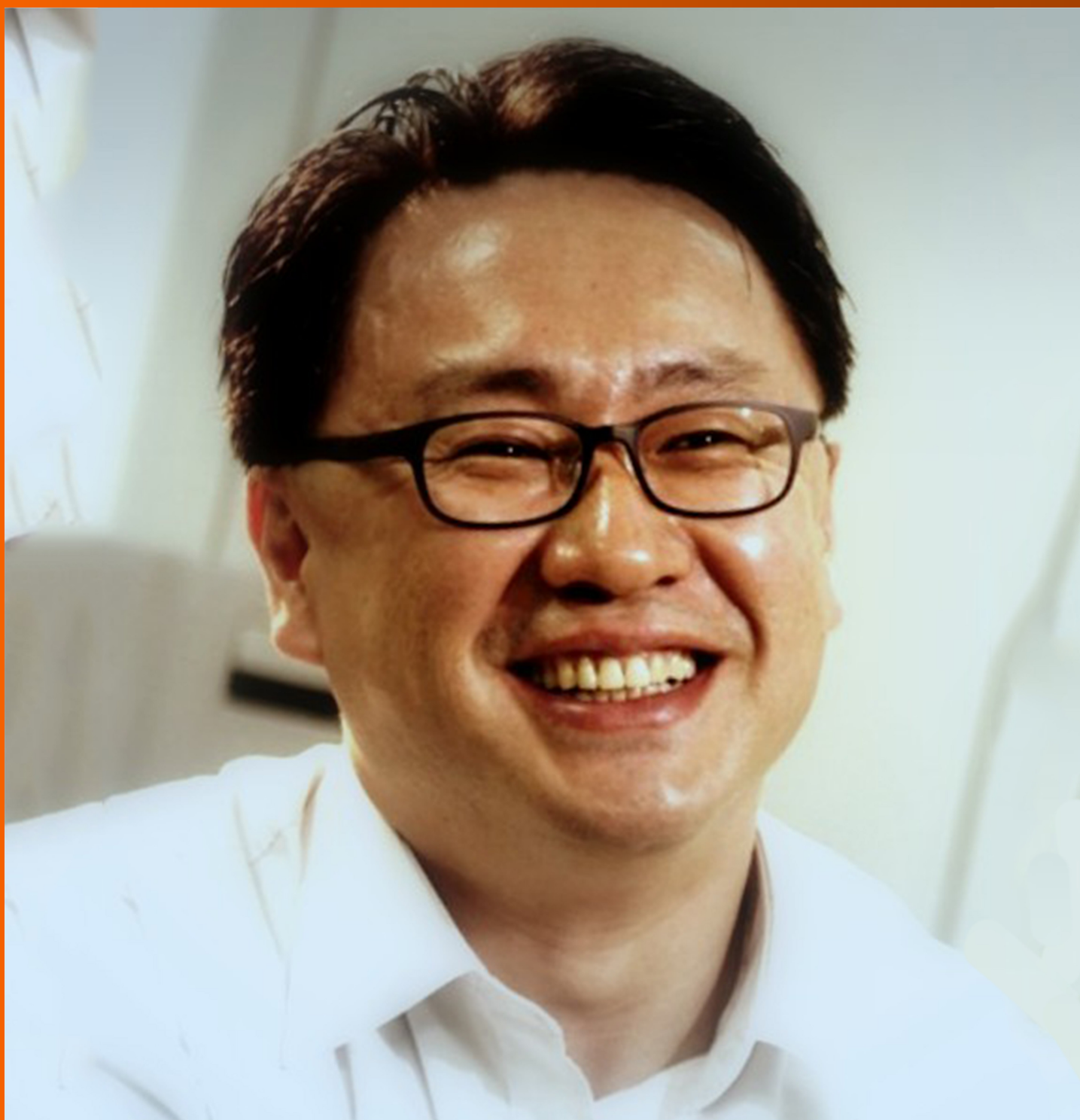


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- 1 On the immunological limitations of hibernation and synthetic torpor as a supporting technique for astronauts' radioprotection in deep space missions

