Increasing physical activity has been shown to reduce cardiovascular morbidity and mortality [1]. More specifically, it has been shown to reduce physiological markers of cardiovascular disease, such as high blood pressure, vascular endothelial cell reactivity and arterial stiffness [2]. A potential mechanism by which exercise training is thought to reduce cardiovascular disease is to increase nitric oxide bioavailability, by either enhancing synthesis or reducing degradation via reducing free radical production. In this issue of Clinical Science, Hägg and colleagues have chosen the spontaneously hypertensive rat model to study these pathways. Traditionally, increasing physical activity in an animal model meant forced running, which is complicated by the high stress levels associated with the induction to run. To alleviate this complication, investigators have used voluntary running wheels placed in the cages of rats [4]. Interestingly, to address issues relevant to human disease, Hägg et al. [3] chose to study SHR (spontaneously hypertensive rats), an animal model for human essential hypertension. In their study, Hägg et al. [3] found that spontaneous running increased aortic compliance and antioxidant capacity with decreased oxidative stress in mesenteric arteries. These results were presented as support for the cardiovascular protective effects of physical activity.

A key aspect of any interventional study is to understand what the intervention is. Hägg et al. [3] found that SHR did run voluntarily (see Figure 1 in [3]). Remarkably, these animals were covering on average 14 km/day after 4 weeks of training. The world would be a much healthier place if only we could get humans to cover similar distances! So the question is, what kind of training intensity does 14 km/day in rats represent? Earlier studies have shown that young rats will voluntarily run much longer durations (up to 34% of the day) and even at higher speeds (up to 67% of maximum speed) than performed by enforced training [4]. A typical enforced training programme can be moderate (30 m/min, 60 min/day, 5 days/week) or rigorous (32 m/min, 90 min/day, 5 days/week) [5]. These programmes will result in the rats running 9–15 km/week, much less than the 98 km/week seen in the study by Hägg et al. [3]. Do all voluntary training programmes produce such high training volumes? Previous studies on normotensive (Sprague-Dawley) rats have shown that young rats will sustain weekly running distances of 38 km/week [5], but running distance varies with the age of the rat, with younger rats running more than older ones [4]. Also, duration of exposure to the running wheel alters behaviour as well, with rats often reported to run very impressive distances on first exposure [6]. Although reaching running distances of up to 40 km/day, running distance declines to 3 km/day after 6 months [6]. Not all rats perform the same and it is common to divide normotensive

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Abbreviation: SHR, spontaneously hypertensive rats.

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rats into high (13.4 km/day), moderate (7.2 km/day) and low (3.2 km/day) achievers [4]. The other question is whether SHR behave differently from other rat strains. This does not seem to be the case, as previous studies report running distances for SHR that are similar to normotensive rats (subjected to the same age and exposure conditions) [7]. Thus it seems that the SHR in the study by Hägg et al. [3] were running as one might expect a young rat to run on initial exposure to a voluntary running wheel. The intensity of running is important as previous studies have suggested that the blood pressure response of SHR to running may depend on running intensity [7].

How does this study by Hägg et al. translate to human health care delivery? They clearly demonstrated that voluntary running will improve several markers of vascular health in hypertensive rats, but the exercise stimulus has to be considered to be far greater in terms of time/day, times/week, and even exercise intensity than the typically recommended exercise programmes for humans (30 min of exercise three times/week, at a moderate intensity). The strength of the study by Hägg et al. [3] is the information on what vascular biochemical changes maybe associated with exercise, but it will remain to be determined if the same biochemical changes occur with a lower intensity training stimulus [8]. Perhaps we should consider ‘activating the wheel’ for selected time periods to more closely mimic human exercise patterns?

Another interesting issue presented by Hägg et al. [3] is the choice of arteries to evaluate. They chose the thoracic aorta as a conduit artery and the second- or third-order branch of the mesenteric artery as a resistance artery. A number of studies have suggested that central conduit arteries provide the best link between arterial stiffness and future cardiovascular events [9]. However, it is important to consider the impact of the exercise on the arteries being studied [10]. The aortic artery should have increased blood flow in response to exercise as it conducts blood to the exercising limbs. However, Laughlin et al. [11] found that mesenteric arteries deceased blood flow during exercise and, furthermore, exercise training did not significantly alter mesenteric artery blood flow. This suggests that changes in the mesentery arteries reported by Hägg et al. [3] may well reflect non-specific responses to exercise training. This highlights the importance of considering the role the artery plays during exercise as well as the general function of artery when evaluating the impact of exercise on arterial structure and function.

REFERENCES