News from NIH: pain management

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As noted by the recent Institute of Medicine report, *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research*, chronic pain affects about 116 million American adults and costs the nation up to \$635 billion each year in healthcare-related costs and lost productivity [1]. As such, research into understanding pain and improving pain management spans the missions of most of the National Institutes of Health (NIH) Institutes and Centers. This column will highlight just a few of the many NIH activities related to pain management. A trans-NIH Pain Consortium initiative is described along with two studies. One study highlights research to test new and improved treatments to control cancer pain. Another study highlights research to advance the field of pain assessment. These studies are just a small sampling of the kinds of translational pain research conducted at NIH but hopefully they serve to illustrate some exciting research directions and the breadth of pain management research at the NIH.

NIH PAIN CONSORTIUM

The NIH Pain Consortium “was established to enhance pain research and promote collaboration among researchers across the many NIH Institutes and Centers that have programs and activities addressing pain” (<http://painconsortium.nih.gov/index.html>). As part of its goals, the NIH Pain Consortium is in the process of establishing “Centers of Excellence for Pain Education” at medical, dental, nursing, and pharmacy schools across the nation, in an effort to give health care professionals a solid understanding of pain as part of their basic education, with the aim of improving pain treatment while reducing the risk of prescription opioid abuse. These Centers will establish curricula on pain which will be used in courses at these Centers, and made available on the NIH Pain Consortium’s website to encourage the adoption of these curricula at other academic institutions. If you would like to join the NIH Pain News listserv, go to <https://list.nih.gov/archives/nihpainconsortiumnews.html> and click the “Join the list” option.

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REDUCING CANCER PAIN

Achieving adequate pain relief without significant physiological, cognitive, and other behavioral side effects is a major problem in advanced cancer. NIH research commitments include pain research, new drug development, and translational research (translating research findings into patient treatment). An example of a research program combining these three NIH goals is the use of resiniferatoxin (RTX) for improved control of pain. This research is a collaboration between the National Institute of Dental and Craniofacial Research, National Institute of Neurological Disorders and Stroke, and the NIH Clinical Center. RTX is derived from a compound occurring in a Moroccan cactus-like plant. RTX is a potent analog of capsaicin, the active ingredient in hot pepper. RTX vigorously activates a calcium–sodium ion channel called TRPV1. Previous experiments have shown that this overactivation of TRPV1 permanently inactivates a subpopulation of pain-sensing neurons. Preclinical studies in rats and treatment of dogs with cancer or severe arthritis pain have shown long-lasting pain relief after a single intrathecal injection. Except for some aspects of heat perception, all other sensory modalities (proprioception, touch, and vibration) were preserved and functional abilities improved. There were no adverse behavioral changes [2].

Despite increasing focus on the use of analgesics and delivery systems, control of cancer pain remains inadequate. The current study is designed to test the safety of intrathecal injection of RTX in cancer patients whose pain is not controlled by standard analgesic treatment. The goal is to try to duplicate the safety and pain-relieving results of the animal studies in humans. If the treatment proves to be safe and effective, testing RTX to relieve other types of pain can be considered.

ABDOMINAL PAIN ASSESSMENT

Clinicians and clinical and translational researchers have an especially difficult task to assess pain and document changes in pain. Pain, for both adults and children, is a subjective, self-reported phenomenon. Clinically, the 0 (meaning no pain) to 10 (the worst possible pain) Likert scale is most commonly used to measure the intensity of pain. The location of pain is documented at the discretion of the healthcare provider. Most studies show that clinicians underestimate pain intensity in their patients [3]. From a clinical research perspective, the short-form McGill Pain Questionnaire [4] is the current research standard to assess pain and utilizes a subjective visual analog scale; however, it does not have an objective component. Objective pain correlates include physiologic measures such as heart rate, heart rate variability, blood pressure, skin temperature, and pupil dilation.

In the USA, up to 20% of individuals suffer from chronic abdominal pain of unknown origin [5]. As with many pain conditions, there is a need for research to improve characterization of pain phenotypes through real-time assessment of both subjective (patient-reported) and objective (clinical observations) pain assessment. One example of the kind of research needed is being conducted in the intramural research program of the National Institute of Nursing Research by Dr. Wendy Henderson collaboratively with the NIH Clinical Center, the National Institute of Diabetes and Digestive and Kidney Diseases, the National Institute of Allergy and Infectious Diseases, and the University of Washington School of Nursing. They developed the Gastrointestinal Pain Pointer (GIPP) for electronic capture of subjective and objective gastrointestinal pain [6]. The GIPP is an electronic medium that allows researchers to capture both the patients' current pain in terms of location, intensity, and descriptors of painful symptom, but also physiologic correlates of pain including blood pressure and heart rate (binary/executable format provided by Psychology Software Tools, Inc.). The patient uses a graphical interface to choose his/her gender and body type, record the location and intensity of the gastrointestinal

distress, and then selects descriptive words for the gastrointestinal discomfort. The clinician simultaneously captures heart rate and blood pressure either manually or through the assistance of an electronic device. It takes approximately 1–2 min to administer. The data are captured and explored together, time stamped into an electronic data storage file for analysis, and may also include an alert system to prompt the user to complete subsequent objective and subjective measurements.

Development and testing of novel electronic assessment approaches, such as the GIPP, hold “promise for advancing the science of managing clinical pain” [7]. Research is needed to continue to develop assessment approaches that are easy to use, time- and cost-efficient, and provide clinicians and researcher to a more integrated resource for pain assessment that includes location, intensity, quality, and physiologic parameters. As noted, the examples highlighted above are just a few examples of the broad pain management research agenda at the NIH that includes advances in education, assessment, and treatment.

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