Reviewer's report

Title: Sleep quality, BDNF genotype and gene expression in individuals with chronic abdominal pain

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Reviewer: Yvette Conley

Reviewer's report:

This is a well-written manuscript that addresses sleep and chronic abdominal pain using a whole genome expression approach as well as a single candidate gene/single SNP association approach. The manuscript has several strengths including use of validated sleep measures, use of appropriate genomic data collection approaches, and report of interesting findings. The manuscript does have some weaknesses that if addressed would further strengthen the manuscript.

Major Compulsory Revisions

1) The manuscript is written with the cohort of 59 subjects in mind; however microarray gene expression data (a major data element for the project) was conducted in less than half of this cohort (n=26). We are never told what this subset looks like…are they different in any manner from the larger cohort that is defined…how many controls were included in that n=26…how was this subset selected and why?

2) The controls for this study are important since most of the evaluations are relative comparisons with controls; however we are given no information about the controls in the manuscript…how was a control defined…were they recruited in the same manner as the cases…were they just as rigorously evaluated for sleep and CAP phenotypes as the cases?

3) Information related to recruitment of subjects in general is thin. It is mentioned that they were recruited through the NIH clinical center during an outpatient visit…but why were they visiting the center in the first place…were they recruited from a specialty clinic…what was the inclusion and exclusion criteria for the study?

4) CAP is a heterogeneous phenotype and how it was defined for the analyses of this project could be better explicated…how many bouts of pain and what level of severity for over 6 months would constitute CAP…any attempts to focus on organic vs functional etiologies (see inclusion and exclusion comment above)?

5) The manuscript does discuss why BDNF was chosen as a candidate for evaluation, but why only BDNF and not other equally plausible candidates…why the chosen SNP in particular…why not variation in the genes that look interesting from the gene expression data?
6) Evaluation of the BDNF polymorphism data was conducted by comparing homozygotes vs heterozygotes and it is not clear why this was done. Given the small sample size it is understandable that they would dichotomize genotypes particularly if the number of homozygote variants were small, however most studies would have dichotomized into presence/absence of the variant allele and not combined the two homozygote groups for comparison. The authors should clearly state why they did the groupings that they did for this analysis.

Minor Essential Revisions

1) Background, 2nd paragraph, sentence “brain-derived neurotropic factor (BDNF) is a neuropeptide located on the gene rs6265…” is awkward and should be reframed.

2) There are a few things that are presented in the results/discussion that are not fully explained in the methods. The methods for the qRT-PCR should mention what genes were evaluated in this manner and why they were chosen. The methods do not mention if/how pathway based analyses were conducted although the results/discussion mention it.

3) Table 1 should list p-values for gender and race.

Discretionary Revisions

1) Given the focus on BDNF and information presented in the background about BDNF expression and abdominal pain scores, it would be interesting, since the data is there, to say what BDNF gene expression looked like in this study.

2) Given that BDNF genotypes factored into the analysis, it would be interesting for the authors to note in the discussion if BDNF in any way is involved with the significant genes identified from the gene expression data.

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'