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THE EFFECT OF SHORT-TERM EXPOSURE TO SIMULATED MICROGRAVITY ON CIRCADIAN CLOCK GENE EXPRESSION IN MOUSE EMBRYONIC FIBROBLASTS

Abstract

Space exploration poses a critical challenge to humanity. Human beings are not evolved to cope with the harsh conditions of microgravity. Numerous physiological, cellular and genetic pathologies are caused by microgravity. With the onset of commercial spaceflight driven by space agencies and global corporations, the need to understand and mitigate these risks for the amateur space traveler is more important than ever.

The human circadian rhythm is subject to change due to variable environmental cues such as gravity changes and high cortisol levels. The environmental cues during spaceflight differ dramatically from those on Earth, and thus they impose many critical adaptive challenges, including those for the human circadian clock. Altered circadian rhythms have been observed across many organisms in space conditions, and circadian misalignment leads to adverse impacts on adaptation, performance, and health. Much is still to be elucidated behind the mechanisms of how our sleep circuitry is affected by the effects of gravitational stresses.

Mouse embryonic fibroblasts (MEF) are an example of peripheral oscillators that undergo circadian rhythm under the influence of the principal oscillator, the suprachiasmatic nucleus (SCN). Here, we conducted an in vitro study on isolated cultured MEF cells to determine how expression of core clock genes, integral to driving biological rhythms, change under short-term simulated microgravity conditions. We targeted the clock genes; Per1, Per2, and Bmal1, and investigated their responses to these conditions across 3 days. Within 24 hours, the sinusoidal diurnal rhythmic expression of cells exposed to the same simulated microgravity conditions was compared to that of control samples in 1G. Hydrocortisone was also injected into the cultured mediums to better simulate the high cortisol level environment.

Significant changes were observed across all targeted clock genes across 72 hours, reinforcing the theory that microgravity plays a role in how mechanical forces affect the clock gene expression in vitro, independent of the external light-dark cycle. Our understanding of how the space environment affects our circadian clock and sleep performance is critical to space medical management, ensuring the safety of future astronauts and missions.