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THE UNFOLDED PROTEIN RESPONSE (UPR) REGULATES PHENOTYPE SWITCHING AND
PROLIFERATION OF VASCULAR SMOOTH MUSCLE CELLS OF CEREBRAL ARTERY UNDER
SIMULATED MICROGRAVITY**Abstract**

Exposure to microgravity results in vascular remodeling and cardiovascular deconditioning in astronauts, which poses a threat to spaceflight safety and the health in astronauts. To elucidate the mechanism for this condition, we investigated whether unfolded protein response (UPR) during simulated microgravity regulates phenotype switching and proliferation in. Hindlimb unweighting rats was used to simulate the pathophysiological effects of cardiovascular system in present study. We examined the biomarkers of endoplasmic reticulum and mitochondrial (UPRER and UPRmt), the mitochondrial oxidative stress, protein abundance of contractile and synthetic makers and structure of cerebral arteries. We found that the levels of CHOP, GRP78, PERK, eIF2 and ATF4, which are makers of UPRER are increased, while ER, SIRT3, FOXO3a, SOD2 and Catalase, which are makers of UPRmt, were decreased in cerebral arteries. Besides, the contractile markers -SMA, calponin, SM-MHC and caldesmon were decreased, while the synthetic makers OPN and elastin as well as PCNA were increased in cerebral VSMCs. These alterations were partially restored by mitochondria-targeted antioxidant MitoTempo. Therefore, simulated microgravity upregulates UPRER while inhibits UPRmt in cerebral VSMCs of simulated microgravity rats, and mitochondrial oxidative stress regulate switching and proliferation of cerebral VSMCs through modulating UPRER and UPRmt differently.