

July 5, 2022

Announcements

- Needed: You! For student panel. July 15 (Friday), 1 pm, CSE2, Room 382.
- Needed: You! As a research participant (Annika P.).
- August 17 presentations will be held in CSE2 G20 (Amazon Auditorium).

Discovery Park



Magnusson Park

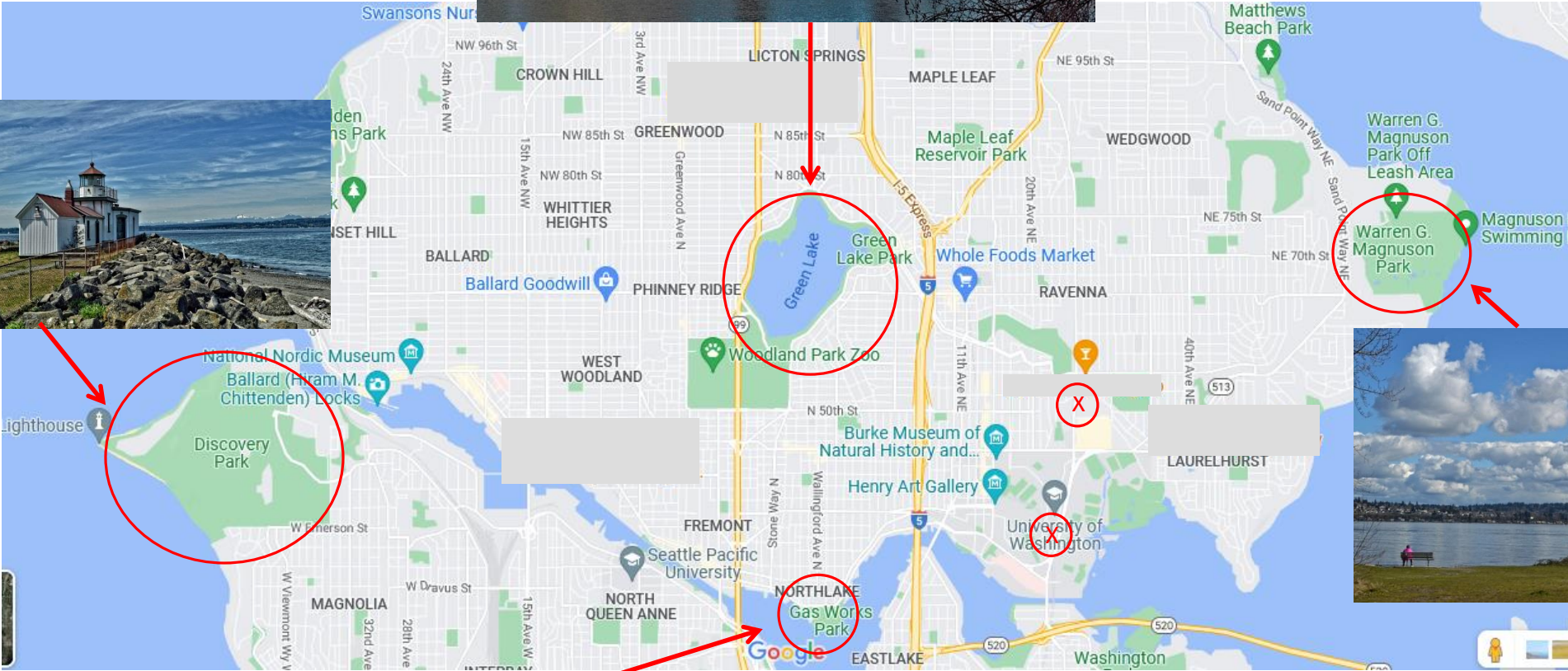


Green Lake



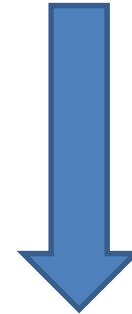
