Bachelor project

Czech Technical University in Prague

F3

Faculty of Electrical Engineering
Department of Circuit Theory

Analysis of overnight electrophysiological recordings from deep brain stimulation

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Acknowledgements

I would like to express my deepest appreciation to my excellent supervisor Mgr. Tomáš Sieger Ph.D. I'm grateful for all the things, I could learn from him.

Declaration

I declare that this work is all my own work and I have cited all sources I have used in the bibliography.

Prague, May 1, 2023

Prohlašuji, že jsem předloženou práci vypracoval samostatně, a že jsem uvedl veškerou použitou literaturu.

V Praze, 1. května 2023

Abstract

Obtaining of overnight recordings from deep brain stimulation is a new source of unique data. The relation between motor activity in sleep in patients suffering from Parkinson's disease and neural electric activity in nucleus subthalamicus is a trending research topic.

This thesis examines the relation between parallel overnight recordings of electromyography and neuronal activity and neuronal activity, and their relation in individual sleep stages. The chosen methods are burst detection in neuronal activity in beta frequency band (13-33 Hz), detection of synchronised activity in electromyographic channels and subsequent parallel analysis of the individual events.

We found presence of bursts in the times of increase in electromyographic activity and specific electromyographic channels affected in different sleep stages.

All the data processing and analysis methods are implemented in the form software for Matlab.

Keywords: Deep brain stimulation, nucleus subthalamicus, Parkinson's disease, sleep, motor activity, electromyography, polysomnography, local field potentials

Abstrakt

Možnost pořizování celonočních záznamů z hluboké mozkové stimulace je záležitostí posledních několika let a poskytuje tedy unikátní data. Vztah motorické aktivity ve spánku u pacientů s Parkinsnovou nemocí a neurální elektrické aktivity v subthalamickém jádře je stále zdaleka nevyčerpané téma.

Tato práce zkoumá celonoční paralelní elektromyografické a neurální nahrávky a hledá mezi nimi spojitost a případnou specifickou vazbu na různá spánková stádia. Jako metody volí detekci salv v aktivitě v nucleus subthalamicus na beta frekvenci (13-33 Hz), detekci synchronní aktivity v elektromyografických kanálech a následnou paralelní analýzu jednotlivých událostí.

Výsledkem je pak nález výskytu salv v časech zvyšující se elektromyografické aktivity a ovlivnění rozdílných elektromyografických kanálů v různých spánkových stádiích.

Veškeré zpracování dat a analyzační metody jsou zpracovány jako softwarový nástroj v Matlabu.

Klíčová slova: Hluboká mozková stimulace, subthalamické jádro, Parkinsonova nemoc, spánek, motorická aktivita, elektromyografie, polysomnografie, lokální potenciálová pole

Překlad názvu: Analýza celonočních elektrofyziologických záznamů z hluboké mozkové stimulace

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ZADÁNÍ BAKALÁŘSKÉ PRÁCE

I. OSOBNÍ A STUDIJNÍ ÚDAJE

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Studijní program: **Lékařská elektronika a bioinformatika**

II. ÚDAJE K BAKALÁŘSKÉ PRÁCI

Název bakalářské práce:

Analýza celonočních elektrofyziologických záznamů z hluboké mozkové stimulace

Název bakalářské práce anglicky:

Analysis of overnight electrophysiological recordings from deep brain stimulation

Pokyny pro vypracování:

1. Familiarize yourself with the treatment of Parkinson's disease (PD) using deep brain stimulation (DBS), and the electrophysiological signals recorded overnight from PD patients treated with DBS: local field potentials (LFP) from DBS electrodes and parallel polysomnography (PSG) signals.
2. Explore LFP and PSG recordings, identify segments suitable for further analysis, and preprocess them, if necessary. Visualize the signals in time and frequency domains with respect to the progression of the patients' sleep.
3. Estimate the relation between LFP and patients' motor activity. Is the relation specific to different sleep stages? Note that while REM and NREM sleep (and motor action during the sleep) differs in healthy subjects, this distinction can be disrupted in PD.
4. Implement the methods used in steps 2 and 3 in the form of well-documented Matlab functions.

Seznam doporučené literatury:

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[5] Baumgartner AJ, et al. (2021) Basal Ganglia Local Field Potentials as a Potential Biomarker for Sleep Disturbance in Parkinson's Disease. Front. Neurol. 12:765203. doi: 10.3389/fneur.2021.765203
[6] Chen R, et al. Clinical neurophysiology of Parkinson's disease and parkinsonism. Clin Neurophysiol Pract. 2022 Jun 30;7:201-227. doi: 10.1016/j.cnp.2022.06.002.

Jméno a pracoviště vedoucí(ho) bakalářské práce:

Mgr. Tomáš Sieger, Ph.D. Analýza a interpretace biomedicínských dat FEL

Jméno a pracoviště druhé(ho) vedoucí(ho) nebo konzultanta(ky) bakalářské práce:

Datum zadání bakalářské práce: **31.01.2023** Termín odevzdání bakalářské práce: **26.05.2023**

Platnost zadání bakalářské práce: **22.09.2024**

Mgr. Tomáš Sieger, Ph.D.	doc. Ing. Radoslav Bortel, Ph.D.	prof. Mgr. Petr Páta, Ph.D.
podpis vedoucí(ho) práce	podpis vedoucí(ho) ústavu/katedry	podpis děkana(ky)

III. PŘEVZETÍ ZADÁNÍ

Student bere na vědomí, že je povinen vypracovat bakalářskou práci samostatně, bez cizí pomoci, s výjimkou poskytnutých konzultací. Seznam použité literatury, jiných pramenů a jmen konzultantů je třeba uvést v bakalářské práci.

