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Commentary

Affective state and quality of life in mice

The International Association for the Study of Pain defines pain in man as a "sensory and emotional experience", but defining pain in animals is both more challenging and controversial [7]. Perhaps not surprisingly, studies involving animal models have been directed largely at measuring the sensory components of pain, rather than the affective or emotional component. Recently, the validity of some animal models of pain has been questioned, particularly those used to evaluate neuropathic pain [10]. It has been suggested that the relative lack of success in developing novel therapies for patients using these animal models is due to their failure to model key components of neuropathic pain in humans. Patients with chronic pain often report bouts of spontaneous pain, and often show increased anxiety and signs of depression. An appreciation of the need to assess these states in animals has led to a number of studies in rat models of neuropathic pain, but little work has been undertaken in the mouse. The article by Urban and colleagues [12] provides a major contribution to this neglected area, but also raises major concerns in relation to the validity of the mouse models of neuropathic pain that were studied. Extensive evaluation of mice with either chronic constriction injury or spared nerve injury demonstrated the development of mechanical hypersensitivity, but showed no difference from controls in any aspects of their behaviour. The measures of anxiety and depression included open field, elevated plus, marble burying, forced swim, and sucrose consumption. In addition, prolonged recording of activity patterns and food and water consumption were made. The authors concluded that since the mice with these injuries showed no significant alteration in the measures used to assess "quality of life", then these models do not properly reflect key components of the human pain experience. This may be the case, but as the authors point out, this finding might also reflect our poor ability to assess changes in affective state in rodents.

The need to measure affective state in animals is not unique to pain research. The assumption that animals can experience negative affective states such as pain, depression, and anxiety is critical to studies of animal welfare [3]. It is also of significance in animal models measuring the negative states associated with drug withdrawal [4]. The measurement of these states in animals has proven challenging. In humans, self-report is regarded as the gold standard for assessing pain and other negative states such as anxiety. It is the subjective components of these states that are the primary determinants of their distressing nature, and this can be measured only by asking people how they feel. Since self-report is not possible in animals, proxy measures of affective state are used. These are based on the assumption that objective measurement of changes in behaviour, cognition, and physiology will correlate with changes in affective state. A number of proxy measures, such as performance in an elevated plus-maze or open-field arena, or use of novel object or forced-swim tests have been widely used in many areas of research. The authors used several of these techniques, and all have also been applied to study rat neuropathic pain (see citations in [12]).

Although widely used, these measures are not considered by many to be accurate assessments of underlying affective states such as depression and anxiety (e.g., [11]), as changes in these measures can be attributed to factors other than changes in affective state, such as arousal. Recently, research has begun to be focused on alternative and potentially more direct measures of affective state [9]. The most promising of these is the measurement of "cognitive bias", which refers to changes in information processing that often occur with negative affective states. For example, negative affective states in humans are associated with an increased attention to threatening stimuli, leading to a tendency for ambiguous stimuli to be interpreted as threats (i.e., a pessimistic outlook) [5]. Thus far, these measures have been used to assess the impact of environmental factors in nonhuman species [1,6,8], but should be applicable to other causes of negative affective state, such as pain.

The other significant component of the study by Urban and colleagues [12] is the use of more extensive behavioural assessment as a potential measure of quality of life. The authors point out the difficulty of obtaining and analyzing long-term data of this type, and used an automated system to circumvent this. Although using automated measures may solve the problem of collecting and analyzing data over a protracted period, it may introduce another, in that the measures obtained are inevitably limited in comparison to those obtained by detailed manual analysis of behaviour. In the future, computer-assisted video analysis may provide more complex assessments of animal behaviour, and overcome the practical resource limitations of manual analysis. For example, one automated system has been shown to have a reasonable correlation with manual analysis of mouse behaviour [2]. If our rodent models of neuropathic pain do model human experience, then we would expect behavioural changes to be associated with the occurrence of ongoing pain. Identifying such behaviour may require detailed and complex assessment of an animal's entire behavioural repertoire. Such assessments may enable the identification of behaviour associated with nociception, but measures of affect will be required in order to interpret them as "pain". Measuring how animals feel therefore becomes the major challenge for many areas of research that utilize animal models.

Conflict of interest statement

The authors have no conflict of interest in relation to this commentary.

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