Gas Works Park



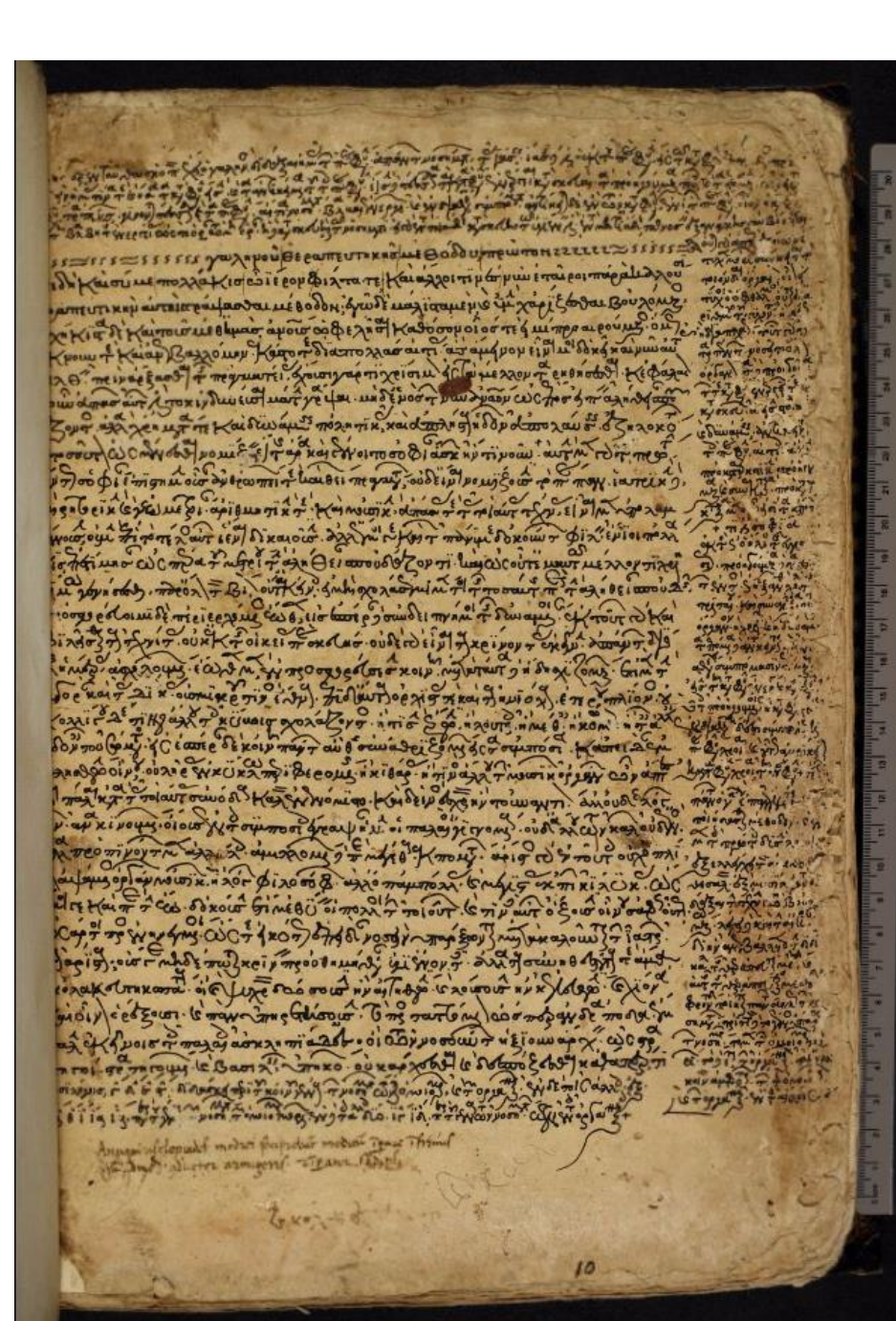


Scientific Manuscripts

- Authorship
- Parts of a paper



- Submitting papers
- Revising papers



Formatting – oh the horror

- Margins
- References
- Spacing
- Font
- Section Titles (order)

Check: Instructions (Guide) for Authors

Different journals have different formats.

