Summer heat too hot for you? What is comfortable?

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Extreme heat or cold is not only uncomfortable, it can be deadly—causing proteins to unravel and malfunction. For many years now, scientists have understood the molecular mechanisms that enable animals to sense dangerous temperatures; such as extremely high temperatures that directly trigger heat sensor proteins known as TRP channels. However, much more poorly understood is how animals sense very small temperature differences in the comfortable range, and choose their favorite temperature.

Reporting this week at *Nature Neuroscience,* Johns Hopkins researchers now have discovered that the fruit fly uses TRPA1 to sense single degree changes in the comfortable range. However, rather than sensing temperature changes directly, TRPA1 functions in the last step of a multistep process that uses many of the same proteins that function in vision. Just as the early events involved in vision allow animals to adapt to different light intensities, the multistep process involved in temperature detection potentially allows animals to adapt to different temperatures in the comfortable range as well.

"It's an exciting discovery, yet in a lot of ways it just makes a lot of sense," says Craig Montell, Ph.D., a professor of biological chemistry and member of Johns Hopkins' new Center for Sensory Biology. "You clearly don't want to hang around or adapt to a temperature that could kill you, but on the other hand, if you can't find your favorite temperature, it is OK to adapt to another comfortable temperature."

Montell and his team use fruit flies as their experimental model because it is easy to perform genetic manipulations on these animals. Temperatures colder than 16 degrees Celsius (61 degrees Fahrenheit) or warmer than 26 degrees C (79 degrees F) are known to trigger an avoidance response. Fruit fly maggots (larvae), explains Montell, prefer 18 degrees C (64 degrees F), but are comfortable at temperatures ranging from 18 to 24 degrees C (64 to 75 degrees F).

To first figure out if the larvae could even sense small temperature differences in the 18 to 24 degree "comfort zone," Montell's team set up a preference test that consisted of a plastic plate where one half of the plate was kept at 18 degrees and the other half at a different temperature, from 19 to 24 degrees. After 15 minutes, they counted the number of larvae on each side of the plate.

"It turns out these larvae can discriminate one degree differences—they prefer 18 over 19 degrees" says Montell. "The question then was: How do they do this?"

Since TRP channels are known to open in response to changes in temperature, Montell's team then tested flies containing mutations in 12 fruit fly TRP genes to see if any were required for the ability to sense temperature changes within the comfort zone.

Eleven of the 12 TRP mutants still preferred 18 degrees to other temperatures in this range. Only the TRPA1 mutant larvae showed no temperature preference, suggesting to the researchers that only TRPA1 is required for comfort zone temperature sensing.

The known "thermoTRPs" all open directly in response to changes in temperature. TRP proteins also are involved in other types of sensory biology, including vision, explains Montell. But rather than being directly triggered by light, a different light sensor molecule activates the TRP vision protein indirectly. Since TRPA1 is not turned on by changes in temperature in the comfortable range, Montell's team reasoned that perhaps, in this range, TRPA1 might be triggered indirectly through a series of steps similar to those that function in vision.

The team then tested flies with mutations disrupting proteins known to work with TRP proteins required for fly vision and found that they, too, were unable to discern temperature differences in the 18 to 24 C range.

Thus, Montell and co-workers have found a new way that TRP channels function in thermosensation, and this "is quite reminiscent of how we detect light."

"We think it's important for adaptation; if a fly finds itself at 34 degrees (93 degrees F), it should never try to adapt to that temperature, because it will die," says Montell. "But flies living at 22 degrees could adapt to this environment because, while this temperature isn't their optimal choice, it still isn't deleterious." The multistep vision-like strategy for sensing changes in temperature could also be well suited for amplifying very small differences in temperature, such as 18 and 19 degrees C. This strategy could allow animals to respond to one degree changes that might otherwise not be possible through a process involving just one protein.

The team's work raises the possibility that similar multistep processes may allow mammals to sense small changes in internal body temperature.

Source: Johns Hopkins Medical Institutions