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On the immunological limitations of hibernation and synthetic torpor as a supporting technique for astronauts' radioprotection in deep space missions

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Abstract

Although human hibernation has been introduced as an effective technique in space exploration, there are concerns regarding the intrinsic risks of the approach (*i.e.*, synthetic torpor) and other factors involved in this procedure. Besides concerns about the brain changes and the state of consciousness during hibernation, an "Achilles heel" of the hibernation is the negative impact of torpor on factors such as the number of circulating leukocytes, complement levels, response to lipopolysaccharides, phagocytotic capacity, cytokine production, lymphocyte proliferation, and antibody production. Moreover, increased virulence of bacteria in deep space can significantly increase the risk of infection. The increased infection risk during long-term space missions with the combined effects of radiation and microgravity affect the astronauts' immune system. With these additional immune system stressors, torpor-induced extra-immunosuppression can be potentially life threatening for astronauts.

Key words: Space radiation; Hibernation; Radioprotection; Synthetic torpor; Immunology

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Core tip: During long-term manned space missions beyond the protective shield of Earth's atmosphere and magnetic field (*e.g.*, a mission to Mars or a long stay on the Moon), while the combined effect of radiation and microgravity affects the astronauts' immune system, torpor-induced extra-immunosuppression can be potentially life

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threatening for astronauts.

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INTRODUCTION

Human hibernation has been introduced as an effective technique in space exploration. Given this consideration, synthetic torpor (*i.e.*, artificially inducing regulated, depressed metabolic states) has been introduced as a method for safely and practically transporting experimental animals to deep space^[1]. Studies show that some chemicals can induce hibernation-like state^[2]. However, in case of humans, there are concerns regarding the intrinsic risks of the artificial hibernation (synthetic torpor) and other factors involved in this procedure^[2]. These concerns include a wide variety of factors ranging from brain changes and the state of consciousness during hibernation^[2] to torpor-induced leukopenia^[3]. Recently, Tinganelli *et al*^[4] have addressed the potential protective role of synthetic torpor in deep space missions. Considering the potential role of synthetic torpor in sparing resources and reducing psychological problems as well as representing a countermeasure against cosmic radiation during a deep space mission, the authors have exposed rats to 3 Gy X-rays in normothermic conditions or synthetic torpor. The rodents' organs were collected four hours after exposure. Tinganelli *et al*^[4] also state that their study is the first experimental evaluation of toxicity and gene expression in laboratory animals irradiated with ionizing radiation under synthetic torpor. Based on the findings obtained in their study, the authors concluded that synthetic torpor can enhance radioresistance in non-hibernating animals and confirm the potential role of synthetic torpor in enhancing radioprotection in living organism during deep space missions. Although this well-structured paper can be considered a significant contribution to space biology, it does not consider the negative impact of hibernation on the human immune system^[3,5] and is the "Achilles heel" of this study. We have previously noted that the limitations of physical shielding and biological protection of astronauts against space radiation are among the key issues that should be properly addressed before a deep space mission is initiated^[6-8]. However, the negative impact of torpor on factors such as the number of circulating leukocytes, complement levels, response to lipopolysaccharides, phagocytotic capacity, cytokine production, lymphocyte proliferation, and antibody production have been already addressed. Moreover, some studies have shown that the virulence of bacteria in deep space can be significantly increased. During long-term space missions, the combined effect of radiation and microgravity affects the astronauts' immune system^[9]. Factors such as immunosuppression, increased bacterial virulence, and presence of particles in suspension are involved in increased risk of infections in space^[10]. It has also been reported that even in the absence of immune dysregulation, factors such as increased microbial virulence during spaceflight^[11], can increase the risk of infectious diseases in space crew^[12].

Given this consideration, as shown in **Figure 1**, torpor can lead to immune system dysregulation and the combination of dysregulated immune system and increased bacterial virulence can be potentially life-threatening for astronauts.

