Reviewer’s report

Title: A Logistic Regression Analysis of Risk Factors in ME/CFS Pathogenesis

Version: 0 Date: 15 Feb 2019

Reviewer: Trudie Chalder

Reviewer's report:

Overall the paper was well written. However, it would benefit from a more nuanced review of the literature where specific well-designed studies are referenced.

An important distinction should be made between more serious viruses and common viruses. For example, there are many prospective studies clearly showing a relationship between specific viruses such as EBV and chronic fatigue or operationally defined CFS. The authors could reference the following paper which reviews the studies.


This review consists of prospective cohorts worldwide and includes infectious mononucleosis (IM), Q fever, giardiasis, campylobacter gastroenteritis (CG), Legionnaires disease and Ross River virus. Risk factors for nonrecovery from PIF included lower physical fitness, female gender, severity of the acute sickness response, and autonomic dysfunction.

A study by Wessely et al showed no association between common viruses and CF or CFS at follow up in a case controlled study nested within a prospective cohort (I was an author on this particular paper). The study was large and designed specifically to answer the question related to causality.

The other issue that needs highlighting when reviewing studies is the methods used. Well conducted prospective studies, where the exposure to a virus is the starting point and participants are followed up should be highlighted. This is important - as indeed the authors have pointed out in their discussion of their paper when highlighting the issue of recall bias.

In the introduction the authors mention evidence of possible heritability. However, they failed to mention the important interaction with the environment.

With regards to childhood trauma there was one very well conducted study published by Heim et al which showed an association between childhood trauma and CFS. It also highlighted the link to the HPA axis and lower cortisol in those who reported trauma. These papers should be referenced specifically as the study was well conducted.

Although described elsewhere, the methods section needs to be more detailed. For example, it is unclear as to where the CFS participants were recruited from and whether the CFS diagnosis had been confirmed by a physician.
The reader is unclear as to how the criteria were operationalised.

It would be important to know how many participants were approached and how many responded. How many people are on the database.

The results appear to have been analysed appropriately but a statistical review would confirm this.

In the discussion a more nuanced discussion is warranted bearing in mind the nature of the methods used. More emphasis on the issues of recall and response bias is needed. More detail on the sample and how it was obtained would help facilitate this process.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

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None declared aside from suggesting a paper I was involved in be included

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