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Differential control of efferent activity in muscle sympathetic single units of humans: a role for pulmonary artery baroreceptors?

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TO THE EDITOR: We read with interest the article by Incognito and colleagues (5), published recently in the American Journal of Physiology. The paper describes differential control over postganglionic single unit sympathetic fibres in healthy humans.

It is widely reported that unloading of low-pressure vagal afferents from the heart and pulmonary vasculature mediates increased muscle sympathetic nerve activity (MSNA) and systemic vasoconstriction in response to mild LBNP (12). However, an alternative explanation is that altered aortic and carotid arterial hemodynamics, acting through the sinoaortic baroreceptors, stimulates sympathoexcitation, without a detectable change in arterial pressure (3, 11). Nevertheless, many in the field attribute vasoconstriction in the skeletal muscle circulation during LBNP to a low-pressure 'cardiopulmonary baroreflex'. This is despite evidence that mild LBNP still elicits increased MSNA and vasoconstriction in cardiac transplant patients (6).

The article by Incognito and co-authors presents some interesting new evidence. Simultaneously occurring increases and decreases in MSNA were recorded from two populations of postganglionic single units in young healthy men and women exposed to LBNP and rhythmic handgrip exercise. Importantly, this is similar to previous findings for healthy middle-aged men (9), and heart failure patients (8). Furthermore, both of these studies by Millar and co-authors (8, 9) also observed two response patterns during mild lower body positive pressure. The so-called "paradoxical" single-unit responses were attributed to unloading and loading of intrathoracic mechanoreceptors, which were presumed to be responsible for sympathetic activation when

stimulated. Notably, these units were relatively small in number compared with those having anticipated firing responses.

With this in mind, we highlight several important findings from studies in animal preparations, which permit careful control of pressure stimuli to reflexogenic areas in the heart, pulmonary vessels, and aortic arch and carotid arteries. For example, it is established that atrial receptors exert little influence over sympathetic vasoconstrictor activity (7). Furthermore, we have demonstrated that responses attributed to ventricular receptors actually originate from mechanosensitive receptors in the coronary arteries (1); notably, reduced ventricular filling has little effect on systemic vascular resistance (2). As a matter of fact, we have shown that coronary artery baroreceptors function as high-pressure receptors, and exert control over sympathetic nerve activity similar to that originating from aortic and carotid baroreceptors (4). Thus, the only receptors within the intrathoracic region with the potential to elicit “paradoxical” sympathetic responses are the pulmonary vascular mechanoreceptors. Moreover, we have observed differential control of systemic vascular resistance in response to rising and falling pressures in the pulmonary and carotid arteries (10).

Pulmonary artery baroreceptors may be of importance in mediating sympathetic activation during exercise, as well as in hypoxic conditions (4). However, modulation of sympathetic outflow by these low-pressure baroreceptors in humans has been largely overlooked. This may be due, in part, to the technical difficulty of applying a discrete physiological stimulus to the pulmonary arteries. Therefore, we commend the work of Incognito, Millar

and colleagues (5, 8, 9) for shedding new light on this possibility. In our view, their data represent exciting first-in-human evidence of a potential role for pulmonary baroreceptors, creating the possibility of differential control of sympathetic outflow by low- and high-pressure baroreceptors. The challenge for those of us working in this area now is to develop an approach that enables discrete stimuli to low- and high-pressure baroreceptors in humans, in order to further investigate differential control of MSNA.

AUTHOR CONTRIBUTIONS

JPM and MJD contributed equally.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

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