POINT:COUNTERPOINT

Rebuttal from Billman on Point:Counterpoint: Exercise training-induced bradycardia

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BOYETT AND COWORKERS (4) identified three potential weaknesses with the autonomic neural hypothesis: 1) the contribution of changes in heart rate (HR) to heart rate variability (HRV), 2) the HR response to atropine, and 3) training effects in cardiac transplant patients.

The authors note that due to the inverse curvilinear relationship between HR and R-R interval (9), changes in HR per se can affect HRV independent of the autonomic nervous system. Sacha and coworkers (11, 12) have extensively analyzed this relationship and have developed mathematical tools to correct both time and frequency domain indices of HRV for prevailing HR. By using these techniques, we found that only ~25% of the HRV could be attributed to prevailing HR (2). We further demonstrated that interventions that reduced or abolished cardiac vagal regulation (pharmacological blockade, exercise, or cervical vagotomy) provoked large reductions in HRV, even after correction for prevailing HR. In a similar manner, baroreceptor reflex activation (to increase cardiac parasympathetic activity) elicited significant increases in HRV corrected for HR (2). Thus HRV with appropriate correction can provide an indirect assessment of cardiac autonomic regulation independent of changes in HR.

Boyett et al. (4) find what they believe to be a lower peak HR response to atropine after exercise training in our prior study (3), which they interpret as evidence for an exercise training-induced change in intrinsic rate. However, the HR and HRV values we reported before and after exercise training were not statistically different (3) and therefore the exercise training response they identify is illusionary. More importantly, HR and HRV after complete autonomic blockade were nearly identical both before and after exercise training and were not different from the values reported for sedentary animals (3). Thus the intrinsic rate as revealed by pharmacological blockade was not altered by exercise training in our prior study (3).

Boyett et al. (4) refer to a single human cardiac transplantation study in which only a subset (8 of 36, identified by a post hoc analysis) of patients exhibited a reduction in HR after exercise training (7), ignoring the studies in which training failed to produce a reduction in HR (some examples, Ref. 1, 5, 6, 8). Furthermore, these exercise-induced HR reductions were not reported in a follow-up study performed on these same patients (6). Ordway et al. (10) also demonstrated that training bradycardia could not be induced in dogs after selective cardiac denervation. Thus training bradycardia is critically dependent on an intact cardiac innervation. Finally, it must be emphasized that we previously reported that exercise training did not alter sinoatrial node function and increased rather than decreased sinus HCN4 expression (3), providing further evidence against the intrinsic rate hypothesis.

AUTHOR CONTRIBUTIONS

G.E.B. drafted manuscript; G.E.B. edited and revised manuscript; G.E.B. approved final version of manuscript.

DISCLOSURES

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