Hypothetical model ignores many important pathophysiologic mechanisms in fibromyalgia

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We would like to respond to the Perspective article by Pinto et al. (Pinto, A. M. et al. Emotion regulation and the salience network: a hypothetical integrative model of fibromyalgia. Nat. Rev. Rheumatol. 19, 44–60 (2023))1 . We feel that the proposed model severely overfits the complicated pathophysiology of fibromyalgia and is not applicable to all or even most individuals with this condition. We are concerned that this theory could inadvertently drive the field backwards despite several decades of research that has begun to illuminate neurobiological mechanisms underlying fibromyalgia and other chronic pain conditions. Our main points are outlined here.

First and foremost, we disagree that psychological stress is the sole cause of fibromyalgia. It is inappropriate and invalidating to imply this is the predominant causal mechanism in fibromyalgia. Many individuals with fibromyalgia do not have a history of trauma, psychiatric comorbidity or even extraordinary stress. Thus, these individuals will not benefit from and may be harmed by this inaccurate and potentially stigmatizing conceptualization of fibromyalgia.

‘Working hypotheses’ should both distinguish between causative and associative factors in the model and directly lead to testable hypotheses, but this piece does neither. The authors state “This proposed integrative model … should be viewed as a working hypothesis with limited supporting evidence available”2 . We agree that the supporting evidence is very limited. There are very few, if any, prospective longitudinal studies that conclusively demonstrate that psychological stress causes fibromyalgia. Longitudinal studies among people with related conditions such as chronic widespread pain (CWP) or temporomandibular disorder suggest that psychological factors are weak predictors of future pain compared to factors such as somatic amplification, interoception, prior pain, poor sleep and smoking2,3 . Furthermore, numerous studies suggest that psychological factors often improve dramatically when pain improves — which would not be expected if this unidirectional hypothesis is correct4,5.

We also disagree with the authors’ proposition that adverse childhood events (ACEs) are key drivers in the development of fibromyalgia. Whereas ACEs are unfortunately ubiquitous in the general population, most individuals who have ACEs do not develop pain, and ACEs are only weakly

associated with the development of fibromyalgia and CWP. The UK 1958 Birth Cohort Study estimated that <10% of CWP cases could be attributed to ACEs6 and a UK case–control study found that only childhood operations and hospitalizations were linked to CWP in adulthood7 .

Placing such significance on psychological stress (which worsens nearly all medical conditions) moves us away from precision medicine approaches. A holistic framework that considers diverse circumstances as well as needs and wishes of the patient is more likely to be effective whether the person has heart disease, diabetes, cancer or chronic pain. We completely agree that a subset of people with fibromyalgia have prominent underlying psychological factors playing a role, and that these individuals should be identified and treated using a variety of psychologically based therapies. But there are a plethora of other important underlying mechanisms and corresponding treatments that need to be considered. We prefer precision medicine approaches, which attempt to align treatments with the underlying mechanisms that are operative in each individual patient. There is a reply to this letter by Pinto et al. Nat. Rev. Rheumatol. https://doi.org/10.1038/ s41584-023-00952-2 (2023)

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Competing interests

The authors declare no competing interest