Cover letter

- Does anybody read it?

Corresponding Author:
University of Washington
Seattle WA 98105

Dear Senior Editor,

Please find attached our manuscript “Spatiotemporal sleep spindle networks reflect the intrinsic connectivity revealed by waking behavior and resting state fMRI,” submitted to be considered for publication in the *Proceedings of the National Academy of Sciences*. In this study we analyzed sleep recordings from subjects implanted with electrocorticography grids for epilepsy monitoring. Taking advantage of the unique combination of resolution and spatial coverage afforded by this recording modality, coupled with a newly developed tool for analysis of large-scale neural data, we are able to report several novel and interesting results. We confirm the existence of two primary spindle sources and map their distribution across the surface of the cortex. Further, we show that sleep spindles cluster into a small number of networks and that these networks span non-contiguous cortical areas. Finally, we compare spindle networks to behaviorally-driven cortical activation patterns and to resting state fMRI functional connectivity maps. Correspondence between these spatial patterns indicates that sleep spindle networks are constrained by the same underlying functional connectivity as waking behavior and resting state fMRI. These results have important implications for our understanding of spindle-mediated functions such as sleep-memory consolidation as well as for pathologies in which abnormal sleep spindles are observed. More broadly, these results help elucidate the intrinsic connectivity of the brain and establishes a new technique for mapping this connectivity.

Thank you for considering our manuscript.