. _____
Datum převzetí zadání

_____
Podpis studenta

Chapter 1

Introduction

Deep brain stimualion (DBS) is a way of treatment for patients suffering from Parkinson's disease (PD). It consists in implanting wires into brain. Tips of these wires serve as electrodes that can stimulate a small portion of brain around them. This modality is used to block pathological activity. New DBS devices have also the option to record local potential. In this thesis I discuss analysis of such recordings in relation to motor activity during different sleep stages.

Motivation

Current research in DBS is focused on developing adaptive close loop systems that would increase the efficiency of stimulation and battery usage. Local field potential (LFP) recording option in neurostimulators is a fairly recent feature and analysed recordings are usually of tens of minutes in length. This makes our overnight 7 hours long recordings very rare and gives this project's results potential to contribute to future implementation of real time symptom-specific adaptive software, which would ease patients from having to switch between stimulating regimes and setting up stimulating parameters [1].

Objectives

1. Familiarize yourself with the treatment of Parkinson's disease (PD) using deep brain stimulation (DBS), and the electrophysiological signals recorded overnight from PD patients treated with DBS: local field potentials (LFP) from DBS electrodes and parallel polysomnography (PSG) signals.

2. Explore LFP and PSG recordings, identify segments suitable for further analysis, and preprocess them, if necessary. Visualize the signals in time and frequency domains with respect to the progression of the patients' sleep.

3. Estimate the relation between LFP and patients' motor activity. Decide if the is specific to different sleep stages.

4. Implement the methods used in steps 2 and 3 in the form of well-documented Matlab functions.

Chapter 2
Medical Background

2.1 Introduction

Deep brain stimulation as a way of treatment of Parkinson's disease is still a relatively young approach. Even though first attempts to electrically stimulate the central nervous system can be dated as far as 70 years back, its widespread clinical use can be seen only in the last 10-15 years. In these years huge advancements in electrode construction and battery life were key for subsequent progress of clinical knowledge [1].

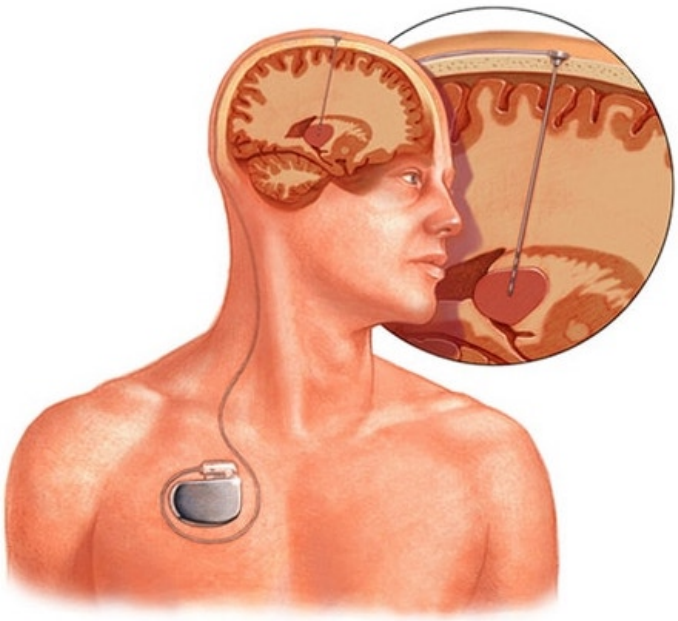

Figure 2.1: Illustration of implanted DBS device, note 3 main parts, battery and wires implanted under the patient's skin and stimulation electrode implanted into the patient's brain [2].

2.2 Parkinson's disease

Parkinson's disease is a chronic neurological disorder with mostly motor symptoms. It's worldwide prevalence is increasing faster than any other neurological disorder. Between 1990 and 2016 the prevalence increased 2.4 times. Peak prevalence age of PS is around 87 with PS occurring very rarely in patients under 50 years. PD is usually diagnosed when motor symptoms such as bradykinesia, rigidity, rest tremor and postural instability occur. Non motor symptoms include loss of smell, sleep dysfunction and psychiatric disturbances such as depression and dementia.

2.2.1 Pathophysiology

Parkinson's disease is characterised by the death of dopaminergic neurons due to intraneuronal inclusions of protein aggregations. These inculions are called Lewi bodies and consist of α-synuclein. Therefore we can see PS as a metabolism deviation. Other neurotransmitter systems such as acetylcholin and serotonin systems are affected as well and can not be affected by dopamine substitution therapy. Degenerative changes start in medulla oblongata and bulbus olfactorius which causes early non motor symptoms such as loss of smell. Later affected area is substantia nigra pars compacta (SNc), which is a part of basal ganglia and its down-production of dopamine causes motor symptoms. Nucleus subthalamicus (STN) is a brain gray matter structure that is hugely affected by dopamine deficiency, degeneration of SNc causes forming of pathological activity in STN that is related to motor symptoms, especially bradykinesia and rigidity. Last symptoms are cognitive, they occur with cortex degeneration [3], [4].

