

## Pain Measurement and Beecher's Challenge

### 50 Years Later

"THERE is a very great and understandable desire on the part of many people for objective indicators of subjective phenomena . . . . It would be wonderfully helpful to have objective signs of subjective change; but it seems unlikely that many such aids will be readily available in any precise way for years to come."<sup>1</sup>

"A relationship between galvanic skin response and intensity of pain has been reported, but it was also found on repetition of the pains that they had lost their effectiveness to produce the galvanic skin response. It is believed that the galvanic skin response is an indicator of the threat contained in the procedure and is thus only indirectly related to pain intensity."<sup>1</sup>

Fifty years ago, Beecher<sup>1</sup> reviewed challenges in use of subjective responses in clinical practice and clinical research. He noted the strong bias among clinicians and clinical researchers towards finding "objective" measures of pain, and he cited some problems with pain measurement based on indices of sympathetic activation. In this editorial, we discuss a proposed pain measure by Hullett *et al.*<sup>2</sup> in this issue of ANESTHESIOLOGY, and we briefly consider the promise of future "objective" pain measures based on brain imaging or brain electrical recording.

Pioneers in pain management and palliative care from the 1940s to the 1970s emphasized interrelationships among nociception, pain experience, impairment, disability, and suffering.<sup>3-5</sup> Different measures are required to assay the sensory, emotional, behavioral, spiritual-existential, and social dimensions of pain.<sup>5</sup> Behavioral measures are widely used for infants and nonverbal subjects of all ages. They are sensitive to fear or anxiety as well as pain, and they may underrate pain intensity relative to self-report measures in patients with persistent pain.<sup>6</sup>

Hullett *et al.*<sup>2</sup> attempt to validate a new pain measure for children, namely fluctuations in skin conductance per second. There are several strengths to this paper. The use of receiver operating characteristics curves and the presentation of statistics such as positive predictive value, are particularly helpful and allow a better interpretation than would be provided solely by calculation

of sensitivity and specificity. Receiver operating characteristics curve analysis should be used more widely. The authors compared fluctuations in skin conductance to age-appropriate standardized behavioral and self-report pain measures. They made a reasonable attempt to control for the effects of anxiety and body temperature, despite the rapidly changing physiologic circumstances during recovering from general anesthesia. The sample size is suitably large.

Nevertheless, the results should give considerable caution regarding clinical use of skin conductance fluctuations as a clinical measure of pain in children. As noted by the authors, the measure shows relatively poor specificity and poor positive predictive value (35.5% for the whole sample and only 28.1% for the 4-7 yr olds). If used as a criterion for analgesic administration, almost two thirds of the total sample would be unnecessarily treated.

Many clinicians and researchers have a bias towards physiologic measures and against self-report, believing that the former measures are more scientific, and more reliable. This bias is often unjustified; machines can lead us into error just as verbal reports can. Surely we would not want to have a patient receive medication because the machine said so, even if they are telling us that they are not in pain. Equipment costs, training costs, and machine failures need to be considered before implementation of any new clinical measurement technology.

Skin conductance can be responsive to many factors unrelated to pain. Sympathetic activation is not a unitary process, and different triggers may activate different components of the sympathetic nervous system. There is a potential for harm in basing clinical decisions on a false-positive pain measure. Consider a hypothetical infant or nonverbal child with well-controlled postoperative pain, but with slowly progressive internal bleeding or septicemia. If early hypovolemic or distributive shock led to sympathetic activation and high scores for fluctuations in skin conductance, then it could be a serious mistake to treat the infant or child with additional analgesics based on these scores.

We agree with the authors that more work needs to be done before this novel measure can be endorsed as a clinical pain measure in children. There are many natural patient groups that one should study to establish that this physiologic measure is specific for nociception/pain rather a range of other physiologic, pharmacological, or psychological processes in children. The authors suggest that fluctuations in skin conductance could be used in children with developmental delays. This measure has not been studied in this population, and these children

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may be particularly vulnerable to physiologic perturbations and to adverse events from overmedication.