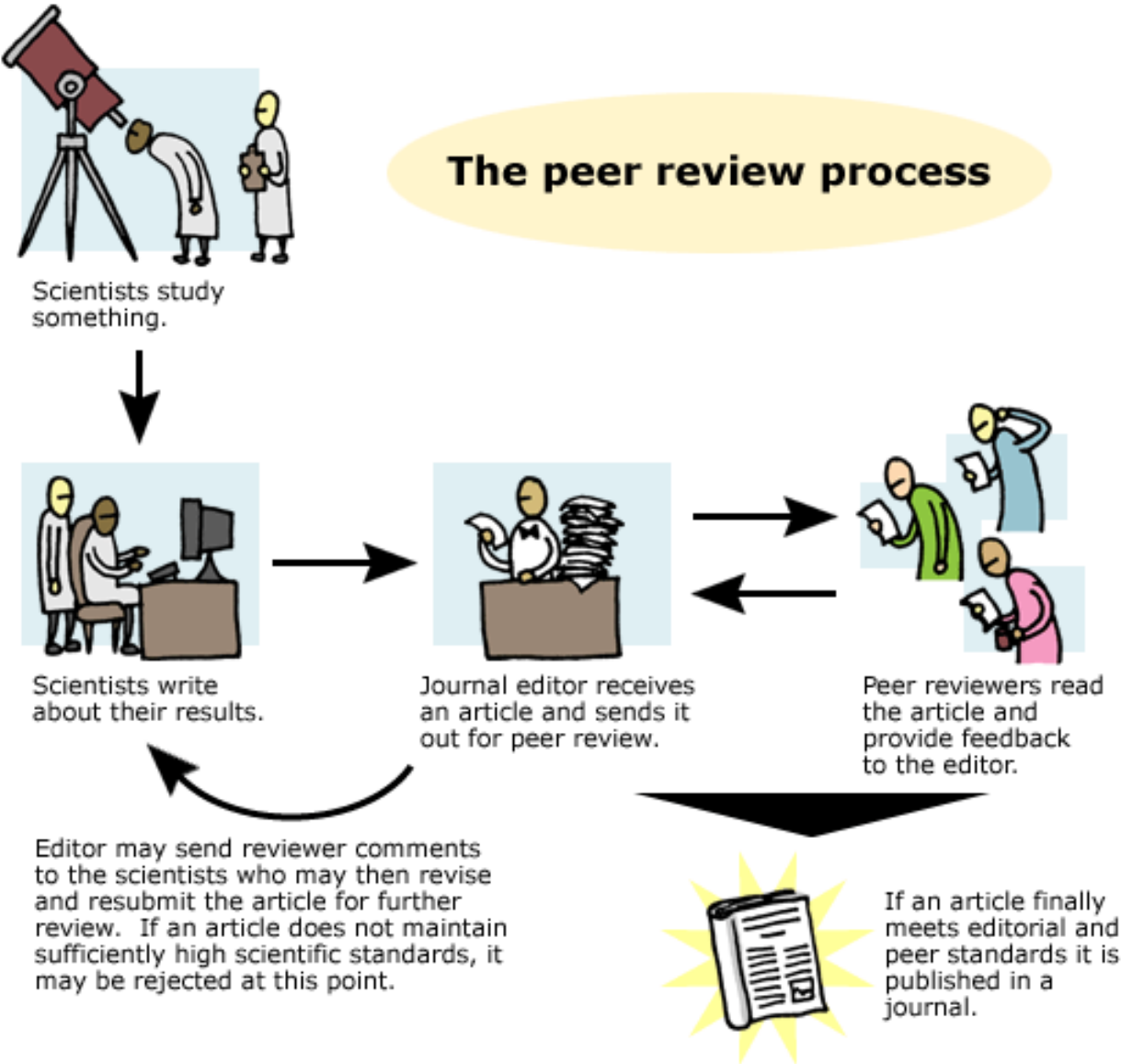
Sincerely,

XXX, YYY, ZZZ

Peer review

- Who are your “peers”

- Some actual reviews:



Reviewer #1 :

This paper attempts to determine the strength of sleep replay of behavioral patterns in the prefrontal cortex as a function of distinct brain states such as down-up shifts, K-complexes, spindles etc.

I can neither understand what the key findings are, nor assess the validity of the central claims. It seems that the manuscript is full of unsupported and arbitrary claims. Following is a partial list.

The prefrontal cortex is surrounded by many different brain regions. Show histological data to demonstrate that the tetrodes were in the prefrontal cortex and not some other area in the forebrain, which are not connected to the hippocampus and hence should not be playing any role in sleep replay or consolidation.

The silica tubing (tip diameter 125um) was much wider than the tetrode (tip diameter 25um). The tubing tip had an area of 15625 square um, whereas tetrodes tip had an area of 625 square um. So, the silica damaged 25 times more tissue than the tetrode. The tetrode protruded 1.5mm out of the silica tubing and the tetrodes reached up to 4mm deep inside the brain. So the silica tubing for each of the tetrode went in about 2.5mm through the cortex above the tetrodes, causing 25 times as more damage than the tetrode alone. Isn't this increased damage of concern? What histological procedure was followed to assess the amount of damage caused by the insertion of wide silica tubing?

Since the results depend on unit identification, provide better description and evidence of unit isolation.

Data analysis methods seem rather ad hoc. Five different methods were used to detect different rhythms: 50ms smoothing of spikes for up-down shift detection, 30ms smoothing of spike density for detecting HVS, and filtering of the LFP for detecting K-complexes and LVS in different ranges with certain thresholds. Further, the K-complexes were separated from up-down states by putting an arbitrary cutoff of 10s period between down states and K-complexes.

These methods seem hoc, highly subjective, very parameter sensitive and without clear physiological justification. The authors should use just one or two methods to do all the segregation of data and provide clear physiological and mathematical justification for the procedures and parameters used.

Yet another set of unjustified parameters (50ms smoothing for EV calculations versus 100ms binning for template matching) are used for the explained variance calculations.

The EV calculation methods refer to "R matrix" that is not defined.

The results about sleep replay of spikes are presented in a very abstract fashion. There is not a single spike raster that demonstrate the key results. This is particularly worrisome when the methods used are so ad hoc and parameter sensitive.

