New role of TRPV1 receptors in locomotor activity regulation

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Research by a Barrow Neurological Institute scientist on the thermoregulatory effects of a receptor more commonly studied for its role in pain is the cover story in the Feb. 2 issue of the *Journal of Neuroscience*. The research was conducted by an international team led by Andrej Romanovsky, MD, PhD, Director of the Systemic Inflammation Laboratory (FeverLab), at Barrow, which is a part of St. Joseph's Hospital and Medical Center.

The featured research discovers a new role of TRPV1 (transient receptor potential vanilloid-1) receptors in the regulation of locomotor activity, or the movement from place to place. These receptors are widely known for their ability to be activated by capsaicin, the compound responsible for the hotness in chili peppers. TRPV1 receptors are located on sensory neural cells throughout the body and can also be activated by high temperature, acidity and other stimuli. Because of their responsiveness to such diverse factors, TRPV1 receptors are thought to serve as sensory integrators of the body's internal and external environments.

The study by Dr. Romanovsky's team was conducted in mice genetically deficient in the TRPV1 receptor. While studying how TRPV1-deficient mice regulate their body temperature, the researchers made an unexpected observation that these animals, when young, exhibit a much higher locomotor activity than control mice. Even during the light phase of the day (when mice are typically inactive), TRPV1-deficient animals were moving in the experimental chamber with an average speed of nearly one yard per minute – faster than the speed of control mice at the

peak of their daily activity.

The researchers then conducted experiments with drugs that block or activate TRPV1 receptors and looked at how these drugs affect general motor activity. These pharmacological experiments confirmed that TRPV1 receptors located outside the brain send signals to the brain to suppress locomotion.

"We all know that the body's propensity for physical activity changes based on numerous factors," explains Dr. Romanovsky. "For example, we do not want to exercise after having a large meal, when it is hot outside, or when we are tired, nauseated or in pain. We all know people who seem to be naturally inactive, as well as people who are more active than others. Our study suggests that the TRPV1 receptors may send signals that play a role in regulating the extent of locomotor activity."

This discovery, which is part of St. Joseph's trauma research, could have wide implications in determining whether TRPV1 receptors are involved in any of several motor and behavioral disorders, as well as the regulation of body weight. Future studies could potentially look at whether TRPV1-activating drugs could be used to decrease the propensity for exercise when people are confined to a limited space for prolonged time periods, as during spaceflight missions, or whether TRPV1-suppressing drugs could be used to boost levels of physical performance and endurance.

Provided by St. Joseph's Hospital and Medical Center