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Thinking about breathing: Effects on respiratory sinus arrhythmia

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ABSTRACT

Respiratory sinus arrhythmia (RSA), the increase and decrease in instantaneous heart rate (HR) with inspiration and expiration, is commonly evaluated as function of breathing frequency *f*. However, to the extent that RSA plays a role in the efficiency of gas exchange, it may be expected to correlate better with HR/*f* ('breathing specific heart rate') than with *f*, because the former is a better reflection of the cardio-respiratory coupling. We measured RSA breath-by-breath in 209 young men and women during spontaneous breathing and during volitional breathing under auditory cues at vastly different *f*. In either case, and for both genders, RSA correlated better with HR/*f* than with *f*. As HR/*f* increased so did RSA, in a linear manner. When compared on the basis of HR/*f*, RSA did not differ significantly between spontaneous and volitional breathing. It is proposed that RSA is a central mechanism that ameliorates the matching between the quasi-continuous pulmonary blood flow and the intermittent airflow, irrespective of the type of ventilatory drive (cortical or autonomic).

1. Introduction

The phenomenon of the acceleration of the heart during inspiration and its deceleration during expiration (respiratory sinus arrhythmia, RSA) has been known for a long time and documented almost two centuries ago (Ludwig, 1847). Since then, numerous studies have been performed to reveal the mechanistic basis of RSA and its possible function. Measurements in dogs, which present a characteristically marked RSA, have shown that RSA improves gas exchange by maximizing pulmonary blood flow in relation to inspiration, with a decrease in physiological dead space and a rise in ventilation-perfusion ratio (Hayano and Yasuma, 2003; Giardino et al., 2003; Yasuma and Hayano, 2004). A decrease in RSA, on the other hand, can be an ominous sign for a variety of cardiac conditions (Fei et al., 1996a,b). In infants, lack of inter-beat variability is considered an indication of poor autonomic control of the heart and a possible risk factor for the sudden infant death syndrome (Schechtman et al., 1992).

The inspiratory increase in heart rate (HR) originates from the temporary inhibition of the nucleus ambiguus (or cardio-inhibitory centre), which causes a reduction of the vagal output to the sinoatrial node and the shortening of the inter-beat interval. Breathing influences the nucleus ambiguus via a number of direct or indirect paths, broadly characterized as peripheral and central mechanisms (Daly, 1986). The former includes the reflex responses to the changes in intra-thoracic and blood pressures and to the activation of the pulmonary stretch receptors with lung inflation, while the latter refers to the interaction between the respiratory and the cardio-inhibitory centers. Since the early work of Anrep et al. (1936a,b) many experiments have given support to one or the other of these mechanistic possibilities (Taha et al., 1996; Schäfer et al., 1998); hence, it is probable that RSA results from a combination of factors (Anrep et al., 1936b; Larsen et al., 2010), each gaining a different level of importance in a particular condition or experimental setting.

Cognitive and emotional activities impact on the automatic function of the respiratory and cardiovascular systems and could interfere with the central cardio-respiratory interaction and the sympathetic control of the heart (Bartlett and Leiter, 2012). Reports that RSA can change during slow-wave sleep, mental exercises or just by thinking about breathing (Bernardi et al., 2000; Cysarz and Büssing, 2005; Jurysta et al., 2006) would indicate that cortical influences modify RSA. However, in all these conditions the changes of the breathing pattern have complicated the interpretation of the results; in fact, breathing frequency (*f*) has a profound influence on RSA (Angelone and Coulter, 1964; Hirsch and Bishop, 1981). Several studies have attempted to control *f* by having the subjects breathing at predetermined values of *f* ('cued breathing'). Larsen and colleagues (Larsen et al., 2010), from a detailed review of ten of these studies, have remarked on the fact that the results

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covered all possibilities, with either no significant difference in RSA between spontaneous and cued breathing (four out of ten studies), or a significant increase or decrease (three studies each).