2.2.2 Treatment

All therapy that is available is symptomatic. Future medication, that targets metabolic pathways and prevents from inclusion forming is still not accessible. The core of toady's therapy is dopamine substitution which helps mostly with motor symptoms, but it also affects psychiatric symptoms. If the patient is resistant to dopamine therapy, or a wear off effect is present, then DBS is a method of choice. Also comorbidities, mobility, compliance and life expectancy are important criteria. Therefore DBS is a therapeutic option that is used in younger patients with well documented and defined PD and its symptoms [3].

2.3 Deep Brain Stimulation

Basic principle of DBS is delivering electric impulses to focal brain region. DBS is an invasive therapeutic option, which requires neurosurgical implantation of electrodes to a very specific location. Precision is achieved by electrophysiological and stereotactical guidance. Neurological programming

and regular neurological checkups done by neurologist specialised in invasive neurology follow after the surgery. There are two paths of improving effectiveness of stimulation, first is electrode engineering and the other are adaptive stimulating algorithms using real time sensing of local activity [1], [5].

2.3.1 Construction

Neurostimulator consists of two main components a battery which is implanted in a subcutaneous pouch under right clavicle and two stimulating electrodes, which are implanted into the brain and connected by a subcutaneous wiring to the battery. Battery life improvement was a huge milestone. It enabled other hardware and later software research to be done. Also thanks to modern neurostimulators lasting more than 5 years without changing battery and therefore preventing from frequent small surgical procedures, it is a huge benefit for the patient's comfort. No official standard is condensed, but representative stimulating electrode is 1.27 mm in diameter and has 4 stimulating circular contacts distanced about 1 mm from each other in the long axis of the electrode. These contacts are radially divided into 3 subparts, that can be controlled individually [1]. The layout is called "directional electrode" and it enables neurologist to arrange stimulating electric field in all 3 space dimensions to achieve best possible clinical effect. But the direction of the electric field is only a secondary positional adjustment, most of the targeting is done during implantation.

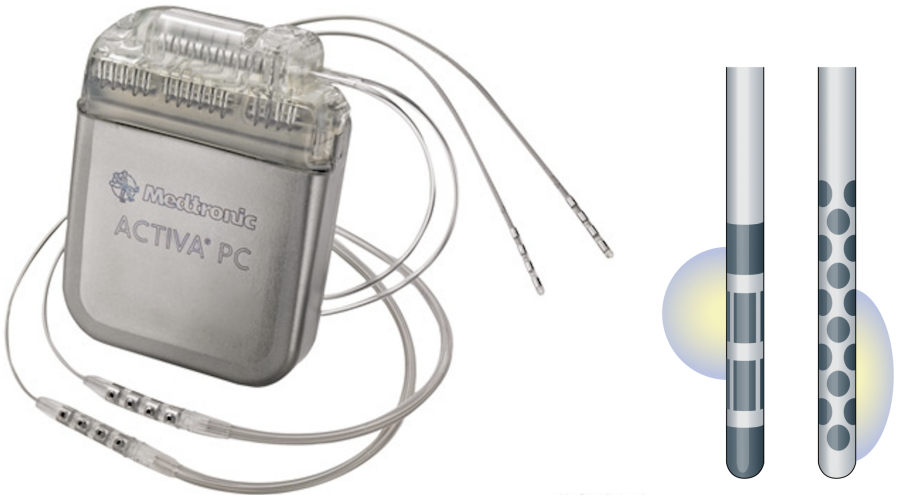

Figure 2.2: Image on the left shows construction of a neurostimulator, wires connect the battery and the electrodes [6]. Image on the left is a scheme of possible contact arrangement of stimulating electordes. [1] Blue object with yellow center is the expected volume of activated tissue (VAT), see in 2.3.4 Programming.

2.3.2 Biocompatibility

Implantation of electrodes, subcutaneous battery and wiring can cause infection and local foreign body reaction. But only in case of the electrodes it can affect the quality of stimulation. Infection can occur days or weeks after surgery and is taken care of by neurosurgeons. Electrodes can be made of platinium-iridium wires and nickle alloy contact are encased in polyurethane sheath as described in literature [1], but no universal standard is present. After implantation an interface between the electrode and the brain tissue develops. The interface changes in time because of oedema and glial reaction. The oedema forms shortly after implantation and lasts for weeks. The glial reaction causes changes in order of months. Also matrix proteins and ionic interactions with electrodes play a role in local impedance. It is not unusual that electrodes can lose functionality of one or more contacts, fortunately it is usually not crucial for the therapeutic effect.

2.3.3 Sensing

New advanced electrodes are capable of sensing local field potentials (LFP). The LFP signal comes mostly from action potentials of the local population of neurons [7]. Because of the periodical nature of the neuronal signal, the most important information about firing activity is the frequency and amplitude. Compared to other methods of recording electric activity in the brain (electroencephalogram (EEG) or even to electrocorticogram (EcoG)) LFP gives much more precise but also very spatially localised information. The sensing capacity never serves as an indication for electrode implanting [8].

2.3.4 Programming

There is a great variability in possible stimulating settings [1]. Besides the above mentioned 3D electric field setting, which changes the volume of tissue activated (VAT) - VAT is a 3D representations of the shape of the current electric field 2.2, also the frequency (around 100 Hz used) and the amplitude (usually around 3 mA) can be specified. Neurologists can also choose between constant current and constant voltage setting, but due to better stimulating consistency with constant current most patient have this set up. Due to inconsistent nature of PD symptoms during the day, during different activities and simultaneous use of medication, there is a need for stimulation that adapts to ongoing situation. One solution that is used today consists of patient manually switching between 2 or more regimes dedicated to specific activities and also manually increasing or decreasing stimulating current amplitude - within limits set by the neurologist. Adaptive and close-loop stimulation based on real time sensing and feedback to bodily movement would greatly improve the overall effect but it is still in development and is not used in patients.

