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Fatigue associated with chronic pain: Further thoughts on the motivational conceptualization of fatigue, and its reciprocal relationship with pain

Stefaan Van Damme^{1,*}, Dimitri Van der Linden², Susanne Becker³

1 Department of Experimental-Clinical and Health Psychology, Ghent University,
Belgium

2 Institute of Psychology, Erasmus University, Rotterdam, The Netherlands

3 Department of Cognitive and Clinical Neuroscience, Central Institute of Mental
Health, Medical Faculty Mannheim, Heidelberg University, Germany

*Corresponding author

Address: Henri Dunantlaan 2, 9000 Ghent, Belgium

Tel.: +32-9-264.91.49; Fax: +32-9-264.64.89

E-mail: stefaan.vandamme@ugent.be

In their letter to the editor, Lenaert and colleagues [6] commented on our recently proposed motivational framework explaining the frequent occurrence of fatigue in individuals with chronic pain [11]. 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 chronic pain patients 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 [4]. 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 (CFS) [7]. However, for these studies the same limitation applies as for the studies on fatigue in chronic pain patients, mentioned by the authors, namely that the samples were selected based upon the diagnosis of CFS, preventing strong causal claims. The authors also referred to a number of prospective studies [1,3,5,8] 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 suppression of pain and the protection of goal-directed behavior against painful distractors. As it has been shown that executive control is compromised by fatigue [12], it is likely that fatigue can interfere with one's ability to self-regulate when experiencing pain (e.g., suppressing pain-related distraction) [10], which might enhance pain [9]. We acknowledge that such a pathway might be a worthwhile addition to the framework. Clearly, more experimental and prospective work is required to scrutinize temporal dynamics and causal mechanisms related to pain and fatigue.

A crucial issue in such endeavor is a clear conceptualization of fatigue. Lenaert and colleagues [6] provided a real-life example to illustrate that it may not be warranted to equate fatigue with reduced motivation or attenuated reward processing. We fully agree and, in our article, did not intend to argue for such an equation. We understand their concern and agree that the description of our framework could be further refined so that it becomes more explicit that an

unfavorable outcome of cost-benefit analyses might induce fatigue, but that this is not the case in every situation. We argue that fatigue is a rather specific sensation that functions to lower the motivation for future effort (similar as hunger being a specific sensation that motivates calorie intake) with the overall goal to optimize effort mobilization. The core of our framework is that an unfavorable costs-benefits analysis of current behavior accelerates the generation of such a fatigue sensation, and that chronic pain can negatively bias this outcome through different pathways. For example, to uphold or persevere goal-directed behavior when having persisting pain requires self-regulatory control, which will increase current as well as anticipated effort, as such adding to the costs of the behavior. These costs could be further enhanced by negative pain cognitions and expectations (e.g., worrying, low self-efficacy), as well as inefficient problem-solving, often observed in chronic pain patients [2]. Furthermore, the experience of pain during goal-directed behavior will attenuate the processing of reward associated with this behavior, reducing its perceived benefits. In sum, when pain patients have to decide whether or not to engage in or maintain goal-directed behavior, unfavorable costs-benefits analyses might lead to quickened generation of fatigue sensations, increasing the likelihood that they will not do so.

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