Anesthetic approach stops pain without affecting motor function

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One of the holy grails of local anesthesia is the ability to achieve a long-lasting nerve block that eliminates pain sensation while not affecting motor function. Now, researchers at Children's Hospital Boston have discovered an anesthetic approach that seems to do just that. If it proves to work in humans as well as it did in rats, it could be useful in a variety of medical applications, providing, for example, a local anesthetic for childbirth that would block pain without interfering with the mother's ability to push, or for musculoskeletal disorders in which it is important to maintain mobility.

The discovery was reported in the online Early Edition of the Proceedings of the National Academy of Sciences during the week of February 1.

The researchers, led by Daniel Kohane, MD, PhD, of the Division of Critical Care Medicine at Children's, originally sought only to find an agent that would prolong the anesthetics' effects. They focused on surfactants, a subclass of so-called "chemical permeability enhancers" that enable drugs to spread more easily throughout a tissue.

In testing three kinds of surfactant along with the anesthetics QX-314 and QX-222 (both derivatives of lidocaine), they found that this approach did prolong the sensory block in rats' sciatic nerves, for up to 7 hours or more depending on the surfactant, but didn't prolong motor impairment; in some cases the motor block was absent or of very short duration. In the rats, this meant they were able to tolerate having their

paws on a hot plate for long periods, yet still able to balance and bear weight on their legs.

"This was a surprise finding," says Kohane, who also directs the Laboratory for Biomaterials and Drug Delivery (LBDD) at Children's. "What we've discovered really is a new approach; the question now is to figure out the mechanism by which it works and look at the effects of other chemical permeability enhancers."

Kohane speculates that surfactant made the anesthetic better able to penetrate sensory nerves, which have little or none of the fatty coating known as myelin, whereas in motor neurons, which have abundant myelin, the active drug gets trapped in the myelin, never entering the nerve itself.

The lab's next steps will be to explore the effects of different permeability enhancers and examine their safety, since at high doses the drug combination could potentially be toxic to the nerves. The eventual plan is to test the approach in larger animals.

A parallel approach to achieving a pain-specific nerve block was proposed in 2007 by Clifford Woolf, MD, PhD, recently appointed director of the Children's Hospital Boston Program in Neurobiology. Woolf's team combined QXT-314 with capsaicin, which opens cellular gates that are only present in sensory neurons, and achieved pain-specific blocks in rats lasting 2 hours or more.

More information: Sagie I and Kohane D. Prolonged sensory-selective nerve blockade. PNAS online early edition, week of February 1, 2010.

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