

FINAL DIGITAL SIGNAL PROCESSING PROJECT

ANALYSIS OF EEG SLEEP SPINDLES IN COVID-19 SURVIVORS

SOFIIA TATOSH
Department of Engineering
University of Padova
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1 INTRODUCTION

The recent pandemic with coronavirus (further - COVID-19) changed the perspective of people's life. It influenced many lives, both mentally and physically. Many who were directly exposed to the virus and were infected with COVID-19 still may suffer from post-disease consequences, so-called long COVID. According to Centers for Disease Control and Prevention (CDC), people who experience long COVID most commonly report tiredness or fatigue, fever, respiratory and heart symptoms such as cough, chest pain, digestive symptoms like stomach pain, as well as neurological symptoms that include headache, difficulty thinking or concentrating, sleep problems, dizziness when you stand up and even depression or anxiety [4].

Sleep spindles are specific brain wave patterns that people experience during certain stages of sleep. They are thought to play a role in brain plasticity, learning, and integrating new memories.

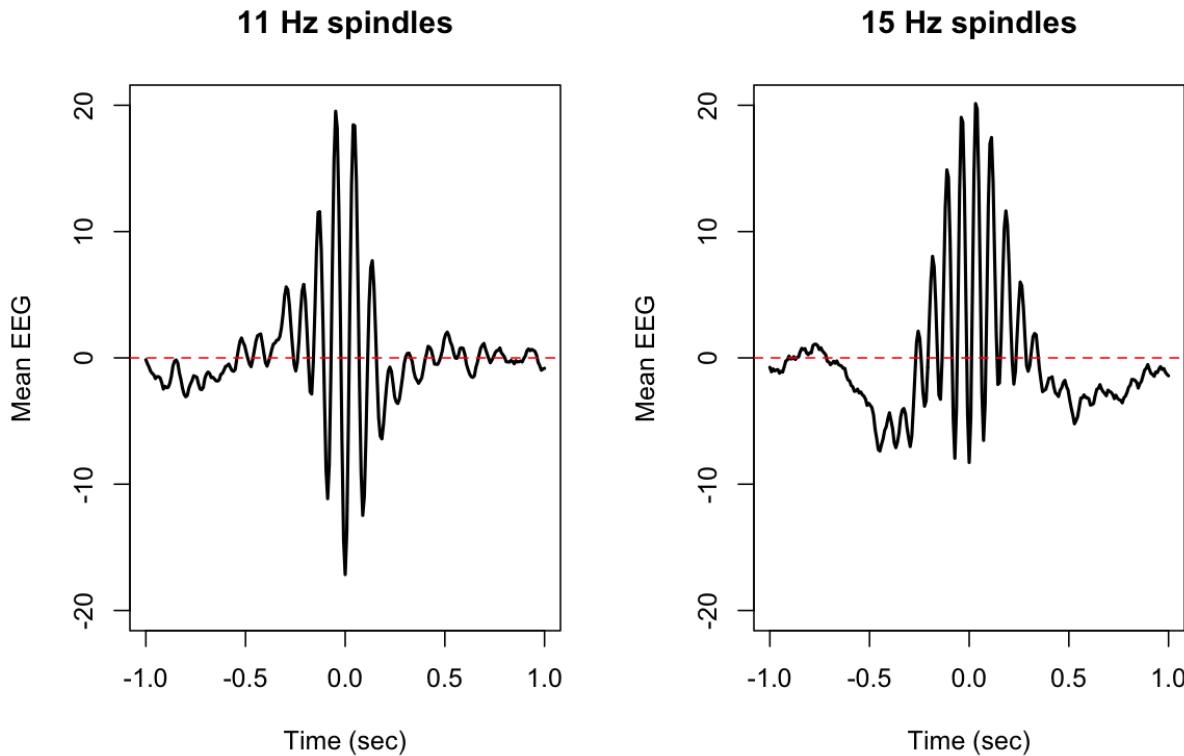


Figure 1: Example of sleep spindle in raw EEG signal [5]

Spindles are most prevalent in stage 2 sleep, which we tend to enter for the first time right after falling asleep. Unusual patterns in spindles may occur due to various factors such as aging,

chronic pain, coma, dyslexia, epilepsy, neurological or psychiatric disorders, and stroke.

