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Commentary

Dissecting post-herniotomy pain – Scratching the surface?

Sensory characterization (QST) of patients with chronic pain conditions of neuropathic and non-neuropathic origin is a promising tool to elucidate pain mechanisms and it is hoped that QST findings facilitate the development of more stratified treatment strategies [13]. QST contributed to the important appreciate that pain is not a single entity but should be differentiated according to symptoms. This perspective accords very well with clinical reality – not every patient with chronic pain responds in the same way to a particular treatment. Steadily increasing evidence suggests that a distinct number of sensory patterns – although different in expression and frequency – can be found across very different pain conditions (e.g. painful neuropathy, post-herpetic neuralgia, complex regional pain syndromes). These findings suggest that patients could be clustered according to their pain symptoms, and that clustering might be a more promising approach to develop and evaluate pain therapies than is grouping patients by disease etiologies [7,13]. In the Aasvang et al. study in this issue of PAIN [1], this concept is carefully transferred to the surgical field. The authors did not study a disease entity but rather a frequent complication of a standardized surgical procedure – namely post-herniotomy pain. The authors' findings of heterogeneous sensory patterns in QST fit well with the above concept of different types of pain despite the same underlying disease or disturbance.

What do we learn from such a detailed investigation of sensation in different patient groups? First, the presence of pain and hyperalgesia in an area with sensory loss detected by QST supports the diagnosis of neuropathic pain [15]. As both characteristics are present in the vast majority of patients with post-herniotomy pain, a major neuropathic pain component can be assumed. Second, in contrast to conventional electrophysiological approaches, QST studies make it possible to identify sensory loss and gain in the thermal and mechanical domains [3,12]. Thus, QST is considered particularly useful for detecting evoked pains such as hyperalgesia and allodynia [5]. Depending on the sensory findings obtained by QST, different pathophysiological mechanisms associated with pain, e.g. peripheral or central nociceptive sensitization are assumed. This seems promising, but there is a limitation when studies rely only on QST. Because QST is purely descriptive, inferences from such studies may only "scratch the surface" of the underlying pathophysiology. For example, is it sufficient to talk about "peripheral" sensitization when there is evidence that the gp120 protein has been implicated in painful HIV-neuropathy [16] but the endothelin B receptor in painful diabetic neuropathy [4]? Moreover, even if mechanical hyperalgesia is generally regarded to be the clinical correlate of "central" sensitization at the spinal level, recent studies also point to the contribution of sensitized peripheral mechano-nociceptors [10] and the involvement of low threshold mechanical C-touch fibres [14]. In other words, distinct sensory phenomena might have very different molecular bases. Even clinically, the finding of sensory loss, if associated with pain, is not necessarily indicative of a nerve lesion, because ongoing nociceptive input from the periphery has been shown to induce not only hyperalgesia but also functional sensory decline, even in the absence of a nerve lesion [6,9]. This presentation might be a sign of plasticity in the spinal cord or the brain.

The authors discuss the fact that the absence of sensory loss does not rule out a nerve lesion; hypersensitivity could mask an apparent sensory loss [7]. Clearly, if the objective is to better understand the precise mechanisms that contribute to neuropathic pain, then, as a prerequisite of a pathophysiologically oriented treatment, sensory profiles obtained by QST should be linked to histological, electrophysiological and/or imaging studies. A useful approach in getting a deeper insight into post-herniotomy pain is to look not only at the pain symptoms but also at anatomy. Indeed, in a recent MRI study by the same group [2] pathologic changes such as "contrast enhancement in groin", "edema," and "increase in spermatic cord caliber" occurred significantly more often in painful versus unoperated groins. No significant difference was found between painful and pain-free operated groins. Thus, although not specific for painful groins, these structural changes might be indicative of different pain mechanisms in post-herniotomy pain – beyond peripheral or central nociceptive sensitization, as defined by QST. These findings should be taken as a call for the development of disease-specific animal models that will allow the investigator to link sensory patterns with molecular mechanisms in a translational approach and thus provide the much sought after evidence for tailored and mechanism-based pain treatment.

Apart from the methodological considerations concerning QST, another aspect is striking: the heterogeneity of sensory phenomena within the painful post-herniotomy subgroup is paralleled by considerable overlap of the sensory findings (i.e. normal 20%, see discussion) between the painful and pain-free post-herniotomy cohort – a finding that is not specific for post-herniotomy pain [8]. This observation points to the fact that there are further pain mechanisms that are not represented by QST. One possibility for such a "pain mechanism", or at least a contributor to the pain, is anxiety, which has been demonstrated to enhance the perception of pain [11]. Although the authors state that a considerable number [5/80, about 6%] of their patients refused to complete the protocol because of anxiety about pressure pain, detailed anxiety and pain scores were not reported in this study. In future studies, these data should be included and correlated with the QST results.

Taken together, the present study increases our understanding of the diversity of symptoms in post-herniotomy pain. But even more importantly, the study points to significant shortcomings in our understanding of post-herniotomy and probably also other

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chronic pains, given the large overlap between painful and pain-free subgroups. This, of course, raises concerns about the specificity of the sensory findings (see also [5]). A promising approach to overcome this lack of specificity is to combine and correlate QST findings with further functional (e.g. electrophysiological, functional imaging), structural (i.e. nerve/skin biopsies, imaging studies) and therapeutic data through multiple assessments. These studies should be individually designed according to the disease condition being studied. In this setting QST will contribute even further to our understanding of chronic pain and to the development of mechanism-based treatments.

Conflict of interest

The authors have no conflict of interest to declare.

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