Reviewer #2 :

XXX et al. have investigated reactivation during nREM sleep by characterizing ensembles of cell firing in the rat prefrontal cortex. A sleep-wake-sleep paradigm was used - this allows for detecting an increase in correlated neuronal firing during sleep as a consequence of behavior prior to sleep. The key contribution of the paper is identifying during which components of the sleep the reactivation predominantly occur. Reactivation is associated with down-to-up state transitions, K-complexes and low voltage spindles - but not high voltage spindles. This is important basic knowledge providing a better understanding of the functional role of the various sleep components during nREM sleep. The data acquisition and analysis is very well done. The key components of the analysis is based on previously published techniques (e.g. explained variance) and seems very robust. The paper is clear and concise; however, the Result section is a difficult read (see below).

Specific comments

From the Table it appears that the time spent in HVS is very little compared to LVS and KC. How does that speak to the claim that reactivation did not occur during HVS; i.e. was there sufficient data to make the case?

Page 3

Introduction. Please define the frequency ranges for HVS and LVS.

Method section. The criteria for how to automatically identify the different sleep stages are clear. It is however not clear how these criteria relate to automatic detection procedures of other laboratories. How generally accepted are the criteria?

The result section is difficult to read. For instance Fig. 2 is only briefly mentioned. What do we specifically learn from the different panels (e.g. what's the point of the last panel in Fig. 2B?). I propose to better walk the reader through the figures. LVS, HVS and down-to-up transitions could be indicated directly on Fig. 3 and 4.

Page 19. 'Not surprisingly, therefore, these two parameters are correlated with each other.' Down states and K-complexes I assume? Where is this shown?

Figure 7. Why are dates for only one rat reported?

I take it is the down-to-up state being of interest. However the abbreviated title refers to only 'down states' - same in Fig 6, Discussion page 20 (line 5 from below).

Reactivation has also been found during REM. Why was REM not characterized?

Table 1. Please list units for the parameters and explain what they mean (e.g. time spent ...).

Spectrograms: color bars with units missing.

Reviewer 1:

In the MS by XXX et al the spatial distribution of spindle activity in subjects with implanted electrocorticography arrays for epilepsy Monitoring was investigated after either training or no-training on a brain-computer interface (BCI). BCI training involved either high-gamma (2 subjects) or beta/mu (1 subject) frequency. These feedback signals were produced by subjects in cortical areas coding for either tongue or hand movements.

The main findings are that the three subjects with BCI training produced on average a significantly higher rate of spindles at the electrode used for BCI control after training as compared to NREM sleep the day before training. The two control subjects did not reveal this pattern.

A second analysis calculated coincidence measures and hierarchical clustering depicted as dendrograms. Here, electrodes revealing increased spindle rate after BCI were largely also part of the same cluster.

The main message of the paper is that BCI training leads to locally increased spindle rate and greater local coincidence in post-NREM sleep as compared to pre-training sleep. An effect not observed in non-BCI training controls. BCI training consisted of positioning a vertically moving cursor within one of several target regions.

There is meanwhile convincing evidence for the local character of sleep spindles (e.g. Nir et al). Also the concept that spindle or slow oscillation activity is locally increased in an activity-dependent fashion is not entirely new. However, most of the latter studies have been conducted using scalp electrodes (e.g. Clemens., Fogel, Huber et al., Bergmann et al) or in animals (Serman et al 1970). The new elements of the present MS is that BCI can increase local spindle activity, and that this was shown with ECoG recordings.

These are very nice findings. I have however some points to be addressed:

Methods.

1. p. 15 (SI) Why was 1-6 hz used for calculating delta band power when the typical range for scalp recorded EEG is (0.5) 1- 4 Hz?

2. Probably because data from different recording devices/lab groups was used there are some reported inconsistencies: in the SOM high gamma is reported as 70-200 Hz, in the main text as 70-100 Hz. Since (in the SI) the low pass was 134.4 Hz higher frequencies could not be fully assessed.

3. Fig. 1 Subject 1 seems to show enhanced spindle rate also over the frontal cortex (a non-coincident group). The authors should investigate whether there possibly is a consistent temporal relationship on a larger time scale between these two clusters (cp. Mölle et al 2011). May the frontal group reflect activity of the (slower) frontal spindles?