Brain fog is one of the most common neurological and brain-related long COVID symptoms and affects 22% – 32% of those who contracted a disease [2]. Due to a potential relationship between sleep spindles and some of the long-term consequences of COVID-19 infection, this project investigates the differences in sleep spindles in healthy and infected subjects.

The project aimed to estimate the averaged slow and fast spindles and localize them in the inverse domain from a high-density EEG recording acquired during a nap. The data we were working on is (i) one participant discharged from an intensive care unit (ICU) due to COVID-19 infection between March and May 2020 and (ii) one participant that has never been infected by the virus.

2 METHODS

2.1 DATA PROCESSING

This section describes the steps taken to process raw EEG data and briefly describes them.

The data we were working with were high-density EEG signals with 204 channels from two subjects - one patient with a COVID-19 history (ICU subject) and the other one with Healthy Control (CTRL subject). The dataset also consists of pre-determined spindles location with 500ms duration each.

Sleep spindles are often classified into two subgroups: slow and fast-track spindles. Slow spindles ([9-12] Hz) are dominant in frontal cortical sites, and fast spindles ([12-16] Hz) are primarily distributed over parietal and central sites [6]. Thus, to work with slow and fast spindles separately, we first performed band-pass filtering for both types of waves. The algorithm was primarily to first apply a high-pass filter on the raw EEG data for the lower bound, 9 Hz for slow, and 12 Hz for fast track spindles. Then, we applied a low-pass filter on the data received from high-pass filtering for higher bound, 12 Hz for slow, and 16 Hz for fast spindles. More specifically, a Butterworth filter of order four was applied.

2.2 SPINDLES IDENTIFICATION

After the filter application, we identified low and fast spindles in our signals. For that, the dataset contains timing [in seconds] of spindles in *spindles_timing_subject_ID.mat* files. The assumption is that the spindle's duration is constant and equal to 500ms (0.5s). Since the spindles' start

points are provided in seconds, in order to extract the correct samples, we applied the following formula:

$$SS_i = \lceil t_i * SR \rceil \quad (1)$$

Where SS_i is spindle i start time in samples, t_i is spindle i start time in seconds, and SR is the sample rate equal to 250 Hz.

In order to be able to investigate and compare the brain's activation of both subjects while experiencing slow and fast spindles, we first need to calculate the power spectral density (PSD) of each EEG signal. The PSD will allow us to measure the distribution of power or energy in a signal across different frequencies. It thus will be a good representation of the filtering we performed in previous steps. Based on PSD results, we can disregard the spindles that are out of the desired frequency range and, in that way, decide which spindles were mislabeled.

We used a Welch method to estimate the power spectral density of a given signal. Because we deal with a high-density EEG with 204 channels, we first average the trial (spindle) signals between EEG channels. Since we have around 200 spindles to check, we created a function **calculate_spectrum** that performs PSD estimation and **disregard_spindles** that selects well-filtered spindles based on the PSD of a given spindle. The main algorithm behind this is after applying the pwelch MATLAB function, we look for all the peaks in estimated PSD, and for each of the peaks, we perform a check on whether this peak lies outside of the specified frequency bounds ([9-12 Hz] for slow spindles and [12-16 Hz] for fast spindles). During peak selection, a minimal peak height is required to be:

$$MinPeakHeight = \frac{(max(psd) - min(psd))}{2} \quad (2)$$

After the computational approach, we also manually reviewed all the results by visualizing the PSD, peaks, and labels (bad spindle vs. suitable spindle) (Figure 2). All the results were accepted, and everything was performed accurately.

2.3 SOURCE LOCALIZATION

In this section, after identifying spindles and disregarding meaningless ones, we look at the topographies of the outcome signal ("good" spindles' average) and perform activity localization on a 3D cerebral cortex using Brainstorm tool. These visualization approaches will enhance our understanding of where the spindles originated and allow us to see the differences between ICU and healthy subjects.

