Tired of pain or painfully tired?

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Animal research has also shown that individuals suffering from chronic pain have lower pain thresholds to pressure and electrical stimulation than healthy controls (which has been ascribed to sensitization of the central nervous system). Thus, in their model, a sensation that is perceived as painful increases effortful control during goal-pursuit, thereby inducing fatigue. Interestingly, pain perception itself may be influenced by fatigue. Research has shown that individuals suffering from chronic fatigue have lower pain thresholds to pressure and electrical stimulation than healthy controls ([11,14,25,27] (which has been ascribed to sensitization of the central nervous system)). Moreover, although exercise usually increases pain thresholds in healthy individuals, ([12,24,26] it has the opposite effect in individuals with chronic fatigue. ([12,24,26]) Animal research has also shown that healthy mice demonstrate hyperalgesia after fatigue induction. ([1,17] These results indicate that, besides pain increasing fatigue during ongoing activity, fatigue during ongoing activity may also exacerbate pain. Therefore, we argue that pain and fatigue may mutually reinforce and perpetuate each other in chronic pain. Future longitudinal and experimental studies should scrutinize this reciprocal relationship.

Finally, the authors seem to equate reduced motivation to fatigue in some instances. We argue that although fatigue may be captured as reduced motivation, not each occurrence of motivational reduction is (or leads to) fatigue. For instance, the authors propose that chronic pain may impair reward processing, which may reduce the weight of the benefits associated with current goal-directed behaviour, thereby inducing fatigue. This conclusion builds on experimental work showing that when the consequences of our actions embody a mixture of reward and (anticipated) pain, this cost–benefit integration leads to attenuated predictive reward signaling in the brain. ([20] To use a real-life example: If a person goes to the dentist to maintain dental health (reward), the anticipation of pain may reduce the weight of the benefits associated with consulting a dentist. However, referring to this attenuated reward processing as fatigue or fatigue inducing may not be warranted. Indeed, although fatigue may manifest itself as reduced motivation to pursue current goals, certainly not every reduction in motivation for goal-pursuit can be conceptualized as fatigue.

The framework presented by Van Damme et al. opens a new research agenda for fatigue in chronic pain. We propose that expanding their model by integrating reciprocal relationships will allow for a better representation of the complexity of real-life symptom interactions.

**Conflict of interest statement**

The authors have no conflict of interest to declare.

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**References**

Letter to Editor:

In their letter to the editor, Lenaert et al. commented on our recently proposed motivational framework explaining the frequent occurrence of fatigue in individuals with chronic pain. We would like to thank these authors for complimenting and complementing our work and take the opportunity to further discuss some of the issues they raised.

Their main argument concerns the direction of the relationship between chronic pain and fatigue. Our framework was guided by the observation that patients with chronic pain often report heightened fatigue and, as a starting point, we referred to a systematic review suggesting that fatigue may develop as a result of chronic pain. We agree with the authors that this review does not provide evidence for an exclusive unidirectional causal relationship between chronic pain and fatigue. Yet, it is important to note that it was not our intention to argue for such a relationship. We acknowledge that several studies have suggested that fatigue enhances pain or increases the risk of developing chronic pain disorders. As such, we do not contend the idea that fatigue may influence pain, but we do, however, ask for caution when considering the evidence provided in that direction. For example, heightened pain sensitivity has been demonstrated in patients with chronic fatigue syndrome. However, for these studies, the same limitation applies as for the studies on fatigue in patients with chronic pain, mentioned by the authors, namely that the samples were selected based on the diagnosis of chronic fatigue syndrome, preventing strong causal claims. The authors also referred to a number of prospective studies indicating that the presence of fatigue increases the risk of developing pain complaints. However, in the samples used, fatigue was often only one of a broader set of symptoms indicating burnout, sleeping problems, or general psychological distress. Consequently, it remains unclear whether it was actually fatigue that caused the pain complaints or whether fatigue was an indicator of broader psychological problems playing a role in the development of pain disorders.

Despite the limitations discussed above, we concur that it is likely that pain and fatigue mutually reinforce each other. Such a view is compatible with our proposed theoretical framework. As stated in our theoretical framework, higher-order cognitive processes such as executive control are involved in the...