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 exemption 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 humans is below ~75 beats/min the best correlation between increasing systolic pressures and heart periods is found for the heart period in which a specific systolic pressure occurs, rather than for the next heart period. It is strange to see that this insight did not make it into practice.

Now suppose that in a sequence of beats as depicted in Fig. 1A, suddenly the central nervous system decides to command the respiratory frequency, one would expect conspicuous respiratory sinus arrhythmia now. 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.

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Now suppose that in a sequence of beats as depicted in Fig. 1A, suddenly the central nervous system decides to command the inspiratory movement and at the same time it inhibits (“gates”) incoming baroreceptor traffic. This would, inevitably, lead to an increase of the next diastolic pressure, as shown in Fig. 1B. Rather than dampened diastolic pressure variability at the respiratory frequency, one would expect conspicuous respiratory blood pressure oscillations.

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...
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 among 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