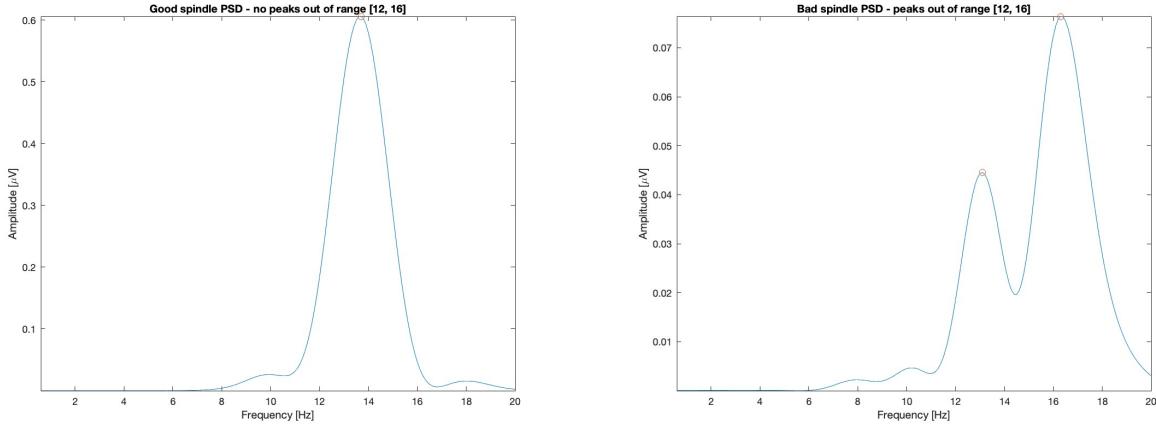


Figure 2: This figure represents two plots of estimated PSD for two different spindles - one considered a "good" spindle and the other one a "bad" spindle. For the "good" spindle, there are no peaks on the PSD plot that go out of range in this particular case (for fast spindles range) [12-16 Hz], whereas the "bad" spindle resulted in incorrect band-pass filtering and thus has peaks outside of the expected frequency range.

Topography is a method to represent how the electrical signals from different electrodes contribute to the overall EEG signal. It refers to the spatial distribution of electrical activity over the scalp. To plot the topographies we first averaged the signal over time having a mean intensity of the spindles at a particular channel.

On the figure below [Figure 3] we can observe topoplots of fast and slow spindles' spatial distribution across the scalp. The signal was obtained by averaging spindles over time at each electrode. The plots provide a visual representation of how the signal varies across different electrode locations on the scalp and hence is a significant tool to visually inspect the differences between a healthy subject and a COVID-infected patient.

While EEG topography is a great tool for investigating the spatial distribution of the measured scalp potentials, it does not involve source localization. It does not account for an inverse problem. Inverse problem in EEG is a challenging task of estimating the underlying neuronal sources of activation in the brain based on the electrical activity on the scalp. Tackling the inverse problem involves determining the spatial distribution and activation patterns of the neural sources on the cortex instead of looking at the scalp 2D plot as in topography maps. Source localization can be performed using a Brainstorm tool, which allows to directly map your data on the brain in 3D. Figure 4 represents the activity localization for ICU and CTRL subjects in slow and fast track spindles.