2.4 Sleep stages

Sleep is a vitally important state of body which is crucial for resting and regeneration of the nervous system as well as almost every other system and tissue in the human body. The sleep is a cyclic phenomenon with a period of one day. It consists of 2 main stages. For one of them rapid eye movement is typical and gives it its name - REM (rapid eye movement). The other is non-REM (NREM) which is further divided into 3 categories. The time structure of sleep has periodic character as well. It cycles through its phases about 5 times with each period having the same phases only with different duration. With each cycle REM stage gets longer at the expense of the other stages. The quality of sleep has a huge influence on the human health but it is also influenced by many neurological (PD) and other medical conditions as well as medication and aging. One of the conditions that is common and heavily affects the quality of the sleep is sleep apnea - a condition in which a lack of breath forces patient to wake up many times at night.

Description of sleep stages

1. N0 or S0 - Wake/Alert is the first stage of every sleep recording. The EEG recorded in this stage demonstrates dominant beta waves (13-30 Hz) when eyes are opened. When eyes are closed and the patient is getting drowsy, alpha waves (8-12 Hz) become dominant.

2. N1 or S1 - While patient is in Light sleep, skeletal muscle tone is present and theta waves (4-7 Hz) are characteristic. This stage usually lasts from 1 to 5 minutes.

3. N2 or S2 - Deeper sleep lasts about 25 minutes and it is the longest sleep stage. Long delta waves are characteristic (0.5-4 Hz) and the muscle tone is decreasing.

4. N3 or S3 - Deepest non-REM sleep, this phase is dedicated to resting and regeneration and also has the highest threshold for awakening. Delta waves with low amplitude are characteristic, the muscle tone is even lower compared to the previous stage.

5. REM - For REM, beta waves are characteristic, all muscles except for muscles in the eye socket are atonic. The first cycle lasts about 10 minutest, each following cycle gets longer and the 5th cycle lasts about 1 hour. [9].

2.4.1 Parkinson's disease and sleep

Sleep disturbances are numerous in patients with PD, about 70% of them suffer from some sleep problem. Compared to healthy people, PD patients have shorter and more fragmented sleep [10].

REM sleep disorder

Some medical conditions including PD can lead to disruption of the atonic state. It can manifest itself only with EMG-registered muscle movements but also with acting out dreams through complex movements or vocal expressions.

Destroyed sleep architecture

The sleep apnea is known to destroy sleep architecture by making the patient wake up many times during the night and therefore not letting him to advance to deeper stages and stay in them. Also, spontaneous arousals (wake up reactions) are more frequent in PD patients [10].

Restless leg syndrome

Higher prevalence than in normal population, makes this syndrome one of possible causes for late onset of sleep [10].

Nocturnal limb dystonia

Nocturnal limb dystonia is a painful limb increased tonus, which can occur as an off symptom (blood level of medication lowers).

Tremor

Termor usually ceases in S1 or its amplitude is decreased.

Other motor abnormalities

Increased muscle tone, blinking and even complex movements can occur during the onset of REM stages. Prolonged tonic contractions can be seen during NREM. [10]

2.5 Polysomnography

Polysomnography (PSG) is diagnostic tool in sleep medicine. it includes continuous recording of multiple parameters during sleep. For the purpose of this thesis only EMG channels were used. Other channels include ECG, oxygenation, eye muscle EMG, breathing and video recording.

Chapter 3

Data

For the analysis we used two sources of signals. First one was DBS sensing and the other were certain EMG channels from PSG. Both of the signals were recorder over night while the patients were sleeping. The recordings were approximately 8 hours long.

3.1 Gathering of the data

A patient suffering from PD was invited for one night to a sleep laboratory. PSG was done by a nurse and DBS recording was done by me (6 patients) or another technical worker. After connecting the communication device to the neurostimulator it was necessary to tap the monitor every 40 minutes to prevent it from aborting the data stream. Another inconvenience was that after 4 hours of recording we had to end the streaming session, disconnect the communication device and restart recording. This was due to the limited capacity of the communication device to hold data before saving them into files.

3.1.1 Hardware

DBS recording setup included Percept™ PC neurostimulator with BrainSense™ technology, a small communicator, that wirelessly received LFP data from the the neurostimulator, created a data stream and send it via Bluetooth to a tablet, where the data was saved into JSON files. [11], [8].

3.2 DBS recordings

We expected to see artefacts from DBS stimulation, which had the frequency of 130 Hz. It was planned to synchronise both recordings by abruptly decreasing the stimulation to 0 mA and then immediately increasing the stimulation back to its former value. But the technique proved wrong, because it was not possible to detect the artefacts in EEG. So this method of synchronisation failed and we had to rely on the time of creation of the files. But there was another problem, now in the DBS communication device, in most cases the

internal time of the device was wrong. This left us with usable recordings from only 2 patients for the thesis out of 20 (6 of them were recorded by me).

3.2.1 Preprossessing the raw data from DBS recordings

Recordings were saved in JSON format, which contained a large structure of data. One 8 hour recording was stored in about 2 to 3 JSON files. I used only the "BrainSenseTimeDomain" (BSTD) record type, which referred to the raw voltage data recorded by the neurostimulator. and "BranSenseLFP" (BSLFP) record type, which referred to the power of the frequency of interest that was set by a neurologist as the marker of pathological activity in the STN, this frequency was unknown to me.

