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HHMI Undergraduate Researcher Turns Up the Heat on Hibernation

If doctors could put people in hibernation and pull them out at will, scientists think they could minimize damage from strokes, help recipients' bodies accept transplanted organs, perhaps even enable astronauts to travel in suspended animation until reaching distant destinations. But up to now, researchers have not understood the molecular mechanism controlling hibernation-like states.

An HHMI-supported undergraduate's research, published in the January 2006 *Journal of Neuroscience*, describes for the first time the specific mechanism mice use to enter torpor, a hibernation-like state that enables them to survive periods of fasting during cool weather. Ross Smith is a co-author of the paper from researchers at Williams College in Williamstown, Massachusetts, and Emory University in Atlanta. Smith conducted the research as an undergraduate in Williams' biologist Steven J. Swoap's laboratory, as part of the college's HHMI-supported undergraduate science education program. A June 2005 graduate of Williams, Smith is now a technician in Gokhan Hotamisligil's laboratory at Harvard University.

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— Steven J. Swoap

We were trying to figure out what signaling pathway was involved in allowing mice to go in and out of torpor, explained Smith. Working with Swoap, he helped show that torpor is controlled by the same system that controls fight-or-flight responses and further, that it involves the stimulation of receptors for epinephrine (adrenaline) and norepinephrine, called adrenergic receptors, most likely those found in fat stores.

The work on torpor began in Swoap's lab when he observed that knock-out mice that cannot synthesize the neurotransmitters norepinephrine or epinephrine do not enter torpor when they fast.

In 2004, Smith joined Swoap's research team as an HHMI summer research fellow. Williams College, like more than 100 colleges and universities throughout the United States, has an undergraduate science education grant from HHMI to encourage and support undergraduate research opportunities.

Swoap said that work by students like Smith is critical to the pace of science at an undergraduate campus like Williams. The undergraduates are the ones that spark the ideas and generate the enthusiasm. They drive the research, the biology professor said.

Smith showed that replacement of epinephrine or adrenaline to the peripheral nervous system, and not to the brain, determines whether an animal enters torpor. We could replace the neurotransmitters in the brain and still not get torpor in these mice, Smith said. Torpor was restored when the neurotransmitters were made available at nerve-endings in the periphery.

The undergraduate also found that the ability to enter torpor could be restored in the knock-out mice through the use of a synthetic amino acid that enabled production of the two neurotransmitters. This was an extremely important control, Swoap said. Smith also generated data showing that low body temperatures achieved during torpor are maintained by the animal and are not just due to heat loss.

Up to now, most research on torpor focused on which animals enter the state. Swoap predicted his team's findings will move the field in a new direction. It's going to draw more basic researchers into studying the mechanism, he said.

Some scientists are already thinking about the human applications of torpor research, Swoap added. It would be extremely beneficial, for example, for a person to have a low metabolic rate during surgery to avoid injury, he said. The ability to pull people in and out of a hibernation-like state at will, if it can be accomplished, is decades away, he said, but, this is a first step in that direction..