Sweet dreams (are made of this)

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In the field of hibernation science, the arctic ground squirrel remains a fascinating enigma. Whereas virtually every species of hibernating mammal spends the majority of its winters in microhabitats that occupy temperatures well above the freezing point (0°C), the permafrost-laden regions of Siberia, Canada, and Alaska in which the arctic ground squirrel resides prevent it from burrowing to depths of more than a meter. As a result, during its 7-month hibernation season, the arctic ground squirrel is often subjected to ambient temperatures approaching −25°C, resulting in body temperatures as low as −2.9°C.^{1,2} Even though these animals often achieve core temperatures well below the natural freezing point of bodily fluids (−0.6°C), however, the blood and tissues of the arctic ground squirrel are able to defy the inhospitable environment from which they have evolved through a unique process known as “supercooling.” Although the exact mechanism of supercooling remains a mystery, the discovery of the phenomenon nearly 30 years ago serves as yet another example of how the natural world continues to challenge our understanding of what is physiologically possible.

In this issue of the *Journal*, Jiang and colleagues³ provide a surprisingly elegant study highlighting the potential neuroprotective effects of a previously unidentified, 40-kd protein derived from hibernating chipmunks. After injecting the protein into preconditioned Sprague-Dawley rats that were subsequently exposed to 60 minutes of deep hypothermic circulatory arrest, Jiang and colleagues³ found that the preconditioned rat group showed an attenuated inflammatory response that resulted in improved gross neurologic function and the preservation of a more favorable neuronal histologic status than seen in nonpreconditioned control animals. They speculate that this specific protein, and perhaps others like it, could be neuroprotective across species through modulation of sirtuin and brain-derived neurotrophic factor pathways.

Historically, it is important to note that the use of nonspecific pharmacologic adjuncts, such as steroids, barbiturates, and various other anesthetic agents, has not been shown to

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Central Message

Protective mechanisms during deep hypothermic circulatory arrest may be developed from hibernation science.

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be efficacious for the purpose of cerebral protection during periods of deep hypothermic circulatory arrest.⁴ Although the exact biochemical structure of the special protein isolated within this study is yet to be determined, the protein may very well offer a mechanism for controllable supercooling physiology, which is why the results presented in this study are so promising. To this end, it would be interesting to observe whether the neuroprotective effect of this protein is present in cases of moderate hypothermia, or even normothermia, and whether this protein could be used in additional clinical applications that are devoid of deep hypothermic circulatory arrest, such as in the postresuscitation management of cardiac arrest or during routine cerebrovascular or neurosurgical procedures. Indeed, the 2017 American Academy of Neurology practice guidelines to reduce brain injury after cardiopulmonary resuscitation now include the addition of moderate hypothermia (32°C–34°C) within the first 24 hours after cardiac arrest for improved neurologic outcome and survival.⁵ Finally, a critical question that has not yet been addressed is whether this protein, or others like it, would be able to transcend the taxonomic divide and exert protective effects in human subjects. For now, and for the sake of our patients, we in the field of cardiothoracic surgery should push forward with a renewed optimism as we continue to “dream” of our own “supercool solution” for cerebral protection.

References

1. Jabr F. What the supercool arctic ground squirrel teaches us about the brain's resilience. *Scientific American*. Available at: <https://www.scientificamerican.com/article/arctic-ground-squirrel-brain/>. Accessed February 25, 2018.

2. Hill RW, Wyse GA, Anderson M. *Animal Physiology*. 2nd ed. Sunderland (MA): Sinauer Associates; 2008:262-7.
3. Jiang X, Gu T, Liu Y, Wang C, Shi E, Zhang G, et al. Protection of the rat brain from hypothermic circulatory arrest injury by a chipmunk protein. *J Thorac Cardiovasc Surg*. 2018;156:525-36.
4. Hiratzka LF, Bakris GL, Beckman JA, Bersin RM, Carr VF, Casey DE Jr, et al; American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines; American Association for Thoracic Surgery; American College of Radiology; American Stroke Association; Society of Cardiovascular Anesthesiologists; Society for Cardiovascular Angiography and Interventions; Society of Interventional Radiology; Society of Thoracic Surgeons; Society for Vascular Medicine. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. *Circulation*. 2010;121:e266-369. Erratum in: *Circulation*. 2010;122:e410.
5. Geocadin RG, Wijdicks E, Armstrong MJ, Damian M, Mayer SA, Ornato JP, et al. American Academy of Neurology practice guideline: reducing brain injury after cardiopulmonary resuscitation. *Neurology*. 2017;88:2141-9.