BSTD

BSTD had the sampling frequency of 250 Hz. BSTD was streamed in the form of packets that usually contained 62 or 63 samples. I observed that some (less than 5) packets were missing in almost every JSON file. To prevent frame shift, I filled the missing packets with NaN values. To create spectrograms in Matlab I chose to replace NaN values with the average non-NaN value of the analysed segment. Other packets were missing during pauses inbetween JSON files. Another difficulty were huge peaks in both right and left BSTD of Patient 1 see in figure 3.1. Fortunately, the recordings of the sleep stages of our interest did not contain any of peaks.

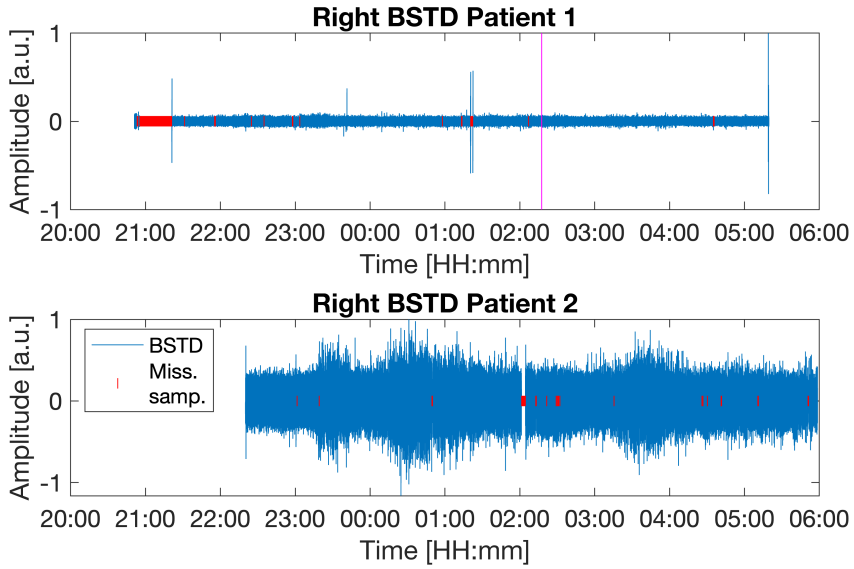

Figure 3.1: BSTD signals from the stimulating electrode in the right hemisphere from both patients. . Huge peaks of LFP in Patient 1 are artifacts. Detail at magenta highlighted time in figure 3.2 and spectrogram in figure 3.3.

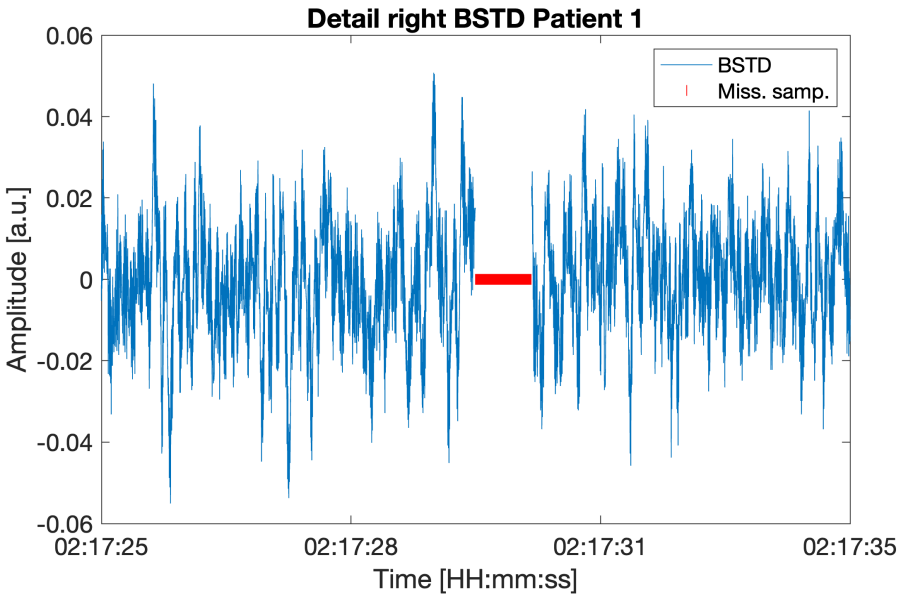

Figure 3.2: Detail of Right BSTD signal of Patient 1 with missing samples. Full signal in figure 3.1.

