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## Invited Letter Rejoinder

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# The role of lifetime stressors in adult fibromyalgia: a response to Joan S. Crawford's letter to the editor

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### Dear Editor,

We would like to thank Dr Crawford for their interest in our paper. In their letter to the editor (Crawford, 2021), Dr Crawford suggests that the extent of the relationship between lifetime stressors and the development of fibromyalgia in adulthood, proposed by our systematic review and meta-analysis (Kaleycheva, Cullen, Evans, Harris, Nicholson, Chalder, 2021), could have been better accounted for by methodological issues in the study. We respectfully disagree and would like to address Dr Crawford's main concerns.

While we concur that retrospective reports are subject to potential recall bias and acknowledge that, in some cases, people experiencing on-going pain and debility may be more likely to report prior stressful experiences, we believe such data are sufficiently reliable to allow aetiological inferences. Notably, an experiment by Hoscheidt, LaBar, Ryan, Jacobs, and Nadel (2014) testing the accuracy of memory recall indicated that, while susceptible to misinformation cues, memory accuracy was greater following exposure to a stressful stimulus. An alternative to asking individuals to recall stressful events is to use measures of exposure derived from national registries. Importantly, studies using this approach to investigate associations between stressors and depression are consistent with retrospective case–control studies using self-report measures in showing a positive dose–response association (Musliner, Andersen, Agerbo, Albiñana, Vilhjalmsson, Rajagopal, … & Supli, 2021), providing convincing evidence that associations between lifetime stressors and complex disorders are attributable not simply to recall bias.

We think Dr Crawford raises an interesting point when it comes to the differences in findings between retrospective case–control studies and prospective studies examining the association between stressful life events and adult fibromyalgia. Our paper focused on case–control studies, in particular, due to the large number of such studies already published in the field. As such, it was our desire to review the methodological quality of those studies, as well as provide insight as to the broader spectrum of stressors associated with fibromyalgia.

We noted that the aetiology of fibromyalgia is poorly understood and hypothesised that stressful life events may either play a role as precipitating factors or predisposing factors. We did not assert the direction of causality. As suggested by Dr Crawford, prospective studies are required to test causal hypotheses. To our knowledge, there are no prospective studies currently looking at the association between fibromyalgia and a range of stressful life events. The lack of such studies could be attributed to the fact that fibromyalgia is a chronic pain condition which has a low incidence rate in the general population and is often difficult to diagnose due to its high comorbidity and nature of symptoms, requiring a specialist clinical examination. For these reasons, a sufficiently large prospective cohort would be required. Furthermore, accurately measuring the rates of stressful life events, such as abuse, as part of a prospective cohort would be a difficult endeavour, as such experiences are less likely to be reported whilst they are ongoing, as disclosure is difficult for many people and the mere mention of some (e.g. those involving childhood abuse) would risk relationships with family members. This could explain why Raphael, Spatz Widom, and Lange's (2001) prospective study did not find a significant relationship with unexplained pain symptoms and prospective reports of abuse.

In defence of the methodological robustness of our meta-analysis, we would like to point out that we used a hierarchy for inclusion of effect sizes, which favoured exposure to stressful events in the lifetime and adulthood in cases where studies examined stress exposure at multiple time-periods. This was done to maximise the number of studies contributing to each stressor type analysis, as well as to minimise the possibility of confounding in terms of recall bias. Moreover, interviews which obtain narrative information about life events can control for

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the over-exaggeration of stressful events by utilising the judgement of trained raters, resulting in greater reliability and validity of recall (Brown & Harris, 1989; Dohrenwend, 2006). They also offer the opportunity to date both symptoms and events in a better attempt to clarify temporal sequence and thus possible causal effects. These aspects were also accounted for within the systematic review section of our paper, whereby we awarded greater points for methodological quality to studies which included interviews, as opposed to checklists and questionnaires, as a method of ascertaining exposure to stressful life events.

Dr Crawford states that we have been led by a confirmation bias in stating that fibromyalgia can be defined as a functional disorder and, therefore, examined the role of HPA-axis dysfunction in fibromyalgia as a possible cause for the disorder. Whilst it is true we described fibromyalgia as a functional disorder due to the lack of clear structural pathology associated with it (Kaleycheva et al., 2021), we did not examine the literature regarding the association between HPA-axis dysfunction and fibromyalgia, as it was not the purpose of our review. However, it is certainly an area which merits further attention.

Finally, we would like to address Dr Crawford's comments regarding the lack of objective evidence that trauma-focused treatment can lead to an improvement in chronic pain and other fibromyalgia-associated symptoms. While evidence may be scarce, this does not mean that trauma-focused therapy would be ineffective in the treatment of a disorder as multifaceted as fibromyalgia. In fact, a protocol for the use of eye movement desensitization and reprocessing (EMDR), a type of trauma-focused therapy, was recently developed by Gardoki-Souto, de la Torre, Hogg, Redolar-Ripoll, Valiente-Gómez, Saduriní, … and Moreno-Alcázar (2021) after demonstrating in a double-blind randomised controlled trial that EMDR was effective in the reduction of pain symptoms in fibromyalgia patients when combined with a non-invasive brain stimulation technique, such as multifocal transcranial current stimulation.

It is apparent that we share similar goals with Dr Crawford – to develop a better understanding of fibromyalgia which will inform the development of effective treatments, in order to reduce the impact of symptoms for patients. Ultimately, we agree that more prospective research is needed to achieve these goals, ideally using interviews with rating systems that capture the full range of stressful experiences and which are sensitive to dating procedures.

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