In appendix 1, we offer a provisional list of criteria that should be met for a candidate physiologic measure of pain intensity. In appendix 2, we list some nonpainful clinical conditions that may influence measurements based on sympathetic activity. Study of some of these patient groups will help evaluate the sensitivity, specificity, and positive and negative predictive value of proposed physiologic pain measures.

Brain imaging is a very active area of pain research that might afford the possibility of improved pain measurement in the future.<sup>7-12</sup> Methods of imaging such as positron-emission tomography, single-photon emission computed tomography, near infrared spectroscopy, and functional magnetic resonance imaging detect signals reflecting regional brain glucose use, blood flow, or regional ratios of oxy- to deoxy- hemoglobin, respectively, as surrogate measures of regional neuronal metabolic activity. Other measures, including magnetic or electric source potential mapping or processed electroencephalographic measures are used as surrogate measures of regional brain electrical activity. Positron-emission tomography and single-photon emission computed tomography require exposure to radioisotopes, and functional magnetic resonance imaging requires prolonged immobility for paradigms with repetitive on-off stimuli to permit signal averaging.

Imaging and electrophysiologic studies have produced surprising findings in patients with several types of chronic pain. Sensory and emotional aspects of pain may show distinct signatures in different patient groups. Along with guiding clinical pain assessment and treatment and drug development, it is conceivable that imaging studies could be used in the future for disability determinations in the workplace, for awards for pain and suffering in lawsuits, or for confirmation of psychiatric diagnoses.<sup>11</sup> Currently, brain imaging techniques are neither sufficiently practical to fit criterion 1 in appendix 1, nor have they been fully evaluated from the viewpoint of defining sensitivity, specificity, and positive and negative predictive value under a range of clinical conditions listed in appendix 2.

In summary, pain assessment and measurement remain imperfectly solved problems for clinicians and researchers. It remains a clinical art to combine patients' reports, behavioral observation, and physiologic measurement with the history, physical exam, laboratory information, and overall clinical context in guiding clinical judgments and therapeutic interventions. In considering the state of our science and clinical practice now 50 yr after Beecher's summary of the problem of measurement of subjective responses, it remains difficult to predict whether advances in brain imaging and other technologies will make assessment of pain and suffering more science than art 50 yr from now.

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## Appendix 1: Some Proposed Criteria for Ideal Physiologic Measures of Pain Intensity

1. Low cost, portable, reliable, easy to use, low risk.
2. Strong agreement with self-report pain scales in articulate subjects ages 4 yr and older. By strong agreement, we mean high sensitivity, high specificity, and excellent positive and negative predictive value over the full range from mild to severe pain intensities. This should include strong agreement for patients/subjects with:
  - a. Experimental pain, including repetitive stimulation
  - b. Acute postoperative pain
  - c. Several distinct types of recurrent episodic pain and chronic persistent pain.
3. Strong agreement with self-report in subjects with experimental pain, acute pain, and chronic pain, under a range of situations such as those listed in appendix 2, items 1-3.

## Appendix 2: Test Situations for Candidate Physiologic Measures of Pain Intensity

1. Children and adults who are afraid or anxious but having no pain.
2. Adults and children ages 4 yr and older with low and high self-reported pain scores with clinical conditions that affect sympathetic responses, e.g., cold exposure, fever, anemia, hypovolemia, shock, congestive heart failure, autonomic neuropathies, sympathetic blockade associated with regional anesthesia, paraplegia with lower body stimuli that evoke autonomic hyperreflexia.
3. Adults and children ages 4 yr and older with low and high self-reported pain scores receiving medications with adrenergic agonist or adrenergic receptor blocking effects.
4. Infants, toddlers, and nonverbal adults with low and high previously validated behavioral pain/distress scores (e.g., Children's Hospital Eastern Ontario Pain Scale, Face, Legs, Activity, Cry, Consolability Scale, Premature Infant Pain Profile, or others, according to age and clinical context) over a range of clinical conditions such as those listed in 1-3 above.