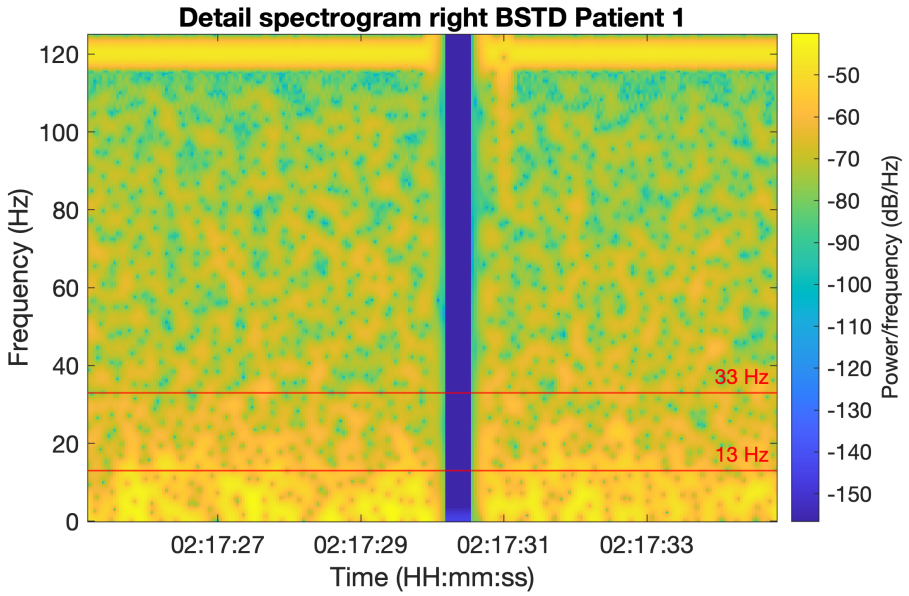

Figure 3.3: Detail spectrogram of right BSTD of Patient 1 in 3.2. Full signal in 3.1. We can see red lines on 13 Hz and 33 Hz, that delimit beta frequency band. I focused on this frequency band wit my analysis.

3.2.2 Pathological Beta

According to prof. MUDr. Robert Jech, PhD., lower beta (13-33 Hz) activity in STN is a reliable marker of pathological activity, and when STN is free from the beta, then the patient is free from the PD symptoms. I found

this information also in literature [12], [13]. In spectrogram 3.3 we see the frequency range that is most likely to cause sleep motor disruptions: 13-33 Hz. We can also observe high power of DBS stimulation (130 Hz), that is aliased on 120 Hz and a gap in data caused by the missing values in BSTD.

BSLFP

BSLFP had the sampling frequency of 2 Hz and had no missing samples, see in figure 3.4. The relatively lower sapling frequency was due to averaging done by the device over unknown window of time.

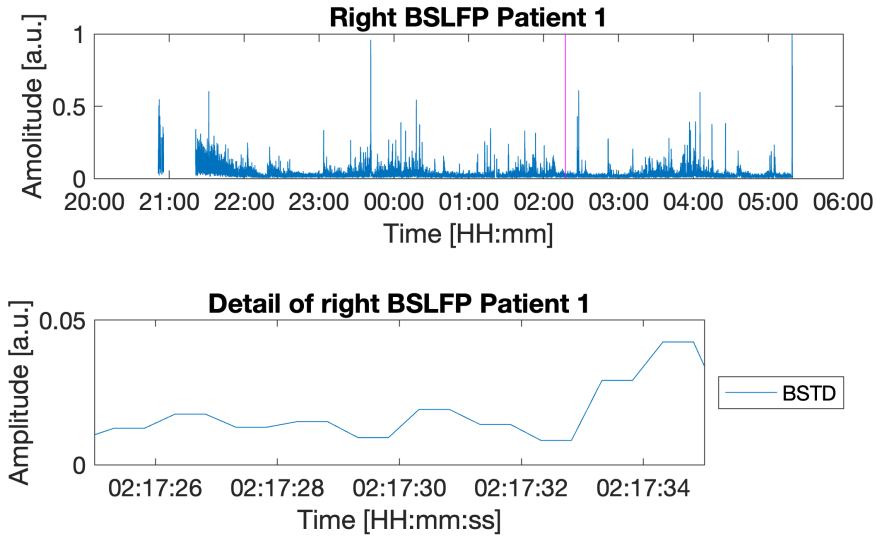

Figure 3.4: Right BSLFP of Patient 1, detail at magenta highlighted time.

3.3 EMG recordings

Recordings were saved in EDF data format. The sampling frequency was 200 Hz. No values were missing. We used only EMG channels of the chin and legs. The chin had 3 electrodes on it, anterior, left and right. Each leg had one electrode detecting action potentials in musculus tibialis anterior.

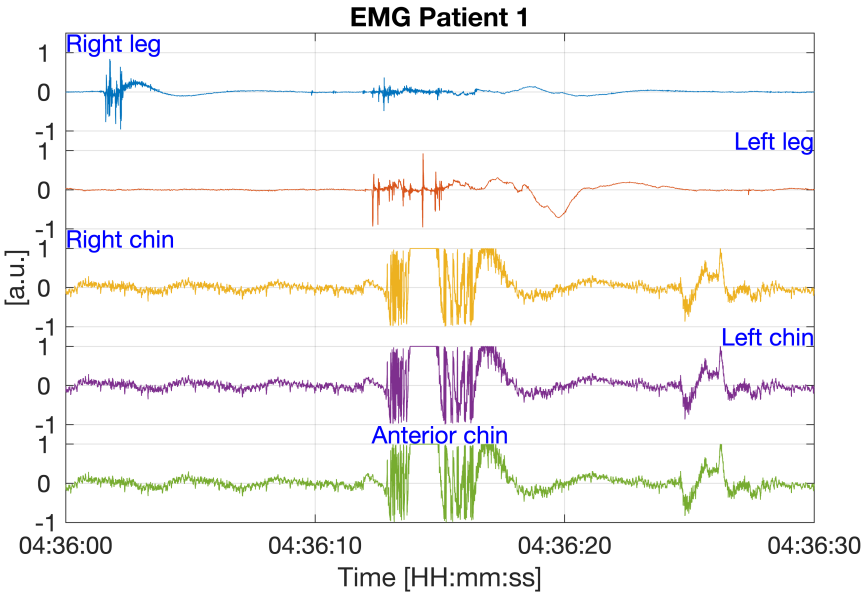

Figure 3.5: All EMG channels of Patient 1, motor activity in all channels at 04:36:15.

