COUNTERPOINT: RESPIRATORY SINUS ARRHYTHMIA IS DUE TO THE BAROREFLEX MECHANISM

In healthy humans blood pressure and heart periods fluctuate at respiratory and other frequencies. The extent of these fluctuations is situation and age dependent. Although literature concurs that most of these fluctuations are reflex driven, some insist on an explanation for the respiratory oscillations. In view of the widespread central nervous activity related to respiration, it is reasoned that in the course of evolution the cardiovascular system has, centrally, become entrained to the respiratory drive. This would, teleologically, improve oxygen uptake by increasing heart rate in the inspiratory phase. Here I make the case that respiratory sinus arrhythmia is mainly a reflex phenomenon, driven by incoming information from baroreceptors. I will base this argument on well-established physiological facts and insight that can be gained from simple computational models.

This will not refute animal experiments that show respiration to modulate centrally the blood pressure to heart period reflex. However, I intend to demonstrate that in awake humans this phenomenon is insufficient to explain respiration-to-heart rate relations.

The beauty of modeling is that it puts physiological insight to the test: does my interpretation of experimental findings fulfill all the requirements; can it describe what has been measured; and, still better, does it correctly predict findings that have not yet been obtained? The problem of modeling is the complexity of most models: they require so many parameters and mathematical formulas that, to the non-expert reader, any desired outcome might be obtained. In this essay I will try to simplify and restrict modeling to the bare minimum; more complex reasoning and models can be found in the literature.

First, let us look at a picture of common baroreflex physiology (Fig. 1A): baroreflex afferent information is in the brain stem relayed to cardiac vagal efferent traffic, leading to sinus node slowing, be it by a full reset of the diastolic depolarization (5) as depicted, or to a slowing of depolarization (2). In any case, if this acts sufficiently fast, the next heart beat will be delayed after a systolic pressure increase, thereby stabilizing diastolic pressure (Fig. 1C). As has been argued by Dr. Eckberg in his Point preceding this Counterpoint, we may assume that this can, in humans, occur within one beat, in view of the latencies involved. Also the founding fathers of the “gold standard” of baroreflex sensitivity (BRS) measurement came to this insight in a later publication (6): if resting heart rate in the respiratory frequency, one would expect conspicuous respiratory drive. This would, teleologically, improve oxygen uptake by increasing heart rate in the inspiratory phase. Here I make the case that respiratory sinus arrhythmia is mainly a reflex phenomenon, driven by incoming information from baroreceptors. I will base this argument on well-established physiological facts and insight that can be gained from simple computational models.

The jumping between frequency and time domain should be done with caution. In treating blood pressure and heart period recordings, it is common practice to reduce the amount of data


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1742
to just a few numbers per heart beat: the duration of the heart period, the diastolic pressure that occurred just after the R-wave that started off the beat, and the systolic pressure that occurred within that beat all get the same sequence number. Consequently, the changed diastolic pressure is found in the next sequence. Alternatively, an increased systolic pressure and the prolonged heart period it provokes end up at the same sequence number. That is not to say that there is no time delay between the occurrence of the systole and the ensuing heart period; we only know the duration of the beat at the moment where the next R-wave occurs. However, when only blood pressures and heart periods are available, it is impossible to measure time delays within the heart beat. For that purpose other experiments are required, like electrical stimulation of the baroreceptor afferent nerves at variable moments within the cardiac cycle (1).

Often the correlation between heart periods and pressure derived parameters is not computed in the time domain by looking at scatterplots but in the frequency domain by looking at phase delays. One should realize that the change of technique does not overcome the shortcomings of the underlying numbers: any correlation that is highest within the same beat will show up as a phase delay of zero, or rather a number within the boundaries of that beat. For instance at the respiratory frequency, any phase difference between two traces are imperfect sinusoids or that the correlation may be jumping from a delay or advance in the upgoing slope of zero beats to that of one beat in the downgoing slope of the traces. The latter would fit well with known vagus nerve physiology (3): the sinus node response to a cardiac vagal volley occurs within ~100 ms, but may linger off after seconds.

Summing up what the extremes of Fig. 1C (baroreflex has it all) compared to 1B (central modulation has it all) imply for daily practice: if all RSA is due to central modulation only, one would expect a conspicuous peak in diastolic pressures at the respiratory frequency. This is not what is observed (4): systolic pressures show a large oscillation at the respiratory frequency, diastolic pressures show only very little. Moreover, the shortened heart period would precede an increased systolic pressure by one beat, implying a negative phase between systolic pressure and heart period of around 90° at the respiratory peak, contrary to experimental findings, where the two signals are in phase. All in all, the first explanation of RSA is that it is due to respiratory induced blood pressure oscillations that are translated into heart rate oscillations by the baroreflex. The same holds true for the slower oscillations around a period of 10 s (0.1 Hz), which are due to a baroreflex-driven sympathetic oscillation. On that oscillation, vagal—and partly sympathetic—heart rate oscillations are “riding” as sign of a healthy baroreflex (4).

I have emphasized the importance of baroreflex physiology to understand blood pressure-heart rate interactions. Of course, reality is more complex than can be fitted into a 1,200-word essay. I did not go into the difference in computed BRS between respiratory and 0.1-Hz oscillations: the former sometimes so much larger than the latter (and even than can be explained by the known numbers for “normal” BRS) that one must consider other mechanisms as well (own observations, in particular in young adults). Also I left out the effects of respiration on venous return to the right and left sides of the heart, each bringing along pressure effects and their own modulation of autonomic outflow. As stated in the beginning, physiological modeling may put belief to the test, but at the same time too complex a model may become a belief of its own.

REFERENCES