One possible reason for the mixed conclusions is that differences in RSA between spontaneous and cued breathing may be *f*-dependent. To test this possibility it would be necessary to construct the *f*–RSA relationship not only during cued breathing but also during spontaneous breathing, and examine their degree of overlapping. If the two *f*–RSA functions differed in slope and crossed over each other, analysis of a narrow range of spontaneous *f* could lead to any conclusion depending on the *f* taken into consideration. A meaningful *f*–RSA relationship during spontaneous breathing necessitates a large number of subjects, not only to cover a wide range of *f* but also to compensate the large variability of RSA among subjects (Mortola et al., 2015) and its age-dependency (Barnett et al., 1999). Because most studies have examined a very limited number of subjects, invariably the RSA during spontaneous breathing is a single value, the average of the whole group (Larsen et al., 2010). Therefore, the possibility that volitional breathing may modify RSA in an *f*-dependent fashion remains untested.

An additional issue is whether or not *f* represents the most correct parameter suitable for the comparison of RSA between volitional and spontaneous breathing. In fact, to the extent that RSA is meant to ameliorate the coupling between cardiovascular and respiratory convection in the process of gas exchange, one may argue that the ratio between mean HR and *f* ('breathing-specific heart rate', beats/breath) may be a better indicator of the cardio-respiratory coupling than the absolute value of *f*. In which case, the comparison of RSA between volitional and spontaneous breathing would be more meaningful on the basis of HR/*f* than on the basis of *f*.

In this study we had the opportunity to measure RSA breath-by-breath in a large group of young men and women of very similar age. The natural variability of the spontaneous breathing pattern among subjects has made it possible to compare RSA between volitional and spontaneous breathing over a range of *f* and HR–*f* ratios to test the following two hypotheses: (a) RSA correlates better with HR/*f* than with *f*, and (b) RSA differs between volitional and spontaneous breathing.

2. Methods

2.1. Ethical approval

Subjects were undergraduate students between 19 and 21 years of age. They were briefed regarding the measurements to be undertaken and the study protocols, and signed an informed written consent to this effect; however, they were left unaware of the specific purpose of the study until data collection was finished. The study conformed to the standards set by the Declaration of Helsinki, and the procedures have been approved by the local ethics committee.

2.2. Participants

A few of the subjects that signed the consent form were excluded from the analysis for various reasons (did not complete the protocols, did not follow properly the acoustic cues or had recording artifacts that precluded a correct measurement of RSA). Consequently, data were obtained from 209 subjects, 91 males and 118 females (Table 1), non-smokers, free from cardio-respiratory disorders or any medical treatment.

Table 1
Numbers and characteristics of the subjects during spontaneous breathing.

	N	Age (years)	Height (cm)	Weight (kg)	*f* (br/min)	Mean HR (bpm)	HR/*f* (beats/breath)	ΔHR (bpm)	RSA (%)
Males	91	19.4 ± 0.1 [18–23]	177 ± 1 [161–196]	72 ± 1 [55–110]	13.8 ± 0.4 [6–24.6]	68.1 ± 0.9 [50.5–95.7]	5.4 ± 0.2 [2.1–12.3]	8.3 ± 0.5 [2.2–24]	12.2 ± 0.6 [2.8–32.4]
Females	118	19.4 ± 0.1 [18–23]	164* ± 1 [150–175]	58* ± 1 [38–118]	14.6 ± 0.4 [5.8–28.4]	68.1 ± 1 [40.5–92.4]	5.1 ± 0.2 [2.2–13.4]	9.1 ± 0.6 [2.8–35.2]	13.5 ± 0.9 [3.6–53.4]
Total	209	19.3 ± 0.1	170 ± 1	65 ± 1	14.2 ± 0.3	68.1 ± 0.7	5.2 ± 0.1	8.7 ± 0.4	12.9 ± 0.5

Values are means ±1SEM. In square brackets, minimum and maximum values recorded. *N*, number of subjects. *f*, breathing frequency (breaths/min). HR heart rate (beats/min). ΔHR, absolute difference between peak and trough instantaneous HR (beats/min). HR/*f*, Breathing-specific heart rate (beats/breath). RSA, respiratory sinus arrhythmia (ΔHR/mean HR,%). * significant difference between genders.