# On the Development of Objective Pain Assessment Tools: What are We Missing?

## To the Editor:

Last year, Wagemakers and colleagues provide us with an overview of the most commonly used devices and techniques for painful stimuli administration (1). The importance of this contribution, specifically to the development of valid and reliable pain assessment tools, becomes evident when we consider nearly 5 decades of research demonstrating that experimentally induced pain elicits autonomic-mediated physiological responses (2). Significant changes in heart rate (HR), heart rate variability (HRV), skin conductance (SC), pupil dilation (PD), and blood pressure (BP), have been reported to be associated with the pain experience. However, some studies (3) point out that those changes may not reflect the severity of perceived pain, but the magnitude of the stimulus that might be perceived as painful. This is consistent with the idea that injury can provoke an autonomic-mediated response that could be described in terms of the damage inflicted, even in an unconscious patient (4). Thus, although it would not be possible to ensure that a patient undergoing general anesthesia can experience pain during the first surgical incision of an operative procedure, the vasoconstriction caused by an increase in the sympathetic tone resulting from a skin incision can be quantified by measuring the photoplethysmographic waveform amplitude, as done by Ben-Israel et al (5). Taken together, all this evidence suggests that fluctuations in autonomic activity do not necessarily reflect the perceived pain intensity, but rather the magnitude of the nociceptive response to injury. Still, the controversy is far from over.

Previous research has reported the existence of statistically significant correlations between autonomic-mediated responses to experimentally induced pain and patients' pain ratings (6,7). On the other hand, in a more recent study (8), it was found that autonomic responses increased when a thermal stimulus, whose magnitude varied across both innocuous and noxious intensities, was perceived as painful. Together, these findings suggest that pain intensity may increase with nociceptive input and autonomic responses to noxious stimulation can be modulated by pain perception (Fig. 1). But what about the autonomic arousal elicited by nonpainful, but salient stimuli? A major limitation of the literature body supporting the use of autonomic markers as pain indicators, is the lack of quantitative comparisons between pain-driven autonomic responses and those triggered by other arousing events. Pain is more salient and arousing than most nonpainful stimuli, it is to be expected that responses to painful stim-

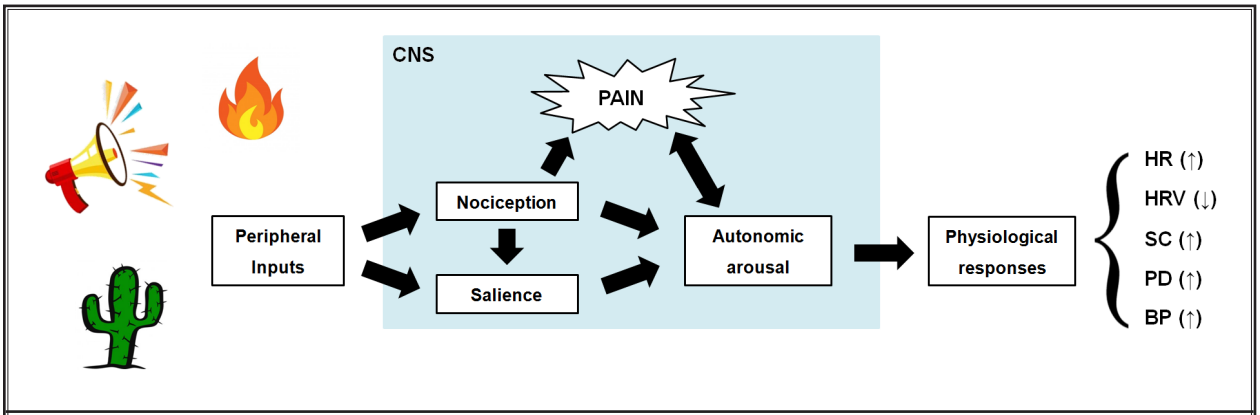


Fig. 1. *Schematic representation summarizing the contributions (3,6-8), which collectively highlight the interactions between pain, nociception, salience, and arousal (9). Cognitive and emotional factors that may influence pain perception and arousal have been omitted for clarity. CNS: central nervous system; HR: heart rate; HRV: heart rate variability; SC: skin conductance; PD: pupil dilation; BP: blood pressure; ↑: increase; ↓: decrease.*

uli will be different from those evoked by nonpainful stimuli (9). To develop reliable pain assessment tools based on autonomic markers, it is crucial to ensure that these measurements are not only pain-sensitive, but also pain-specific. In this regard, some efforts have recently been made. For instance, it has been found that electrodermal responses to electrical driven pain can be distinguished from those generated by emotion-inducing pictures and sounds (10). Another study showed that features extracted from HR, HRV, SC, skin temperature (ST), and blood volume pulse (BVP) can be used for differentiating boredom, surprise, and pain (11). However, as important as it is to compare autonomic responses to pain with those elicited by other arousing modalities, is to avoid over-reliance on peripheral measurements when attempting to identify pain-specific responses. Pre-existing health conditions and severe illness may limit the ability of peripheral autonomic markers to differentiate pain in both adults (12) and children (13), so limiting the search for pain-specific responses to the observation of only peripheral markers could provide incomplete and inaccurate data. As Jhon Tukey is reported to have said: "…when the right thing can only be measured poorly, it tends to cause that the wrong thing to be measured well. And it is often much worse to have a good measurement of the wrong thing, especially when it is so often the case that the wrong thing will, in fact, be used as an indicator of the right thing, than to have a poor measure of the right thing (14)."

As suggested by Lee et al (9), the uniqueness of the pain experience may lie on the relative balance between nociception, salience, and emotional arousal, which have been shown to overlap at the functional and anatomical level. Nevertheless, it is the brain that has the last word in the interpretation of these interacting contributions. Pain is a perceptual experience and, as such, it occurs in the brain. Therefore, pain-specific information that may be revealed by autonomic innervated organs (heart, skin, eyes, blood vessels) might be better acquired directly from the brain. Future research endeavors should point in this direction, combining functional magnetic resonance imaging with electroencephalography data.

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