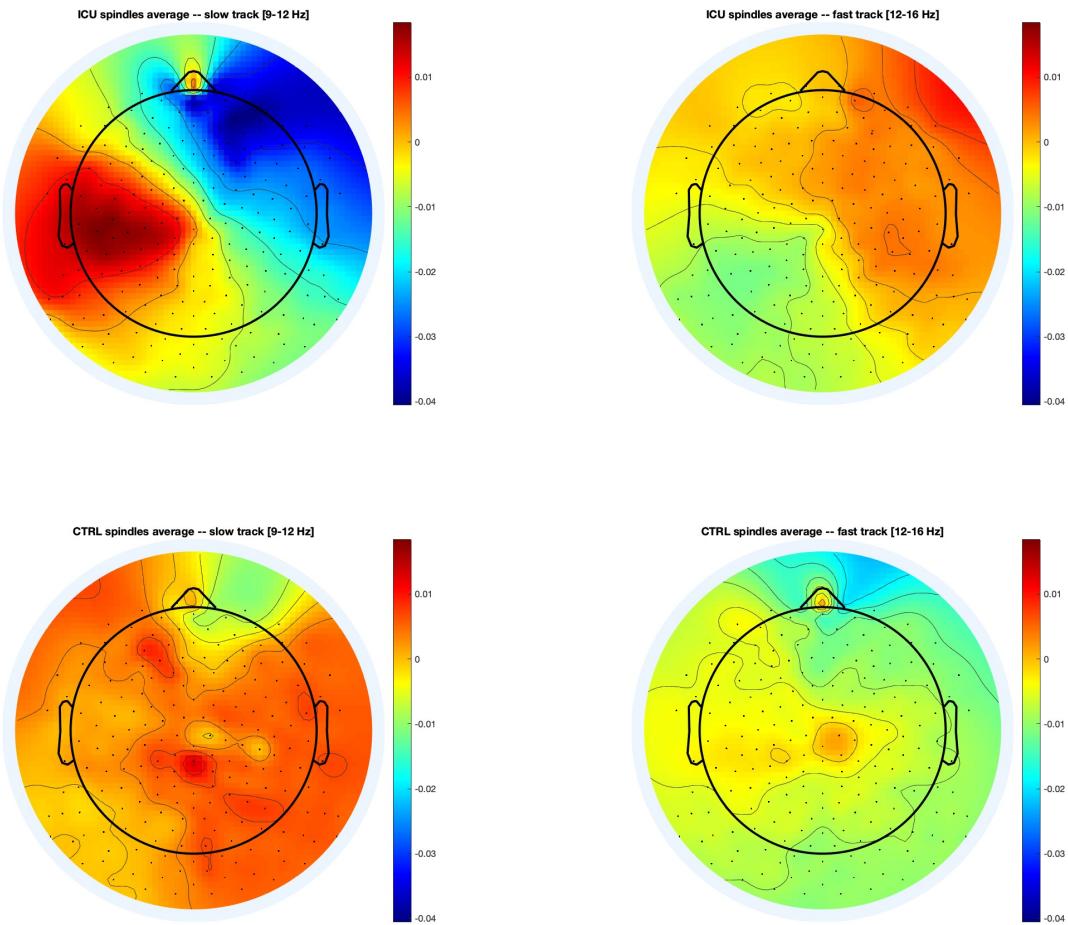


Figure 3: This figure depicts four topographies of slow / fast spindles for ICU and healthy subjects.

