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COMMENTARY

A closer look at temporal summation of second pain in healthy persons.

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Quantitative sensory testing (QST) is an important tool in pain research. Using these methods, quantitative data regarding the perception of pain associated with pain states, treatment and other factors can be studied using the application of controlled sensory stimuli to the subject. One limitation of research employing these techniques, however, is that evoked stimuli typically stimulate multiple types of receptors and pain modulatory systems, making it difficult to pin down the types of pain processing mechanisms that might be responsible for any observed differences or changes.

Based on the existing literature, temporal summation of second pain (TSSP), or wind-up, is an exception to this as the methods are proposed to predominantly stimulate C-fibers (Vierck et al., 1997), allowing researchers to make more specific inferences about the neurophysiological mechanisms underlying the stimulation and responses. As noted in the manuscript, repetitive C-fiber stimulation is believed to promote excitatory neuronal activity in the dorsal horn of the spinal cord. Prior research has demonstrated that that wind-up is attenuated by N-methyl-D-aspartate receptor antagonism (Price et al., 1994) and may reflect central sensitization, a process believed to contribute to the development and maintenance of chronic pain (Latremoliere and Woolf, 2009). Thus, the study of TSSP provides insight into the functioning of specific processes associated with pain and pain conditions.

Anderson et al. expand on the existing literature on TSSP by taking a critical look at the prevalence of TSSP in a large group of healthy subjects and defining TSSP according to different criteria. Furthermore, the authors employ empirical techniques to group subjects based on TSSP responses as well. The authors found that a high proportion of healthy subjects do not display TSSP. In fact, in some subjects, ratings were observed to decrease over time. In addition, there were disparities in the prevalence of TSSP between the calculation methods and empirical method. When simply looking at numerical increase in pain ratings across repeated stimulations, the prevalence of TSSP was higher. However, the empirical method grouped small responders with no responders, suggesting that this may be a homogeneous group of subjects. Such a finding raises an important question: do small increases in pain reporting reflect TSSP, or normal variability in responding? Since it is likely that some normal variation occurs, it remains unclear what level of increased pain reporting reflects TSSP. This is an important question that needs to be addressed in future research.

One might also question the robustness and validity of this phenomenon if it only occurs in a minority of subjects as suggested by the empirical analysis of the data. However, one could also argue that if TSSP is a pathological process, it might not be highly prevalent in a pain-free population. As stated in the paper, it would be beneficial to examine the prevalence of TSSP in samples with pain conditions. Observing a high prevalence in clinical samples would suggest the study of TSSP has relevance to understanding chronic pain conditions. Indeed, the authors mention that several studies have found differences in TSSP magnitude between subjects with different chronic pain conditions compared with healthy controls.

In the discussion, the authors debate the pros and cons of examining TSSP as a concrete phenomenon or a continuous variable. There is potentially considerable merit in looking at the former. While it is important to look at mean differences between samples of interest, such analyses do not always address the clinical significance of the findings. While studies have found significant differences in TSSP means between pain samples and controls, the percentage of clinical

patients who display TSSP compared with pain-free subjects is relatively unknown. If the percentage is not the majority of the sample with pain, how well do the findings characterize the pathology that underlies the pain disorder being studied? Even within a particular pain diagnosis, persons with chronic pain are viewed as being highly heterogeneous (Valluci, 2012). If the abnormalities that underlie pain in a sample are varied, QST methods might be used to try and characterize the types of dysfunction that underlie a person's pain and tailor treatment. These questions can not be fully answered by simply looking at TSSP as a continuous measure.

In summary, the Anderson et al. paper provides us with an important reminder that we need to closely examine the methods we use to evaluate pain. While the methods used to produce TSSP are novel and innovative, they also need be more carefully examined in both healthy and clinical populations in order to better understand the meaning of the findings.

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References

Latremoliere, A., Woolf, C.J. (2009). Central sensitization: A generator of pain hypersensitivity by central neural plasticity. *J Pain* 10, 895–926.

Price, D.D., Mao, J., Frenk, H., Mayer, D.J. (1994). The N-methyl-D-aspartate receptor antagonist dextromethorphan selectively reduces temporal summation of second pain in man. *Pain* 59, 165–174.

Valluci, R. (2012). Heterogeneity of chronic pain. *Clin Drug Investig* 32 (Suppl. 1), 3–10.

Vierck, C.J., Jr, Cannon, R.L., Fry, G., Maixner, W., Whitsel, B.L. (1997). Characteristics of temporal summation of second pain sensations elicited by brief contact of glabrous skin by a preheated thermode. *J Neurophysiol* 78, 992–1002.