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Editorial comment

Quantitative sensory tests (QST) are promising tests for clinical relevance of anti-nociceptive effects of new analgesic treatments

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1. Introduction

In this issue of the Scandinavian Journal of Pain, Juerg Schliessbach and coworkers [1] report the findings in several quantitative sensory tests (QST) assessing nociception compared to clinical treatment effect in 50 chronic low-back pain patients randomized to receive oxycodone or placebo in a double-blind RCT with cross-over design. Acute anti-nociceptive QST effects of oxycodone were assessed against its clinical analgesic efficacy, with special emphasis on the ability of QST findings to predict and differentiate clinical responders from non-responders. This is a novel approach to utilize QST measures in a relevant clinical setting, which might prove useful for future preclinical and clinical trials on analgesic drugs.

2. Difficult task of assessing pain and measuring analgesia

Pain is a multifaceted subjective experience, which cannot be assessed with external objective measures nor easily be reduced to one-dimensional figures. Both in clinical research and practice, analgesic treatment efficacy is evaluated with subjective symptom severity scales whereas experimental preclinical studies apply different QST measures. Due to differences in these testing algorithms, there is disappointingly often a mismatch between promising preclinical but failing clinical outcomes for novel drugs. This might be improved by validating and assessing the predictive value of anti-nociceptive QST alterations against clinical analgesic efficacy in human patients. This hasn't been systematically evaluated before, but is the ambitious aim of the current study.

3. QST – current state of conduct

It would be useful to get reliable numeric, more objective means to assess the efficacy of old and new analgesic drugs, both in the clinical and especially in research settings. QST, although not totally objective as it depends on subjective patient report, has already been shown to improve the diagnostic accuracy in peripheral neuropathy and chronic pain [2–6]. As QST offers numerical results, and reference values for various modalities have been published [7–9] and the method validated in large clinical patient samples [10–12], it is of great interest whether it might be useful in predicting and assessing clinical response when developing new analgesic treatments.

4. QST-detected anti-nociception of the analgesic drug agree well with clinical analgesia: QST is a promising bridge between preclinical and clinical trials of new analgesic treatments

The study by Juerg Schliessbach and coworkers [1] is important as it opens a new line of research with the aim to build a bridge over the gap between preclinical and clinical trials by means of validated QST methods. Although nearly all the nociception related QST variables applied in this study were found to be in line with clinical efficacy, heat pain detection (HPDT), electrical single-stimulation pain (ESPT), and pressure pain detection (PPDT) thresholds were found to best reflect the clinical analgesic response. However, the anti-nociceptive changes in QST, even with the best performing HPDT, ESPT and PPDT, were rather modest in their ability to predict clinical response. According to the ROC AUC results, from any given two pain patients, HPDT could correctly predict responder status in 65% of the cases, ESPT in 64%, and PPDT in 63%; the lower 95% confidence limits were below 0.50 (ranging between 0.43 and 0.48). The highest sensitivity for ruling in drug responders was found for ESPT (75%), but otherwise the QST variables may perform better in ruling out non-responders to oxycodone; the specificity ranged from 82% to 91% for HPDT and PPDT, depending on the pre-set cut-off points for QST variables and clinical response limits (20% vs. 30% vs. 40% decrease in NRS scores). It is noteworthy that 30% decrease in symptom severity, lately often considered to reliably reflect clinically meaningful response, performed optimally in these analyses supporting its use as a response limit in clinical trials.

The approach introduced in this study [1] should be encouraged as it will hopefully improve analgesic drug development, and provide new quantitative tools for measuring efficacy of pain-relieving treatments in the future.

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Conflict of interest

The author declares no conflict of interest.

References

[1] Schliessbach J, Siegenthaler A, Bütikofer L, Vuilleumier P, Juni P, Arendt-Nielsen L, Curatolo M. Quantitative sensory tests fairly reflect immediate effects of oxycodone in chronic low-back pain. Scand J Pain 2017;17:107–15.

[2] Forssell H, Jääskeläinen S, Tenovuo O, Hinkka S. Sensory dysfunction in burning mouth syndrome. Pain 2002;99:41–7.

[3] Teerijoki-Oksa T, Jääskeläinen S, Forssell K, Virtanen A, Forssell H. An evaluation of clinical and electrophysiologic tests in nerve injury diagnosis after mandibular sagittal split osteotomy. Int J Oral Maxillofac Surg 2003;32:15–23.

[4] Jääskeläinen SK, Teerijoki-Oksa T, Forssell H. Neurophysiologic and quantitative sensory testing in the diagnosis of trigeminal neuropathy and neuropathic pain. Pain 2005;117:349–57.

[5] Løseth S, Lindal S, Stålberg E, Mellgren SI. Intraepidermal nerve fiber density, quantitative sensory testing and nerve conduction studies in a patient material with symptoms and signs of sensory polyneuropathy. Eur J Neurol 2006;13:105–11.

[6] Ørstavik K, Norheim I, Jørum E. Pain and small-fiber neuropathy in patients with hypothyroidism. Neurology 2006;67:786–91.

[7] Rolke R, Baron R, Maier C, Tölle TR, Treede R-D, Beyer A, Binder A, Birbaumer N, Birklein F, Bötefur IC, Braune S, Flor H, Huge V, Klug R, Landwehrmeyer GB, Magerl W, Maihöfner C, Rolko C, Schaub C, Scherens A, Sprenger T, Valet M, Wasserka B. Quantitative sensory testing in the German Research Network on Neuropathic Pain (DFNS): standardized protocol and reference values. Pain 2006;123:231–43.

[8] Neziri AY, Scaramozzino P, Andersen OK, Dickenson AH, Arendt-Nielsen L, Curatolo M. Reference values of mechanical and thermal pain tests in a pain-free population. Eur J Pain 2011;15:376–83.

[9] Becser N, Sand T, Zwart J-A. Reliability of cephalic thermal thresholds in healthy subjects. Cephalalgia 1998;18:574–82.

[10] Freynhagen R, Rolke R, Baron R, Tölle TR, Rutjes A-K, Schu S, Treede R-D. Pseudoradicular and radicular low-back pain – a disease continuum rather than different entities? Answers from quantitative sensory testing. Pain 2008;135:65–74.

[11] Baron R, Maier C, Attal N, Binder A, Bouhassira D, Cruccu G, Finnerup NB, Haanpää M, Hansson P, Hüllemann P, Jensen TS, Freynhagen R, Kennedy JD, Magerl W, Mainka T, Reimer M, Rice ASC, Segerdahl M, Serra J, Sindrup S, Sommer C, Tölle T, Vollert J, Treede R-D. Peripheral neuropathic pain: a mechanism-related organizing principle based on sensory profiles. Pain 2017;158:261–72.

[12] Vuilleumier PH, Biurrun Manresa JA, Ghamri Y, Miekusch S, Siegenthaler A, Arendt-Nielsen L, Curatolo M. Reliability of quantitative sensory tests in a low back pain population. Reg Anesth Pain Med 2015;40:665–73.