



The heart cannot pump blood that it does not receive

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A commentary on

Neurohumoral mechanisms associated with orthostasis: reaffirmation of the significant contribution of the heart rate response

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Orthostatic gravitational stress results in a decrease in venous return. Because the heart cannot pump blood that it does not receive, ventricular stroke volume and cardiac output decline, but until the point of presyncope, there is little change in arterial pressure. There is little doubt that the vasomotor outflow to the resistance vessels and presumably the splanchnic capacitance vessels are of fundamental importance in the prevention of hypotension (Rowell, 1993; Wieling and van Lieshout, 2008), but there is also a concomitant increase in heart rate and the significance of this is much less clear (Hainsworth, 2000).

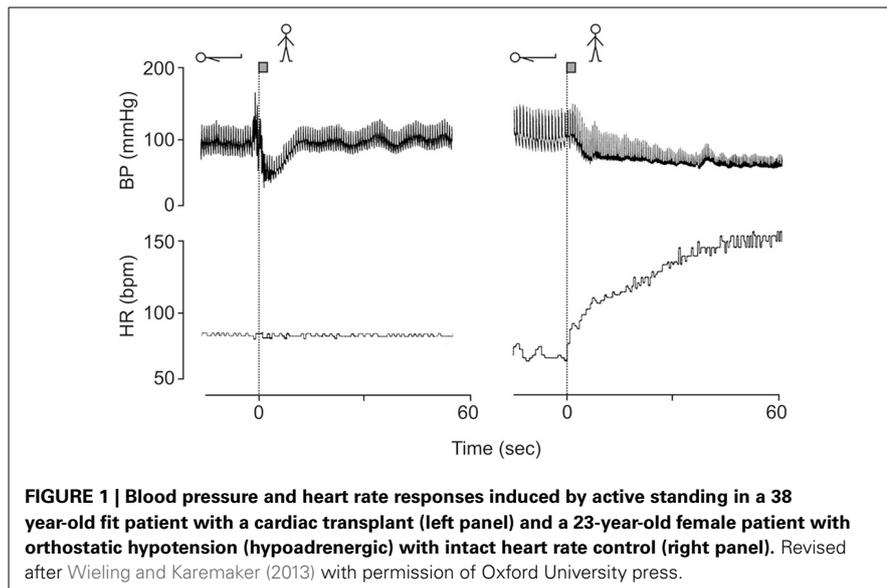
In a recent issue of *Frontiers in Physiology*, Convertino focussed on the physiology of maximal compensation to orthostasis studying high and low tolerant healthy subjects. Exposure to a maximal lower body negative pressure (LBNP) test was used to quantify orthostatic tolerance. The author argues that this stressor is equivalent to actual orthostasis. However, recent studies suggest that pooling in the splanchnic area during actual orthostasis (standing/head-up tilting) is more important than previously reported in studies using simulated orthostasis by applying lower-body negative pressure up to the levels of the iliac crest (Taneja et al., 2007).

More pronounced splanchnic pooling during orthostasis may result in more stimulation of vascular subdiaphragmatic receptors that are postulated to play a role in orthostatic adjustment by causing vasoconstriction and augmentation of the carotid baroreflex (Doe et al., 1996). Other obvious differences with LBNP are that during free standing the carotid baroreceptors are always above the heart and the static increase in skeletal muscle tone during active standing opposes pooling of blood in limb veins (Wieling and van Lieshout, 2008; Wieling et al., 2014). Increases in skeletal muscle tone are a key factor in orthostatic adjustment. Accordingly, a static increase in skeletal muscle tone by leg-crossing during a maximal LBNP test increases time to presyncope considerably (Krediet et al., 2006). Therefore, a device which combines head-up tilting with negative pressure to the lower part of the body (Hainsworth, 2000) seems a more physiological approach to quantify orthostatic tolerance in a reproducible way. Although LBNP (in the horizontal position) is a deficient model for studying orthostasis, it can be used to simulate loss of central blood volume (hemorrhage) (Johnson et al., 2014).

As far as the physiology of maximal hemodynamic compensation in high and low tolerant healthy subjects, the author reaffirms the concept that the heart rate response contributes significantly to orthostatic tolerance (Convertino, 2014). The observations of Convertino are of considerable interest, but it is important to realize that they are based on studies in young adult healthy subjects exposed to a maximal LBNP stress. The observations

cannot be generalized to the adjustment to the upright posture during free standing. Based on clinical observations the following data indicate that neural heart rate control is not important for orthostatic tolerance.

- (1) Weissler studied the effects of posture and atropine on the cardiac output in six young adult male subjects. He documented that atropine administered in the supine position increased heart rate on average by 44 beats/min. The heart rate increase was accompanied by a cardiac output rise of about a factor 2 with an increase in mean arterial pressure. After administration of atropine in the upright posture heart rate increase by 65 beats/min, but no effect on cardiac output and blood pressure was observed. When pooling of blood in the upright posture was prevented by sustained inflation of an anti-gravity suite, the cardiac responsiveness to atropine in tilted subjects was restored, in part (Weissler et al., 1957a). In another study it was documented that administration of atropine could not prevent an impending vasovagal faint (Weissler et al., 1957b).
- (2) Patients with a cardiac transplant have no increase in heart rate on standing, but intact orthostatic blood pressure control (**Figure 1**, left panel) (Van Lieshout et al., 1989; Wieling and Karemaker, 2013).
- (3) In patients with sympathetic vasomotor lesions, but intact vagal heart rate control pronounced orthostatic



hypotension occurs despite an impressive postural tachycardia (Figure 1, right panel) (Wieling and Karemaker, 2013).

- (4) Atrial tachypacing at best has marginal effects on hypotension in patients with severe orthostatic hypotension due to autonomic failure (Sahul et al., 2004) and cardiac pacing does not improve orthostatic tolerance in patients with vasovagal syncope (El-Bedawi et al., 1994). However, benefit from rate-drop pacing in older patients with documented prolonged asystolic syncope has been reported (Brignole et al., 2012).
- (5) Another example of the disconnect between the heart rate responses and orthostatic tolerance are patients with the postural orthostatic tachycardia syndrome in whom very high orthostatic heart rates are associated with orthostatic presyncope. The treatment in these patients is aimed at decreasing postural complaints by decreasing the postural tachycardia (Joyner, 2011).

These data strongly support the view that the central venous reservoir is an important determinant of cardiac responsiveness to changes in heart rate i.e., a heart cannot pump blood that it does not receive. In fact, very high heart rates would decrease cardiac filling time and during conditions of impaired venous return

such as orthostatic stress, could actually impair cardiac output (Hainsworth, 2000).

The positive correlation between orthostatic tolerance and the maximal sympathetically mediated heart rate before syncope in high and low tolerant healthy subjects observed by Convertino may have been because in this situation heart rate is a marker for enhanced sympathetic drive to resistance vessels, which provide the main defense against hypotension (Rowell, 1993; Hainsworth, 2000).

In conclusion, The arterial (and especially carotid) baroreceptor control of sympathetic motor tone of resistance and splanchnic capacitance vessels in combination with the central blood volume are the most important components in the maintenance of postural normotension in humans (Rowell, 1993; Wieling and van Lieshout, 2008). Activation of the skeletal muscle pump in the lower body can compensate in part for defects in control of vasomotor tone and a reduction of central blood volume. Cardiac effector mechanisms appear not to be important for the adjustment of arterial pressure to the upright posture.

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