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Peer Review

Review of: "The Hypno-PC: Uncovering Sleep Dynamics Through Principal Component Analysis and Hidden Markov Modelling of Electrophysiological Signals"

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This study presents the decomposition of exceptionally high-density PSG recordings of 29 healthy subjects from an open database using a partly described combination of feature extraction, PCA, (G)HMM (and also ICA, the role of which is not clear in this context).

The procedure (as far as I was able to understand it from the text):

In the first step, 83 channels of EEG and accompanying EOG, EMG, and ECG are parametrized in 30- or 4-second epochs by computing several candidate measures known to correlate with behavioural states. It is not disclosed whether these features were computed separately for each of the EEG channels, which would yield the dimension of the input vector over the order of hundreds.

In the second step, these input vectors are probably combined into time series of respective resolutions (30 and 4 seconds) and subjected to PCA.

The major observation of this study, reflected in the title, seems to refer to the fact that the time course of the first PC, in this particular dataset explaining over 40% of variance, resembles visually the shape of corresponding hypnograms.

In the next step, a GHMM is fitted to the above time series (mainly 30-sec resolution) in a leave-one-recording-out cross-validation applied to the 29 analyzed recordings, for several numbers of hidden

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states, and the optimal number is chosen from information criteria, yielding 4 for 30-seconds data and 7 for 4-seconds series.

In the following step, the estimated above hidden states are assigned to traditional sleep stages via a procedure which the Authors call "*minimal supervision*". For each recording, a segment with the higher posterior probability of a given state was taken as a representative. The next step is described as "*We then assigned each hidden state the most frequent sleep stage label among these representative segments across all training subjects.*". We have 4 hidden states and 19 subjects; does that mean that for each of the 4 states the most representative segment is assigned to a sleep stage that was assigned to this epoch in most of the 19 recordings? If so, what was the variability across subjects? The hypnogram is made of 5 sleep stages, so how were the four hidden states able to distinguish them all in such a simplistic procedure?

Overall, while the level of English is good, the clarity of expression, scientific rigor, and respect for reproducibility are unsatisfactory, especially given the lack of sharing the software scripts used in this study.

Scope and results:

Authors seem to propose 3 major types of impact for their results:

1. automatization of sleep staging
2. observation of “novel features”
3. reduction of dimensionality?

As for (1.), the Authors quote relatively good concordance with human scorers — however, it was achieved only for "good" recordings of healthy subjects, with the procedure tuned for this particular set of recordings. The Authors do not seem to mention or discuss any attempt to use this model for recordings from other datasets, in the Conclusion assigning their scheme unfairly to the group of _unsupervised_ methods. There is a great multitude of less or more blind approaches to automatic sleep staging, yielding better, more generalizable, and robust results, described in articles over decades. This should be stated and addressed clearly.

As for (2.), there is an infinite number of different permutations of preprocessing/stat/ML/SP methods, which may — and many of them do — yield results somehow coherent with the tradition of

visual EEG analysis. Proposing yet another one, the authors show several plots that might provide insights into the meanings of e.g. some PCs or other parameters, but this approach does not seem to solve any real-world problems: if we find exactly that for this dataset PC2 refers to feature Y, what knowledge do we gain, and what is the relevance of such a finding for other datasets? The authors should address this question explicitly. (*I personally believe in approaches that build directly on the notions derived from the indispensable knowledge base of decades of the visual analysis of EEG, rather than trying to replicate some of its features via exotic measures of unknown neurophysiological relevance, but this is just a personal disclosure not impacting the review.*)

As for (3.), the authors indeed reduce the dimensionality from 80+ EEG channels. However, there is no hint or explanation of why such a huge number of EEG derivations was needed in the first place. It is extremely uncommon in polysomnography, which in most clinical cases relies on 1-2 EEG channels. Recording so many channels during sleep, even in a research setting — not to mention clinics – is very tedious and complicated, so this additional burden should be strongly motivated. As mentioned above, it is not disclosed what the original dimension of the features vector for each epoch was, but taking only parameters for the C3-A2 derivation (or, at most, from the 19 electrodes from the 10--20 system) might provide a simpler way of 'dimensionality reduction'. The influence of the number of EEG derivations and the size of the input vector should be very easy for the authors to verify by changing a few lines in the processing pipeline.

Clarity and other issues:

- Math/SP procedures, which seem to be the major topic of this study, are not described with clarity and reproducibility in mind, which renders them almost useless for those trying to replicate it; given that the methods are the main value in the absence of neurophysiological findings, this is a major flaw.
- There is no information on the actual dimensions of the "standardised feature matrix," that is, the actual number of parameters being fed to the next stages.
- Notation in an (unnumbered—??) equation in the section "Statistical Analysis" is not explained.

- Labels on some plots (e.g., the right panels of Fig.1) are absolutely illegible, and others are often just too small.
- "Multiple time scales" are repeated in the text several times, but only 30 and 4 second epochs were analysed, with inferior performance from the shorter epochs — ?? Such statements should be reviewed.
- What was exactly the aim of presenting ICA time courses and topographies of PC-transformed vectors of some specific parameters?

Conclusion:

At this stage, the authors should decide what the main scope and results are (for example, just to support the title — what kind of Sleep Dynamics was uncovered) and rewrite the text accordingly, possibly adding some of the suggested computational experiments. Descriptions of the methods, as the most important part of the paper, need far better clarity, which can be done at the cost of the inflated Introduction and the most speculative parts of the Discussion.

PS

Note to Editors: It is hard to refer to particular features of the manuscript, which has no page, line, and equation(!) numbers. Also, the organisation of the Supplementary Material into separately downloadable figures and a separate file with captions is very inconvenient.

Declarations

Potential competing interests: No potential competing interests to declare.