Thank you very much for asking me to review this interesting paper.

Here the authors investigated cerebral activation in FMS patients by functional near-infrared spectroscopy (fNIRS). A key finding was that FMS patients displayed a stronger contralateral activity over the dorsolateral prefrontal cortex in direct comparison to patients 15 with MD (p<0.05). Overall they claim that their findings provide evidence for altered central nervous processing in patients with FMS allowing a separation between FMS and MD.

Major Revisions

I have some areas I would like the authors to address:

1. In much of this literature FMS is classified as a medically unexplained syndrome. There is an increasingly sophisticated literature that is attempting to unpick the mechanisms underlying these enigmatic conditions. A cursory review of this highlights foci on attentional neurobiology and relationships to the neurobiology of anxiety and abnormal attention, as oppose to major depressive disorder. All tend to have numerous, persistent unexplained symptoms with poor functioning and respond poorly to medical intervention. Functional MRI studies have found increased activity in areas of the brain that attend to symptoms, a reflection of potential hypervigilance (1). A relatively recent position paper in Brain by Edwards et al (2) advances a Bayesian approach to understanding mechanisms here. I’m concerned that this approach advanced here is a little behind the curve and more extensive survey of the biological literature in this field would be helpful.

2. My major methodological concern is that the comparison group sued here is depressed (MD). Given that a key research question is around pain, a group with a known pathophysiology of pain would be more logical. A perhaps better psychiatric comparator would generalised anxiety disorder.

3. There is an implicit suggestion in this manuscript that FMS is a variant of, or is conflated with MDD. I’m not aware that this is the case – at least at the biological level. This means that it’s difficult to understand the meaning of a difference in fNIRS signal between the two groups.
4. I’m also rather worried about the limitation of functional near-infrared spectroscopy (fNIRS), acknowledged by the authors. This can only realistically measure surface cortical activity.

5. I wonder if fMRI data prior to the use of this technology would be a more effective approach. This leads me to the issue of power. These are small sample sizes and I’m not sure they permit the authors to substantiate the claims they make for their data. Again, a more detailed fMRI approach may allow a power calculation to be made on the basis of possibly biologically meaningful data.

6. I cannot see where the drug therapy for the patients has been recorded. I would regard this as a potentially crucial confound for this kind of imaging signal.

Refs

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
'I declare that I have no competing interests'