New insights into orthostatic hypotension

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We are approaching the 50th anniversary of manned spaceflight, which began in 1961 when Yuri Gagarin and Alan Shepard flew into space within a month of each other; much has been learned about the health risks associated with microgravity. One of the first indications that space travel could have adverse health consequences was in the U.S.A. Mercury program, when an astronaut experienced a near-syncopal episode upon return to Earth after only 34 h in space (4). In subsequent 14-day Gemini missions, postflight head-up tilt tests were aborted due to presyncopal symptoms of hypotension (2). The etiology of postflight orthostatic hypotension is multifactorial and may include blood volume loss, cardiac dysfunction, diminished baroreflex sensitivity, altered vestibular-autonomic function, and increased vascular compliance or decreased vasoconstrictor responsiveness. The relative contribution of each of these factors to orthostatic intolerance may vary within each individual (3) and may vary as a function of various factors, such as flight duration and gender (8, 12).

Although much work has been done to understand the causes and underlying mechanisms of postflight orthostatic hypotension, there are still considerable gaps in our knowledge regarding possible mechanisms contributing to this phenomenon. One such gap is the possible role of the splanchnic circulation. Vasoconstriction of the splanchnic circulation is normally responsible for ~33% of the decrease in total vascular conductance needed for the maintenance of arterial pressure during an orthostatic stress (11), and the mesenteric circulation is one of three arterial branches that make up the splanchnic circulation (10).

The focus of the work by Colleran et al. (5), published in this edition of the American Journal of Physiology: Regulatory, Integrative and Comparative Physiology, was to investigate the possible role of the mesenteric circulation in the cardiovascular deconditioning that is associated with spaceflight and bed rest in humans. To accomplish this goal, these investigators used the tail-suspended hindlimb-unloaded rat, which exhibits many of the hallmarks of cardiovascular deconditioning that are evident in humans, including resting and exercise tachycardia (7), diminished maximal aerobic capacity (9), and orthostatic hypotension (13). Two significant findings were presented in this study. First, they found that the rate of norepinephrine-induced vasoconstriction of mesenteric resistance arteries is diminished in hindlimb-unloaded rats. Other studies have reported the effects of hindlimb unloading on the maximal response and sensitivity to vasoconstrictor stimuli in various conduit and resistance arteries. However, this study is the first to describe a slower rate of constriction, which may be physiologically significant in terms of the need to rapidly elevate peripheral vascular resistance in order to maintain cerebral perfusion pressure during standing. Second, the investigators tested various vasoconstrictor responses working through different signaling pathways to discern the mechanism for the diminished adrenergic vasoconstriction. The results indicated that hindlimb unloading impaired an intracellular Ca2+-release mechanism associated with the sarcoplasmic reticulum in the smooth muscle cells. This conclusion was further supported by the findings of diminished ryanodine-2 receptor mRNA and protein expression in mesenteric arteries from unloaded rats. Hence, this study is the first to fully describe the effects of hindlimb unloading on the adrenergic vasoconstrictor dynamics of mesenteric arteries and the first to describe the impairment of the Ca2+-release mechanism in the dysfunction of the vasoconstrictor response.

One of the unique features of the mesenteric circulation is that this vascular bed is not subjected to altered blood flow and pressure gradients that occur in many tissues when a cephalic fluid shift is induced by the hindlimb unloading treatment (6, 7, 13). In the absence of changes in mesenteric perfusion or intravascular pressure, it is unclear what the stimulus for the change in mesenteric vasoconstrictor dynamics might be. Previous work from this laboratory has suggested that alterations in the concentrations of circulating hormones associated with the fluid shift, such as atrial and brain natriuretic peptides, may play a role in altering vasoconstrictor responses in arteries and veins, and possibly smooth muscle contraction in lymphatic vessels and uterine tissue as well (1). These observations may serve as the basis for future investigation and insight into the problem of orthostatic hypotension associated with spaceflight and bed rest in humans.

REFERENCES


