PERSPECTIVES

Exercise training and orthostatic intolerance: a paradox?

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Standing upright imposes a major stress on the cardiovascular system. The gravitational displacement of blood away from the thorax to dependent regions of the body initiates orthostatic pooling of venous blood. The fall in venous return affects the central blood volume and thus the volume directly available to the heart. Despite this assault, humans can usually stand erect as long as they are supported by cardiovascular reflexes to maintain arterial pressure and to limit lower extremity fluid accumulation by increasing vasomotor tone. These reflexes cannot, however, do the job without leg muscular activity ('the muscle pump') and movement is a prerequisite for maintaining the central blood volume.

In patients suffering from pure autonomic failure, cardiovascular reflexes are malfunctioning; the carotid baroreceptor unloading by orthostatic stress is not or is inadequately translated into enhancement of sympathetic vasomotor outflow, leading to orthostatic hypotension with symptomatic cerebral hypoperfusion. By contrast, there are subjects who, when standing, develop symptoms suggestive of cerebral hypoperfusion despite well maintained mean arterial pressure. Related signs are a postural tachycardia and a normal to excessive increase in vascular resistance. This entity is called idiopathic orthostatic intolerance to underscore that we do not know what the defect is – whether it is deficient peripheral vascular responses, noradrenaline (norepinephrine) transporter deficiency, abnormal baroreflex responses or a reduced blood volume. Notwithstanding fundamental pathophysiological differences, patients with autonomic failure or orthostatic intolerance may benefit from the same therapeutic approach aiming at expanding extracellular fluid and plasma volumes.

Improving the aerobic capacity of moderately fit individuals increases the plasma volume and is usually associated with improved orthostatic tolerance (Wieling *et al.* 2002). The beneficial effect of a training programme in improving orthostatic tolerance was elegantly demonstrated by Allen *et al.* (1945) in identical twins who fainted on the tilt-board. After a three-week training programme consisting of abdominal and trunk exercises applied to one of them, a subsequent head-up tilt faint could be elicited in the untrained twin only. This observation contrasts to the propensity of highly trained individuals towards a lower tolerance to orthostatic stress than untrained people. 'Trained men can run, but they cannot stand' may be common knowledge but we are still in search for the how and why.

In this issue of *The Journal of Physiology*, Ogoh *et al.* (2003) contribute two important pieces to the puzzle. First, they demonstrate that under circumstances of progressive depletion of the central blood volume by orthostatic stress, the physiological increase in carotid baroreflex responsiveness to the heart and blood vessels is attenuated in endurance-trained subjects. It is known that athletes may develop structural cardiac changes with a steeper slope of the left cardiac pressure–stroke volume relationship. This may be of benefit when exercising but it leads to a considerable reduction in stroke volume during orthostasis (Levine *et al.* 1991). A second finding of importance by Ogoh *et al.* (2003) is the changed central venous pressure–central blood volume relationship indicating changes in the mechanical properties of the right heart as well. The implication is that highly fit subjects depend more tightly on maintenance of their venous return to maintain the upright body position.

It appears that the effects of fluid expansion related to endurance training as an intervention to improve orthostatic tolerance may be paradoxically offset by cardiac remodelling and reduced effectiveness of baroreceptor control mechanisms. Baroreflex function was, by design, quantified by relating changes in estimated carotid sinus pressure to heart rate and blood pressure. We should, however, not exclude the possibility that a lower response may be also explained by altered sympathetic vascular transduction. This is supported by the finding in endurance-trained subjects that carotid baroreflex control is normal when expressed as changes in muscle sympathetic nerve activity, but reduced when quantified as vasomotor response (Fadel *et al.* 2001).

To summarise the present view, orthostatic intolerance in deconditioned subjects is related to hypovolaemia and possibly to cardiac atrophy (Pawelczyk *et al.* 2001) and to attenuated carotid baroreflex responsiveness and a larger compliance of the heart in the highly fit. The debate as to the effect of physical training on an individual's tolerance to orthostatic stress may come to an end by accepting the existence of an 'optimal level of fitness', ill-defined as it is, located between the deconditioned and the highly trained state. To advise people who do not easily tolerate standing to exercise seems logical but to what extent they should exercise is less certain (Wieling *et al.* 2002). Intuitively leg resistance training may reduce venous pooling by increasing muscle tone but e.g. swimming training does not lead to greater orthostatic tolerance than running training (Franke *et al.* 2003). Tensing the leg muscles attenuates the postural reduction in cerebral perfusion (van Lieshout *et al.* 2001) and the instructions given to students in military schools to 'walk' in their shoes and to stand on the balls of their feet during parade may also be of relevance to athletes.

Where are the crossroads of aerobic fitness and orthostatic intolerance to be found? Given the results of Ogoh *et al.* (2003) we have to realise that three hours of aerobic training each day is apparently capable of establishing a new operating set point for human cardiovascular function that may be of disadvantage for orthostatic tolerance.

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