What Do Experimental Pain Models Tell Us about Aging and Clinical Pain?

During presentations about aging and clinical pain, almost invariably, someone will ask, “Does pain threshold change with age? Wouldn’t that explain your results?” These are complicated questions, and there is rarely time in the few minutes usually allotted for “Q and A” to give an adequate response. Instead, more than once I’ve replied, “What would age differences in pain threshold tell you about clinical pain?” This is not intended to challenge the audience member but rather to reflect the pain research community’s long struggle to understand the relevance of data from experimental pain models to clinical pain.

Most experimental, or laboratory, pain models involve the application of carefully controlled stimulation. Experimental participants are asked to indicate when they first feel the sensation (detection threshold), when it first becomes painful (pain threshold), and if stimulation is continued or its intensity increased, when they would like it to be terminated (pain tolerance) [1]. In these studies, participants are informed that they will suffer no permanent damage from the stimulation and may terminate it whenever they choose. Critics have suggested that the experimental situation cannot adequately mirror the clinical situation, especially in regard to the affective and evaluative dimensions of pain [2]. For instance, while a healthy older person may experience some transient anxiety about an upcoming shock which they have been assured will cause no permanent damage and can be easily terminated, this is far from the anxiety an older person with cancer might experience in the face of an exacerbation of pain. This person may fear disease progression, uncontrollable pain, physical disability that may necessitate institutionalization, and the impact of the pain on their quality of life and death. Proponents of experimental pain models do not deny this limitation. Instead, they point out that there are important questions that can only be answered, whether for methodological or ethical reasons, using experimentally applied noxious stimulation [3]. In addition, there is evidence that some experimental pain parameters may have important predictive value in the clinical situation (e.g., [4]). Therefore, it is evident that both experimental and clinical studies are necessary to further our understanding of pain mechanisms [3].

There is a long history of studies comparing pain sensitivity in younger and older volunteers, with reports that sensitivity increases, decreases, and does not change with age (see Gagliese and Melzack [5] for a review). The findings may be dependent on the modality of stimulation such that age differences in sensitivity to noxious electrical, pressure, and ischemic stimulation are not uniform, even when measured in the same groups of younger and older people [6]. Nonetheless, the preponderance of the data suggests that older people have a similar or slightly higher pain threshold and lower pain tolerance than younger people. What does this conclusion, tentative as it might be, imply about the clinical situation? Do older people experience less pain than younger people in response to the same injury or disease process? Clinical data suggest that older people are less likely than younger people to experience pain associated with acute pathologies [7]; however, age-related patterns in the intensity of most types of clinical pain remain unclear [5]. Does reduced tolerance of experimentally applied pain imply that clinical pain is more difficult to tolerate for older than younger people? Do older people cope less well or experience more distress than younger people with chronic pain? The clinical data suggest that this is not the case [8,9]. Therefore, it appears that the patterns of age differences in pain threshold and tolerance observed among healthy volunteers may not directly translate to the clinical situation. Studies of pain threshold and tolerance in younger and older people with clinically relevant acute or chronic pain are needed to examine this issue.

Another class of experimental pain models assesses behavioral proxies of the important neuroplastic changes that underlie central sensitization and may be more relevant to clinical pain. One of these models, temporal summation, involves an increase in perceived intensity after repeated exposure to a series of noxious pulses of constant stimulus intensity and is conceptualized as a correlate of wind-up in animals and a behavioral proxy of central sensitization [10]. In this model, participants rate the intensity of pain...
They found increased temporal summation in the arm in younger and older healthy volunteers. for thermal and pressure pain applied to the forearm temperatures than younger people. Recently, Lauten applied at the arm, and they did so at lower temperatures than younger people to thermal stimulation older people exhibited greater temporal summation than younger people at the arm, but that older people showed temporal summation at lower levels of stimulation than younger people. These data suggest that with age the threshold for inducing central sensitization may decrease and behavioral responses may increase.

Returning to the original question, what does this mean for our understanding of clinical pain? Although the relevance of temporal summation to both central sensitization and clinical pain remains to be fully characterized, it is regarded as an important correlate of pain-related neuroplasticity and central sensitization [10]. Therefore, if age differences in temporal summation were to be demonstrated in a clinically relevant model, it would have important implications. Enhanced neuroplastic changes may be associated with permanent neurotoxic and neuropathological changes [14] that may contribute to prolonged acute postoperative pain [15] and increased risk of chronic postsurgical and neuropathic pain with age [16,17].

However, caution is necessary in extending the results described above to clinical pain. In clinical settings, it is not unusual for older patients to be frail with multiple comorbidities requiring multiple pharmacological interventions; yet experimental pain studies have included predominantly healthy participants, routinely excluding older people with significant chronic pain or other important comorbidities. It is easy to imagine that these differences would impact on responses to experimental pain models, but research is needed to address this. Many other empirical questions in older adults with clinical pain beg investigation. Are there age differences in temporal summation among people with acute or chronic pain? Do these differences predict recovery, transition to chronicity, response to interventions, or psychosocial and physical function? Are there age differences in the effects of interventions designed to block or reduce temporal summation? The results of such investigations would enhance our understanding of the neurobiology of pain and aging and of the relationship between experimental and clinical pain models. Until then, the answer to the question of whether age differences in sensitivity
to experimentally applied pain underlie the differences seen in the clinical setting must remain open.

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