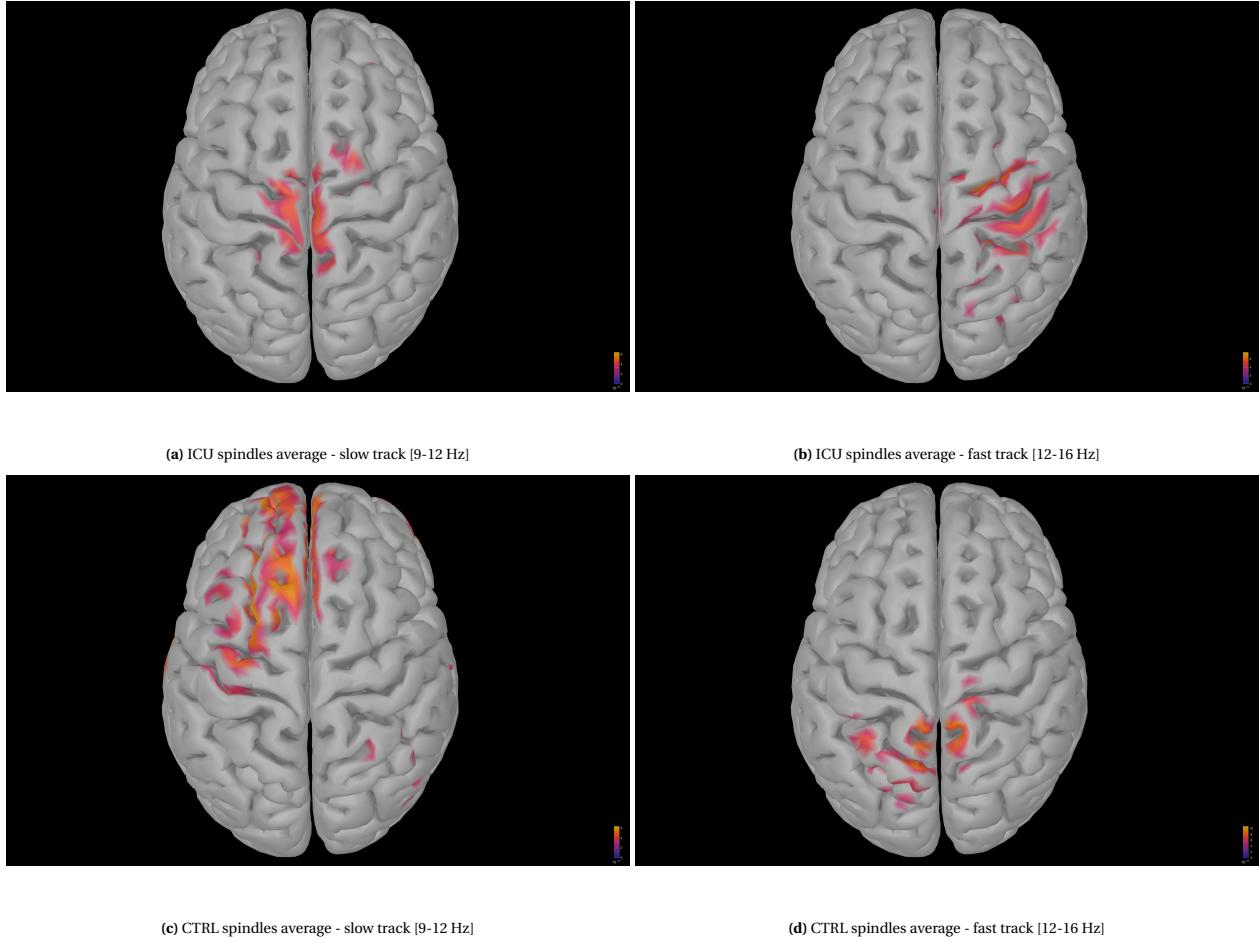


Figure 4: This figure depicts four plots of cortical activations displayed on cortex of slow / fast spindles for ICU and healthy subjects.

3 RESULTS AND DISCUSSIONS

According to the literature, sleep spindles occur due to activity in the thalamus, thalamic reticular nucleus and neocortex. Notably, slow spindles are more prevalent in the frontal region, closer to the forehead, whereas fast spindles are found in the centroparietal region [8], [7], [3]. We observe on the Figure 3 that for the healthy control, fast spindles spatial distribution across the scalp is mostly concentrated on centroparietal and temporal left lobes. For the same subject, in case of slow spindles, high levels of brain activation are located all across the scalp with prevalence in parietal and frontal lobes. Comparing the conclusions above with the topoplots of ICU subject slow and fast track spindles, we can say that the behavior of neural activity of the ICU subject is abnormal and may indicate certain cognitive deficits.

The source localization on cerebral cortex is much clearer to investigate as the activity is directly mapped on the model of the brain. From Figure 4 we can see that for the control subject, slow spindles activity is primarily generated by the frontal lobe, whereas the fast spindles are seen in a central / parietal lobes. This localization of spindles activity is expected and has been discussed above. Notably, we observe a prevalence of neural activity for ICU patients in completely different brain regions compared to the healthy control. We see that slow spindles are generated in central part of the brain and the fast spindles - in left central / parietal lobes. We can notice that for the ICU patient, both spindles are localized in the roughly the same region, which is not common for this type of wave pattern. EEG study on source localization of sleep spindles in healthy controls (Alfonsi et al., 2019) has revealed two broadly distinct cortical areas for slow and fast spindles, respectively placed in the anterior and posterior cortical brain areas. The most active source of slow spindles was found in the frontal cortex, while fast spindles range reached the absolute maximum in the parietal cortex. According to this study, the pattern observed at cortical level mirrors the appearance of spindles at the scalp level [1]. This is consistent with the idea that EEG activity reflects the synchronous activation of brain electrical generators. Indeed, this is exactly what we observe in our study.

4 CONCLUSIONS

In this work, we presented a high-density EEG data processing and analysis to investigate the differences between a healthy subject and a COVID-19 survivor. As mentioned before, sleep spindles are the main EEG patterns we analyse in this study as they are thought to be one of the primary indicators of cognitive dysfunction. In this study we researched potential consequences of a so-called long-COVID. Based on the analysis, we concluded that significant differences

present in the neural activity during sleep may indicate potential issues with memory loss, brain fog and / or neurological or psychiatric disorders.

The localization of the brain activity during experiencing brain spindles showed that the brain activation in ICU patient behaves unexpectedly compared to a healthy control, as depicted on Figure 3 and 4. Sleep spindles are known for to play a significant role in learning, memory consolidation, and sensory processing. Consequently, abnormal spindles activity result in a dysfunction of the above.

This study showed the differences between sleep spindles activity of COVID-19 survivors and those who have never had coronavirus infection. The outcomes could be exploited in further research as a template of analysis of sleep spindles, development of biomarkers of long-COVID cognitive disorders.

5 Bibliography

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