Sex-dependent blood pressure regulation in acute hypoxia

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Received: 22 July 2021 / Accepted: 1 August 2021 / Published online: 27 September 2021
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We read with great interest the recent observations by Jiang et al. [1] who found that physiological testosterone levels may protect against hypoxia-induced hypertension through inhibition of nuclear respiratory factor 1, which transcriptionally regulates angiotensin-1-converting enzyme (ACE) and endothelin-1 (ET-1) expression. It remains to be elucidated whether these novel findings could be transferred to human beings, i.e., whether men would actually be more protected from systemic blood pressure elevations (hypertension) than women when acutely exposed to hypoxia, such as at high altitude. We recently reported blood pressure elevation only in men following acute high-altitude sojourn [2], indicating that the contrary would be the case, possibly because factors other than testosterone levels, e.g., the autonomous nervous system, importantly contribute to blood pressure regulation in hypoxia. On the one hand, hypoxia directly provokes vasodilation (hypoxic vasodilation), which is, on the other hand, counteracted by sympathetic vasoconstriction. For instance, the hypoxia-induced stimulation of arterial chemoreceptors in freely breathing humans causes elevation of both cardiac sympathetic activity and sympathetic vasoconstrictor outflow to skeletal muscles but also to splanchnic and renal beds [3], resulting in higher heart rate, myocardial contractility and vasoconstriction in the aforementioned tissues. Additionally, rapid breathing (hypoxia-induced hyperventilation) adds to the increase in sympathetic activity [4]. Thus, the net result on blood pressure depends not only on the complex interplay between hypoxic vasodilation and sympathetic vasoconstriction but also on individual aspects such as age, preexisting disease, medication, and likely sex. Sympathetic nerve activity is usually enhanced in men when compared to that in women of the same age [5], and sex differences may also exist with regard to the interaction between sympathetic nerve

activity and responses of the vasculature. This is indicated by a positive relationship between muscle sympathetic nerve activity and total peripheral resistance only in men, meaning that a high sympathetic tone may not translate into high blood pressure in women [6]. The association of testosterone with systemic blood pressure in humans is still controversial, and data on testosterone effects on hypoxia-induced hypertension, as demonstrated by Jiang et al. in rats, are lacking. Thus, the findings by Jiang et al. will certainly promote future research on this interesting and clinically relevant topic. It will be of particular interest to investigate potential sex differences in the reported mechanisms in animal models (as only male rats were studied by Jiang et al.) and to design studies in humans (of both sexes) to understand possible interspecies differences.

Compliance with ethical standards

Conflict of interest The authors declare no competing interests.

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