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SCIENCE FOR BED REST: GENDER DIFFERENCES IN PHYSIOLOGICAL AND PATHOPHYSIOLOGICAL RESPONSES TO INACTIVITY AND EXERCISE AFTER BED REST

SHORT-TERM BED REST SHIFTS DNA METHYLATION AGE IN A SEX-SPECIFIC MANNER: IMPLICATIONS FOR MOBILITY MEDICINE

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Prolonged bed rest is a well-established human model of extreme physical inactivity, reproducing key features of accelerated aging, including muscle atrophy, metabolic dysregulation, low-grade inflammation, and oxidative stress (1,2). DNA methylation–based epigenetic clocks (DNAmAge) provide a sensitive tool to detect early biological aging responses to environmental stressors (3). DNAmAge was assessed in healthy subjects at baseline and after 21 days of bed rest, with paired analyses performed in the overall cohort and after sex stratification. In the whole sample, DNAmAge increased after bed rest compared with baseline. Sex-stratified analyses revealed a significant acceleration of DNAmAge in women, whereas no significant change was observed in men. The findings that will be presented strongly suggest that short-term bed rest triggers a sex-specific acceleration of epigenetic aging, with women showing greater sensitivity to muscle disuse. Sex- related differences in the biological response to unloading, including inflammatory, metabolic and mechanotransducive pathways, will be discussed as potential mechanisms underlying these epigenetic changes.

Keywords: *Bed rest, epigenetic aging, DNA methylation age, sex-specific effects, mobility medicine.*

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