulation. However, we believe the article contains an erroneous conclusion that we would like to help correct. The article repeatedly states that relatively lower lower body negative pressure (LBNP) tolerance in women is associated with a reduced heart rate response to carotid baroreceptor stimulation. This conclusion is based on data from a technique that employs changes in R-R interval per unit carotid distending pressure. Women exhibited a maximum slope of 2.61 ms/mmHg, whereas men averaged 3.93 ms/mmHg (P = 0.047). These R-R interval results may be mathematically converted to heart rate results to see if the conclusion regarding heart rate is true.

Reported resting heart rate averaged 65 beats/min for women, which corresponds to an R-R interval of 923 ms, and heart rate averaged 52 beats/min for men, which corresponds to an R-R interval of 1,154 ms. The operational point (resting heart rate) on the R-R interval—carotid distending pressure curves occurred within the span of the reported maximum slopes, as is commonly the case (e.g. Ref. 2). To correspond to reported R-R interval slopes to heart rate slopes, we first added the change in R-R interval for a 1-mmHg increase in carotid distending pressure (the R-R interval slope) to the corresponding resting R-R interval. We then divided 60,000 ms/min by the resulting R-R interval to convert it to a heart rate value, and we subtracted resting heart rate to get the change in beats per minute for a 1-mmHg increase in carotid distending pressure (the heart rate slope). For women

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923\ ms + 2.61\ ms = 925.61\ ms
\]

60,000 ms/min/925.61 ms = 64.82 beats/min

64.82 beats/min − 65 beats/min

= −0.18 beats/min for a 1 mmHg increase in carotid distending pressure

Applying the same calculations to data from men yielded the same value: −0.18. Therefore, no gender difference exists in heart rate responses to carotid baroreceptor stimulation. Data from the LBNP tests in the study actually suggest that women's arterial—cardiac baroreflexes may be more sensitive than men's. The reported "heart rate slope" in response to graded LBNP equaled 0.58 for women vs. 0.37 beats·min⁻¹·mmHg⁻¹ LBNP for men (Ref. 1, Table 3; P = 0.057). "MAP slopes" in response to LBNP were essentially identical (women: −0.16 mmHg/min/mmHg LBNP; men: −0.15). From Ref. 1, Fig. 2, it also appears that men and women experienced identical drops in mean arterial pressure between 0 and 50 mmHg LBNP, yet the women's heart rate increased ~29 beats/min, whereas the men's heart rate increased ~17 beats/min. Therefore, LBNP responses also strongly suggest that women's arterial—cardiac baroreflex operates at a gain similar to or even greater than that of men.

R-R interval is inversely and hyperbolically related to heart rate, which can lead to confusion when drawing conclusions about one variable from the other (3), as in the present article. Also, using changes in R-R interval to assess baroreflex function ignores the important influences baseline heart rate exert on such assessments. These problems are not unique to the present article. For example, some prior studies using the same method as the present work erroneously concluded that carotid-cardiac baroreflex function is compromised after aerobic training and space flight (see Refs. 3 and 4 for discussions).

We thank Dr. Convertino for his hard work and comprehensive study. With the exception of the prob-
lem described above, the article provides a very thorough and interesting examination of gender differences in blood pressure regulation.

REFERENCES

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REPLY
To the Editor: In their letter to the Editor, Drs. Watenpaugh and Raven raise issue with reference in the manuscript entitled “Gender differences in autonomic functions associated with blood pressure regulation” (Ref. 1; abstract; line 24; DISCUSSION; paragraph 1, line 18; page R1918, paragraph 6, line 5) that lower LBNP tolerance in women was associated with reduced heart rate (HR) response to carotid baroreceptor stimulation. The observation by Watenpaugh and Raven is valid in that R-R interval rather than HR response to carotid baroreceptor stimulation was measured in this study. This is an important distinction, because R-R intervals provide more linear indications of vagal-cardiac activity than does HR (5). Although it might be reasonable to conclude that lower vagal response to baroreceptor stimulation should translate to a lesser HR response, it would be most accurate to replace the terminology “lesser HR response” with “lesser vagal-cardiac nerve traffic response.”

Because HR is a calculated reciprocal of R-R interval and cannot be measured, the calculations of Watenpaugh and Raven may compound our understanding of differences in responsiveness of this reflex in different populations or experimental conditions and the physiological significance of such differences. HR is an arbitrarily calculated variable that has important physiological meaning in respect to cardiac output. This issue was addressed in paragraph 7 of the paper (1). The data suggest that reduced cardiac-vagal nerve traffic response may reflect an inappropriate HR response than the response that might be expected in subjects with lower blood volume and stroke volume.

On the basis of their calculations, Watenpaugh and Raven contend that use of R-R interval has resulted in “erroneous” conclusions “that carotid-cardiac baroreflex function is compromised after aerobic training and space flight.” By reporting an attenuated R-R interval response under various experimental conditions, previous investigators have correctly concluded an alteration in the carotid-cardiac baroreflex in reference to vagal-cardiac nerve traffic. The physiological meaning or significance of this alteration is less clear. Because attenuated vagal-cardiac nerve traffic response to baroreceptor stimulation in humans has been associated with less orthostatic tolerance (1–3, 6, 7), attenuated R-R interval responses may reflect a more general integrated role of the carotid baroreceptors in blood pressure regulation. This notion is consistent with the observation that R-R interval has linear relations with both sympathetic and vagal nerve activities (5) and may underscore the significance of attenuated R-R interval responses under specific experimental conditions.

Paragraph 2 of the letter by Watenpaugh and Raven may confuse the issue by discussing an integrated orthostatic response in context of the isolated carotid baroreflex response. Bed rest can attenuate the carotid-cardiac baroreflex response (Ref. 2, calculated by changes in both R-R interval and HR), whereas total arterial-cardiac baroreflex response is increased (4). Smaller tachycardia has been reported in fainters with attenuated carotid-cardiac baroreflex response (2). Therefore, the issue is not magnitude of tachycardia during orthostasis, but whether an attenuated carotid-cardiac baroreflex response may contribute to blunting an appropriate HR elevation.

I thank Drs. Watenpaugh and Raven for the opportunity to discuss these issues and, particularly, for their complimentary comments regarding this paper.

REFERENCES

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