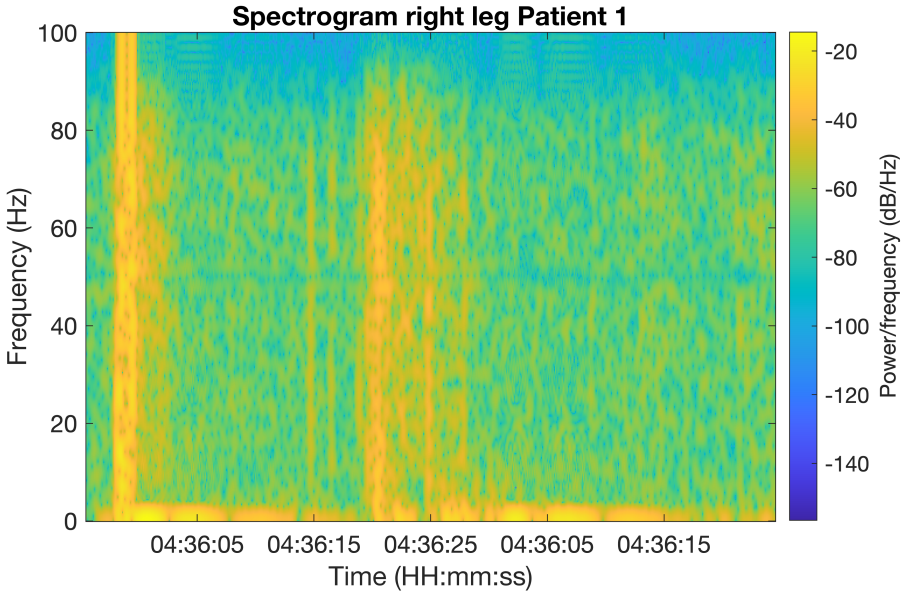

Figure 3.6: Spectrogram of EMG channel left leg Patient 1 shows no specific frequency related to motor activity.

While observing spectrogram of EMG channels I did not find any specific frequency related to the motor activity, example of motor activity in EMG 3.5 and spectrogram 3.6. Therefore I decided to find motor activity in EMG in time domain.

3.4 Sleep and motor activity annotation from expert

We were provided with sleep stages annotation and in case of one patient also with movement activity annotation done by a neurologist. It had the form of a table in TXT format. To be sure, that annotated segment are not disrupted by the activity from different sleep stage, we had to crop 10 minutes in the beginning and at the end of the segment.

Chapter 4

Methods

Introduction of the main methods, that were used to process and visualise the signals and to find connection between motor and LFP activity in different sleep stages.

4.1 Fourier analysis

Fourier analysis is a mathematical approach, that is based on decomposing any function into a sum of sinusoids with complex coefficients. Each of these sinusoids has a different oscillation frequency. We can assume on what kind of information is represented in each sinsoid based on its frequency. Low frequencies hold most prominent contours whereas high frequencies hold information about detail contours of the function. In case of frequency of 0 Hz the sinusoid hold information about constant shift on y axis equal to the coefficient of the sinusoid. The set of coefficients is called spectrum, it holds information about how much are different frequencies represented in the analysed function and about the phase shift of each frequency.

Summed potentials from neuronal populations recorded over meaningfully long period of time tend to have periodical nature. Our data is no exception and given the information about pathological beta in subsection 3.2.2, we can assume, that frequency analysis is a good approach for fulfilling the goal of this thesis.

4.1.1 Discrete Fourier transform DFT

Discrete Fourier transform is a way to compute the coefficients of sinusouids for a discrete finite signal. Therefore is widely used in digital signal analysis and a suitable method for our data (BSTD).

$$X[k] = \sum_{n=0}^{N-1} x(n) e^{-j\frac{2\pi nk}{N}}, k \in \langle 0, N-1 \rangle \tag{4.1}$$

Equation 4.1 describes DFT, X[k] is a discrete spectrum, N is number of samples of the original signal, x(n) are samples of the original signal.

$$x(n) = \frac{1}{N} \sum_{k=0}^{N-1} X[k] e^{j \frac{2\pi n k}{N}}, n \in \langle 0, N-1 \rangle \tag{4.2}$$

Equation 4.2 describes an inverse discrete Fourier transform (DFTINV), which is a way of reconstructing discrete finite signal from discrete finite spectrum. x(n) is a a reconstructed discrete signal, N is number of samples of the discrete spectrum, X[k] are coefficients of the sinusoids (discrete spectrum).

4.1.2 Fast Fourier transform FFT

Is on of the most important algorithms in digital signal processing. It has been published in 1965 and has been heavily used in signal analysis since then. It introduced fast reliable algorithm, that has been implemented, among many others, into MATLAB. Time complexity of FFT is $\mathcal{O}(N \log N)$ and time complexitiy of DFT is $\mathcal{O}(N^2)$, where N is number of analysed samples.

4.2 Spectrogram

Spectrogram is a convenient tool for observing frequency changes in time. It is widely used in signal analysis and relies on FFT.