CONCLUSION

Moreover, the experimental exposure duration in the study conducted by Tinganelli *et al*^[4], is an acute exposure. Extended duration spaceflight will involve a chronic exposure. The biological repair processes for both should have been addressed. Exposure to x-rays is not representative of a deep space environment. Galactic cosmic radiation and solar particle events source terms contain protons, light ions, and high charge and energy particles that produce different biological effects than an acute x-ray exposure^[13,14]. Synthetic Torpor is only a single variable associated with a long-term mission. The effects of microgravity, spacecraft atmosphere, and spacecraft

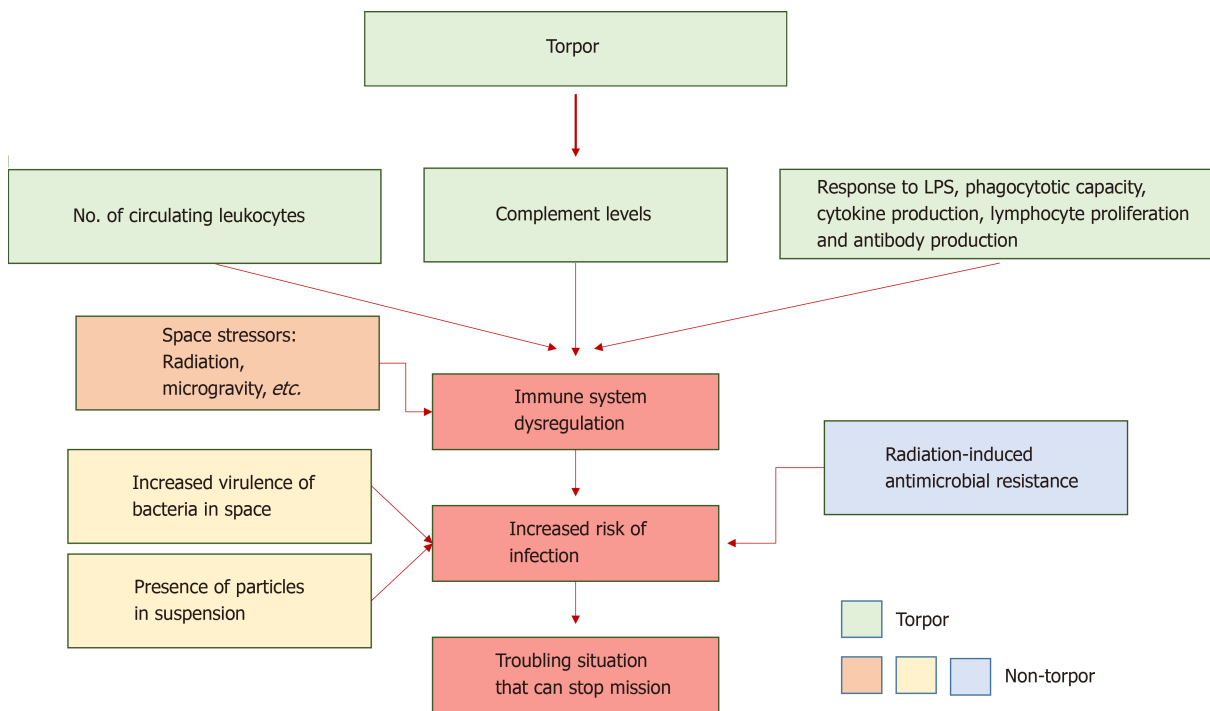


Figure 1 Hibernation (synthetic torpor) can lead to immune system dysregulation and the combination of dysregulated immune system and other factors such as increased bacterial virulence, presence of particles in suspension and radiation-induced antimicrobial resistance can be potentially life-threatening for astronauts. LPS: Lipopolysaccharides.

environment should also be addressed. Given these considerations, during long-term manned space missions beyond the protective shield of Earth's atmosphere and magnetic field (e.g., a mission to Mars or a long stay on the Moon), while the combined effect of radiation and microgravity affects the astronauts' immune system, torpor-induced extra-immunosuppression can be potentially life threatening for astronauts.

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