When do newborns first feel cold?

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Cold sensing neural circuits in newborn mice take around two weeks to become fully active, according to a new study.

The finding adds to understanding of the cold sensing protein TRPM8 (pronounced trip-em-ate), first identified in a *Nature* paper in 2002 by David McKemy of the University of Southern California.

McKemy's latest study, published online by *Neuroscience*, shows that the cold sensing circuit starts to develop in utero but does not mature until well after birth.

"About three or four days before the animal is born, the protein is expressed. However, the axons of these nerves going into the spinal cord are not fully formed until probably two weeks after birth," McKemy said.

The delay in development of cold sensing is plausible, McKemy added.

"In the womb, when would we ever feel cold?"

By contrast, mice are born with a keen sense of smell, which they need to breast feed successfully.

Direct study of the cold sensing protein TRPM8 in humans is not yet possible. While sensory development differs in mice and humans - mice are born blind, for example - the study suggests a possible biological basis for findings of altered cold sensitivity in children.

In a 2008 study of temperature sensation by the Institute of Child Health at University College London, researchers found that 11-year-old children born prematurely were less sensitive to temperature than those born at term.

"This is consistent with our observations that the circuitry is not fully developed until after birth, thus anything that disrupts this formation at this important stage could have long term effects," McKemy noted.

"There are other reports that injury and inflammation in rodent models that occur during the (prenatal) period lead to altered temperature sensitivity as well as altered neural circuits."

The USC researchers tracked development of cold sensing through mice genetically engineered to express a green fluorescent protein whenever TRPM8 was produced.

TRPM8 is one in a class of proteins known as ion channels. Their purpose is to "turn on the cell" when they receive a stimulus. TRPM8 senses both painful cold and the soothing cold of menthol-based creams.

How one protein can convey both sensations is unknown. McKemy speculated that neurons differ in their internal architecture, with each tuned to accept either painful or pleasant cold signals from TRPM8.

One goal of TRPM8 research is to understand the molecular mechanisms of sensation, in the hope of developing better drugs for relief of chronic pain states, such as the extreme sensitivity to cold experienced by some diabetes patients.

"If you want to understand conditions like cold allodynia, which is cold pain, you need to find exactly what are the targets," McKemy said.

"If we understand the basic nuts and bolts of the molecules and neurons and how they detect pain normally," McKemy said, "then perhaps we can figure out why we detect pain when we shouldn't."

Provided by University of Southern California