In search of the optimal measure for assessment of parasympathetic control of heart rate

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Parasympathetic control of heart rate is mediated via acetylcholine-dependent muscarinic receptor signaling at the sinoatrial node. Stimulation of the muscarinic type 2-receptor slows sinoatrial rate through G_i -coupled activation of inward rectifying K_{ACh} channel activity and indirect adenylyl cyclase-dependent inhibition of the hyperpolarization activated I_f current [11, 15]. Parasympathetic control of heart rate can be indirectly assessed in human subjects by measurement of resting heart rate (with or without pharmacological blockade of muscarinic and adrenergic receptors), assessment of heart rate variability in time- and/or frequency domains, measurement of cardio-ovagal baroreceptor sensitivity in response to physiological maneuvers or pharmacologically induced changes in blood pressure, and assessment of the early phase of post-exercise heart rate recovery [1, 2, 12, 13]. All of these measures have been utilized to assess parasympathetic control of heart rate in a variety of human research settings, but there are few published data comparing multiple measures within the same individual.

The two most commonly reported non-invasive measures of parasympathetic function are resting heart rate variability (HRV) and post-exercise heart rate recovery (HRR). Both of these measures are known to respond dynamically to various modes of physical training, and to be associated with clinical outcomes in patients with cardiovascular disease [6, 9, 14]. Nonetheless, there is accumulating evidence that these measures are frequently discordant within a given individual and thus may be

independently linked to parasympathetic control of heart rate. Javorka et al. [10] first reported a lack of association between the measured HRV and HRR in 17 untrained healthy men (mean age 20.3 ± 0.2 years, maximum power output 164 ± 5 W) in 2002. Bosquet et al. [3] confirmed these findings in 28 middle- and long-distance runners (mean age 30–33 years, mean VO_{2max} 58–60 ml/kg per min). Buchheit and Gindre [4] studied 55 healthy subjects (mean age 30.8 ± 1.8 years) grouped according to their fitness level (assessed as VO_{2max}) and training load (assessed by the Baecke sport score). HRV was significantly greater in more fit individuals (those with higher VO_{2max}) regardless of training load, whereas HRR was greater in more highly trained individuals (those with higher Baecke score) regardless of the level of fitness. Dewland et al. utilized the acetylcholinesterase inhibitor pyridostigmine to augment parasympathetic signaling at the sinoatrial node in ten sedentary subjects (mean age 37 ± 7 years, mean VO_{2max} 29.4 ± 6.2 ml/kg per min) and ten endurance-trained athletes (mean age 27 ± 8 years, mean VO_{2max} 53.3 ± 11.3 ml/kg per min). These investigators demonstrated that pyridostigmine increased HRR in sedentary subjects, but not in trained athletes, and did not alter HRV in either group [7].

In this issue, Esco et al. [8] report the findings of a cross-sectional study that further supports the viewpoint that HRV and HRR are independent measures of parasympathetic function. The investigators recruited a sample of 66 healthy subjects (mean age 22.74 ± 3.64 years, mean VO_{2max} 46.39 ± 8.23 ml/kg per min) and demonstrated no association between any time domain or frequency-domain measure of HRV and HRR in this population. Moreover, there was no relationship between VO_{2max} and any measure of parasympathetic control of heart rate. This study is an important addition to the existing literature, as it is the

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first undertaken to prospectively test this specific hypothesis regarding the independence of HRR and HRV in a large population that convincingly rules out the possibility of even a small correlation between these two measures of parasympathetic function. Unfortunately, the authors did not provide any information on the training habits of the study subjects; so, the results cannot be compared directly with previous data reported by Buchheit and Gindre.

The mechanisms to account for the lack of association between these two measures have not been fully characterized. One plausible explanation is that HRV measures parasympathetic modulation of heart rate (primarily related to the phasic changes in acetylcholine concentrations associated with the respiratory cycle), while HRR measures the parasympathetic tone (the mean level of acetylcholine at the sinoatrial node) [5, 7]. It is also possible that both of these measures are influenced by other unmeasured central and peripheral factors that modulate heart rate oscillations. Further work is needed to better characterize the underlying mechanisms of heart rate control and to determine which measure or combination of measures may be most useful for monitoring response to physical training or other interventions, and for assessment of prognosis in cardiac disease.

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