4. For subjects 1 and 2 high gamma activity was used for BCI, whereas for subject 3 only beta/mu activity could be used. Also the BCI control electrode was positioned over the premotor (subjects 1 and 2: primary motor) cortex. One might assume that the strategy of subject 3 was different? Did the relationship of movement vs. imagery for BCI control possibly differ between subject 3 vs. 1 and 2?

5. Please report whether there were any consistent changes in any of the other frequency bands during the BCI task as compared to controls. This may

not be statistically assessable due to the small subject count, but at least in the SI a descriptive account should be given.

6. The discussion following Figure 1 needs streamlining. The authors summarize "The generalized nature of these results" before having given all the results. It is not until farther down that the dendrogram results are described and shown. Also the relevance of the spindle

Findings in regard to the task ("One of the unique aspects of BCI") should be given before the summary.

Reviewer 1:

This article is an important proof of concept of ECoG electrical stimulation for brain computer interfaces, and translation from animals to humans. The flow is clear, the article is well written and the results are very interesting.

However the IRB limitations prevented longer term experimentation. I am wondering whether one would see long term adaptation to the stimulation if the BCI was to be used on a day to day basis. Since ECoG stimulation is a routine test for somatosensory mapping in those patients, it would be interesting to look into the repeatability when patients have to be mapped several times, or comparing responses of a few trials with the same stimulation parameters. **This would still be far from the "continuous" stimulation needed for a BCI, but provide some insight in the adaptation.**

Reviewer 2:

In this manuscript, XXX and colleagues use ECoG arrays, implanted in human subjects over sensorimotor cortex for clinical purposes, to address whether various electrical stimulation parameters are discriminable (they are) and to inquire about the qualitative nature of the evoked percepts as parameters were varied (the subjects reported variations in intensity). **These are important results which act as a critical confirmation of and elaboration on classic findings in humans and animals. I am generally happy with the manuscript as is, but I have some comments and concerns.**

Revisions

- Be nice
- Do what you can, defend what you can't
- Respond to everything

Piled Higher and Deeper by *Jorge Cham*

www.phdcomics.com

ADDRESSING REVIEWER COMMENTS

BAD REVIEWS ON YOUR PAPER? FOLLOW THESE GUIDELINES AND YOU MAY YET GET IT PAST THE EDITOR:

Reviewer comment:

"The method/device/paradigm the authors propose is clearly wrong."

How NOT to respond:

✗ "Yes, we know. We thought we could still get a paper out of it. Sorry."

Correct response:

✓ "The reviewer raises an interesting concern. However, as the focus of this work is exploratory and not performance-based, validation was not found to be of critical importance to the contribution of the paper."

Reviewer comment:

"The authors fail to reference the work of Smith et al., who solved the same problem 20 years ago."

How NOT to respond:

✗ "Huh. We didn't think anybody had read that. Actually, their solution is better than ours."

Correct response:

✓ "The reviewer raises an interesting concern. However, our work is based on completely different first principles (we use different variable names), and has a much more attractive graphical user interface."

Reviewer comment:

"This paper is poorly written and scientifically unsound. I do not recommend it for publication."

How NOT to respond:

✗ "You #&@% reviewer! I know who you are! I'm gonna get you when it's my turn to review!"

Correct response:

✓ "The reviewer raises an interesting concern. However, we feel the reviewer did not fully comprehend the scope of the work, and misjudged the results based on incorrect assumptions."

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JORGE CHAM © 2005

Dear Senior Editor,

Please find attached our revised manuscript “Spatiotemporal sleep spindle networks reflect the intrinsic connectivity revealed by waking behavior and resting state fMRI.” The authors wish to thank the reviewers for their careful reading and thoughtful criticism of the manuscript. We have taken their suggestions under consideration and believe the manuscript is improved as a result. In response to the comments we received we have significantly revised the text, included a new Supplementary Methods section, and created several new Supplementary Figures. In particular, we have made substantial efforts to clarify the methods and quantify the results. Please note that in order to accommodate the new text we have reworked figures 1 and 4 to include only example data from one subject. The full data for all subjects has been moved to the supplementary information.

