Reviewer’s report

Title: Long-term CPAP treatment partially improves the link between cardiac vagal influence and delta sleep.

Version: 3 Date: 20 December 2012

Reviewer: Scott A Sands

Reviewer’s report:

The current study follows the authors’ previous cross-sectional study that revealed interesting differences between patients with SAHS and healthy controls: There is a weaker link between sleep and heart rate dynamics as measured by a reduced gain, coherence and increased delay between EEG (delta power) and heart rate variability (HFnu). Here the work is extended to examine whether long-term treatment of SAHS with CPAP reverses the differences seen between SAHS and controls.

The study is well performed, and despite the small sample size, the authors report a clear finding: The gain value – representing the sensitivity of vagal predominance (HFnu, a marker of autonomic balance) to sleep cycles (delta power fluctuations) – completely normalizes with treatment of SAHS. This work demonstrates conclusively that the strength of the relationship between sleep and autonomic balance is reduced as a consequence of SAHS. By contrast, differences in coherence and delay are not altered by CPAP treatment, suggesting that such differences could be irreversible consequences of SAHS, or instead might be intrinsically different in patients that have SAHS.

Major Compulsory Revisions

Discussion length

The 9-page discussion is quite long and appears unfocused. An exhaustive review on spectral cardiac components of HRV in OSA and effects of CPAP is provided (para 5 to para 14), yet this discussion does not directly pertain to the major focus of the study: examining the effect of sleep (delta power) on cardiac parasympathetic predominance in OSA. I suggest this particular section could be reduced by ~2/3rds while keeping all essential information. This would provide greater focus on the discussion of the key findings and their context in the available literature.

Normalization and HFnu interpretation:

The authors define HFnu as the “cardiac vagal component of heart rate variability” in the title and intermittently thereafter, but also describe that LF/HF is a measure of cardiac sympatho-vagal balance \[HFnu=1/(1+LF/HF)\]. Yet since these two variables are direct mathematical transforms, it appears contradictory to interpret HFnu as a measure of the cardiac vagal component and then its reciprocal as a measure of sympatho-vagal balance. Given that HFnu can vary
with LF as much as with HF, I feel that interpreting HFnu as the “cardiac vagal component” is misleading and that “vagal predominance” would be a more appropriate term for use throughout. The latter interpretation acknowledges that the dynamics associated with HFnu could reflect changes in the LF component with no necessity for a change in absolute HF.

On the same topic: Regarding the text: “HFnu is also considered as a better reflection of the cardiac vagal influence than absolute HF power” – is a statement that requires a reference.

Meaning of stability:
It is not clear what the authors mean by stability/instability (Abstract/Discussion). Specifically, what is stability and what data are used to make inferences regarding stability?

Alternative possibility to lack of reversibility:
Please acknowledge the general possibility that the persistent differences in EEG-ECG coherence and delay in SAHS may be because patients with SAHS and healthy controls have intrinsic differences to begin with (perhaps related via obesity or associated co-morbidities), as an alternative to the explanation that SAHS promotes reduced coherence and increased delay in a manner that is irreversible.

Minor Essential Revisions
There are many data in table form, but few figures. The major outcome variables: gain, coherence and delay might be best presented in a 3-panel figure. (The remaining data in Table 4 - fNREM-REM and Phase shift - could then be written as text.)

Figure 1.
It is not clear what comparisons the $ symbols / P value refer to.

Methods.
Incomplete sentence: “dry throat, cough …”

Discussion
Re: “However, improved parameters of the relationship between cardiac sympatho-vagal balance and delta sleep, such as the gain between both signals, probably could prevent cardiovascular events in severely apneic patients treated with long-term CPAP”. -The last clause seems overstated. Please tone down to “may help prevent…” or “may contribute to the prevention of” or similar.

This small paragraph seems isolated/incomplete: “The absence of statistical differences in cardiac sympatho-vagal activity in untreated patients versus controls could be explained by the relative proportion of mixed and central apnea [observed in the current study].”

This paragraph is confusing: “Mixed apnea with the central component could
explain why our group of SAHS patients showed the same HRV changes during the night as patients suffering from severe OSAS without reaching the statistical threshold.” -Are not the SAHS and OSAS the same? What is the implied separate group of OSAS that is referred to here?

Discretionary Revisions

Methods
Re: “occurrence of modifications” seems a bit awkward e.g. “…between the occurrence of modifications in HFnu and the occurrence of those in the delta power band”. Perhaps consider: changing to “…between the fluctuations in HFnu and fluctuations in the delta power band”.

Discussion
Re: “..in disfavour of the relative sympathetic activity”. -Is the word ‘disfavour’ appropriate given that sympathetic activity is not considered favourable here?

Level of interest: An article of importance in its field

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'