The Innovation

## **Back to Earth**

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Received: February 23, 2023; Accepted: April 20, 2023; Published Online: April 23, 2023; https://doi.org/10.1016/j.xinn.2023.100429

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Citation: Cerri M., Bereiter-Hahn J., Heldmaier G., et al., (2023). Back to Earth. The Innovation 4(3), 100429.

On behalf of the Topical Team Hibernation of the European Space Agency, we would like to provide some comments on the recently published article "Primate preoptic neurons drive hypothermia and cold defense" by Zhang and colleagues.<sup>1</sup>

We read the manuscript with high interest and acknowledge that the authors were able to conduct their experiment on non-human primates, a challenging model for both practical and ethical reasons, hereby striving to expand the validity of many experiments in rodents. Interestingly, the authors report that chemogenetic activation of excitatory neurons within the preoptic area induces a form of hypothermia, while simultaneously, the body is trying to defend its body temperature by increasing locomotor activity, shivering, heart rate, and activating cellular metabolism. Commonly, this is not observed in rodents and poses the question of whether primates may have a more complex brain network controlling metabolic rate. This is most definitely an area of investigation worth pursuing since the metabolic rate was not measured but, certainly, was affected and probably increased as well: an effect that goes in the opposite direction than torpor and that will have to be addressed. The authors expressly referred to torpor as a space-oriented technology in the graphical abstract, and on that, we recommend using caution: a very modest drop in body temperature accompanied by the activation of cold defense mechanism seems not to mimic torpor in an adequate way. In fact, natural torpor proves to be an endogenous metabolic reduction followed by a regulated lowering of body temperature, as it has also been reported for multiple non-human primates.<sup>2</sup>

We are excited to see hibernation research addressed now across the globe, which relates well to the expectation that enabling hibernation can become a game changer for many medical conditions, as well as space missions. We may point out and encourage this scientific community to work on this topic to foster the exchange and share knowledge. It might be an added value to the readers of this journal and this article explicitly that a European Space Agency Topical Team has been addressing hibernation since 2014, providing a scientific forum to discuss and exchange scientific and engineering advances related to hibernation research, including papers describing possible engineering approaches for a spaceship with torpor technology.<sup>3</sup>

Indeed, developing a functioning technology for torpor induction in humans would be a tremendous achievement for humanity.

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