We believe that these changes address the concerns raised by the reviewers and greatly improve the overall quality of our submission. Below we have provided point-by-point responses to the reviewer comments.

Thank you for considering our manuscript.

Sincerely,

XXX, YYY, ZZZ

Reviewer #1:

Comments:

This is a well-written study with appropriate introduction and discussion. The questions addressed by this study are important and the method is original. The results are, at first glance, important and fit well with an emerging picture of spindles as distinct entities engaging different cortico-thalamic systems. However, essential elements of the methods are not disclosed, and the results are descriptive.

Methods

1. An automated method for grouping spindles would be quite useful but the actual process and results of the DMD method are unclear.

Response: We have now included more details about the DMD method both in the Methods section as well as in a new Supplementary Methods section. We have also included a supplementary figure outlining the method as a block diagram.

2. The Archiv paper states that the DMD method is actually applied to an augmented matrix (the original matrix augmented with additional time-shifted replicas of the data). Was that the case in the current study and if so how many replicas were used in the augmented matrix?

Response: Yes, the DMD method is applied an augmented matrix. We chose the number of stacks to be the smallest integer h so that $hn > 2m$ where n is the number of channels and m is the number of data points in the window. This stacking provided enough DMD modes to capture the observed dynamics. This information can be found in the Methods section of the manuscript.

3. As far as I can tell, there is nothing in the method per se that focusses on different frequencies; rather this emerges implicitly as a result of the operator relating the data matrix to its replica shifted one delta t into the past. Is this correct? If so, were modes found that were not related to spindle frequencies? What proportion of the accepted modes (i.e., accepted into the most explanatory group) were associated with spindles and what proportion were associated with other phenomena such as K-complexes, interictal spikes, or artifacts?

Response: No, it is not correct that nothing in the method focuses on different frequencies. Modes are selected based on their frequency, which must be in the subject-specific spindle band. Modes are extracted at many different frequencies; these modes form the basis of the DMD power spectrum for each window. Presumably some modes are related to K-complexes, interictal spikes and artifacts but these modes should not form a significant portion of the accepted modes because they are either in a different frequency range (K-complexes), span the entire spectrum (artifacts) or are not periodic at the spindle frequency (interictal spikes) and therefore rejected by the autocorrelation constraint. We believe that the inclusion of a schematic diagram of our detection method (figure S16) makes these points clear to the reader.

Proficiency

- Practice!
- Read some papers!



The background of the slide is a collage of various playing cards scattered across the surface. Visible cards include the 10 of diamonds, 4 of hearts, 10 of diamonds, 4 of hearts, 9 of hearts, 8 of diamonds, 4 of clubs, 7 of hearts, 5 of clubs, 8 of hearts, 3 of hearts, 5 of clubs, 6 of spades, and 10 of spades. The cards are partially overlapping and oriented in different directions.

Quiet Sorting

Nonverbal communication

Understanding your audience

- **Do not show your card to anyone.**

Without talking, sort yourselves into common “suits” (hearts, diamonds, clubs, spades)

* You **cannot** touch anyone or use anything to write.*

Without talking, sort yourselves in a line in order from low to high number.

Public Speaking



https://www.ted.com/talks/hugh_herr_the_new_bionics_that_let_us_run_climb_and_dance?language=en



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https://www.ted.com/talks/ed_boyden_a_new_way_to_study_the_brain_s_invisible_secrets/



https://www.ted.com/talks/mary_lou_jepsen_could_future_devices_read_images_from_our_brains

Public Speaking

<https://www.youtube.com/watch?v=8S0FDjFBj8o>



Will Stephen

Play (k) **NOVEMBER 2014** **NEWYORKNEWYORK**

0:24 / 5:55

CC