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Author: Mrs. Jingyu Wang

State Key Laboratory of Space Medicine Fundamentals and Application, China Astronaut Research and Training Center, China

Mrs. Zhang Shu

Department of Neurology, General Hospital of Armed Police Forces, China

Mrs. Yuan Min

State Key Laboratory of Space Medicine Fundamentals and Application, China Astronaut Research and Training Center, China

Prof. Wu Shiwen

Department of Neurology, General Hospital of Armed Police Forces, China

Prof. Jiang Shizhong

China Astronaut Research and Training Center, China

Dr. Ming Yuan

China Astronaut Research and Training Center, China

SIMULATED MICROGRAVITY INHIBITS THE CONTRACTILE RESPONSE OF RAT FEMORAL ARTERIES—ROLE OF ENDOTHELIAL AND VSM PI3K

Abstract

Objective: Many evidences suggest that vascular hyporesponsiveness contributes to microgravity-induced orthostatic intolerance, however, the mechanisms of impaired vascular contractility induced by microgravity or simulated microgravity remain incompletely understood. Phosphatidylinositol 3-kinase (PI3K) can regulate the vascular contractility by activating endothelial nitric oxide synthase (eNOS) and mediating vascular smooth muscle(VSM) contraction. In this study, We tested the role of endothelial and VSM PI3K in the decreased femoral artery contractile response to G protein-coupled receptor (GPCR) agonist induced by hindlimb unloading(HU) in rats.

Methods: Microgravity was simulated in Wistar rats by HU. After 30 days of HU treatment, femoral arteries from both HU and control rats were cut into 3-mm rings and mounted in tissue baths for the measurement of isometric contraction. In each ring, contractile responses were normalized as a percentage of the isotonic high K⁺-containing physiological saline solution (KPSS) response. We studied contractile responses of femoral arteries to the GPCR agonist phenylephrine (PE) in the presence or absence of the PI3K inhibitor LY294002(10⁻⁵ M) in endothelium-intact and-denuded vessel rings.

Results: HU decreased the PE-induced contractile response of femoral arteries in both endothelium-intact and -denuded rings, moreover, the contractile responses were higher in endothelium-denuded rings than that of endothelium-intact rings after 30d HU. In the endothelium-intact and -denuded rings, PI3K inhibitor LY294002 significantly inhibited the contractile response to PE, and decreased the contractile response sensitivity to PE in both Con and HU groups. However, compared with HU, only in endothelium-denuded rings, LY294002 had higher inhibitive effects to maximal contractile response to PE in Con group.

Conclusion: These data suggest that the role of VSM PI3K in modulating GPCR agonist-induced vascular contraction is impaired in rat femoral artery after 30d HU. (Funded by Advanced Space Medico-Engineering Research Project of China, Grant NO.2011SY5406018)