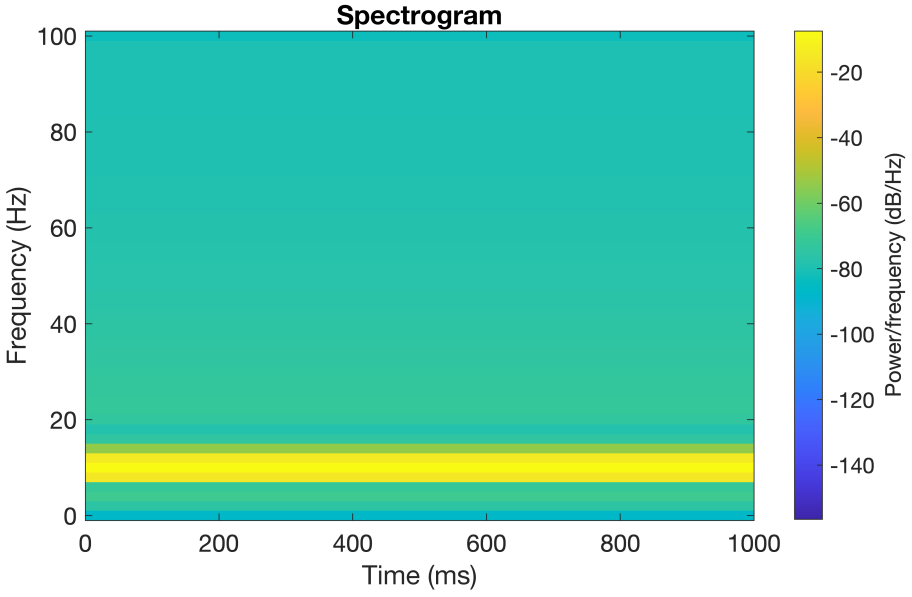

Figure 4.1: Example of spectrogram of signal $sin(10 \cdot 2\pi t)$, see in figure 4.2, no overlap, time window is 100 ms (20 samples). We can see a high power band around 10 Hz.

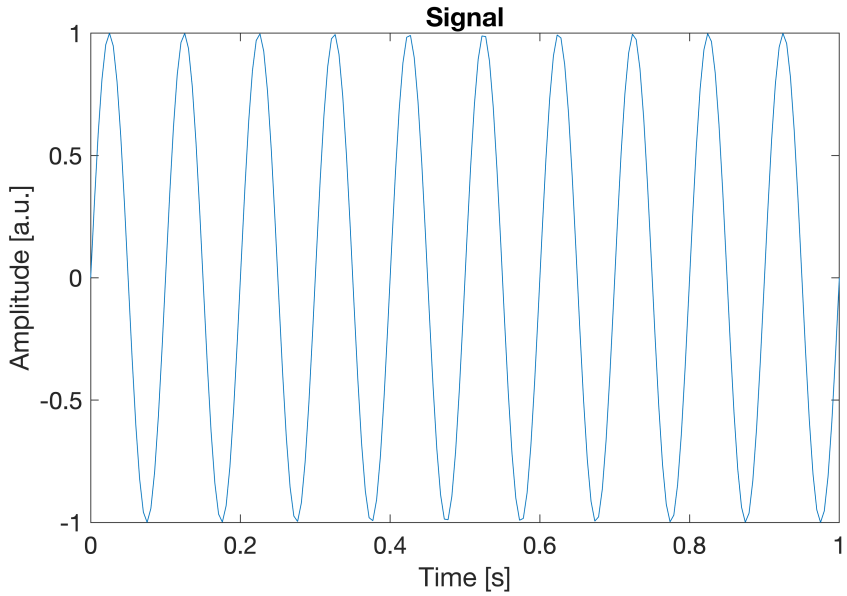

Figure 4.2: Example of signal $sin(10 \cdot 2\pi t)$ for spectrogram, the frequency of the signal is 10 Hz, the sampling frequency is 200 Hz.

4.2.1 Principle

Signal is split into segments of beforehand specified duration. On each segment is applied FFT. This provides us with an 2 dimensional array, where one axis represents time segments and the other corresponding spectrum. Spectres get usually squared to obtain power and for highlighting differences in absolute coefficient values.

Both time and frequency axis are discrete and we have the option of setting parameters of frequency and time to affect resolution in both dimensions. But we are limited by uncertainty principle, higher resolution in one aspect is at cost of the resolution in the other one.

Frequency axis

Frequency axis can be influenced by 2 parameters, sampling frequency and length of the segment of the signal. Because of Nycquisg - Shannon sampling theorem we can represent on spectrogram only frequencies, that are at least twice lower than the sampling frequency.

$$f_{max} < \frac{f_s}{2} \tag{4.3}$$

The longer the segment of the signal is the better frequency resolution we get. It is due to the equation 4.1, which states, that more signal samples mean more spectrum samples. But there is a method to increase frequency resolution without setting wider time window, it consists in extending each segment with nulls. This operation results in "inserted" samples into the spectrum.

Another way to increase information value is to apply Hamming window on each segment, which decreases weight of samples on the edges of the segment.

We have also the option to use spectrogram for extracting certain frequencies. Then we are provided with power of the signal in the specified frequency band.

Time axis

Time axis resolution can be increased by the length of the segment. Also implementing overlap in the signal segments can increase time resolution, but lowers the differences in amplitude between each segment.

4.3 EMG activity

My approach to define what is a motor event was based on both my observations of the signals and on annotations provided by neurologist. Unfortunately the annotations form neurologist were not completely covering the whole recording. Because the amplitude of EMG signals can be either positive and negative, but both mean motor activity, I applied square on the signals.

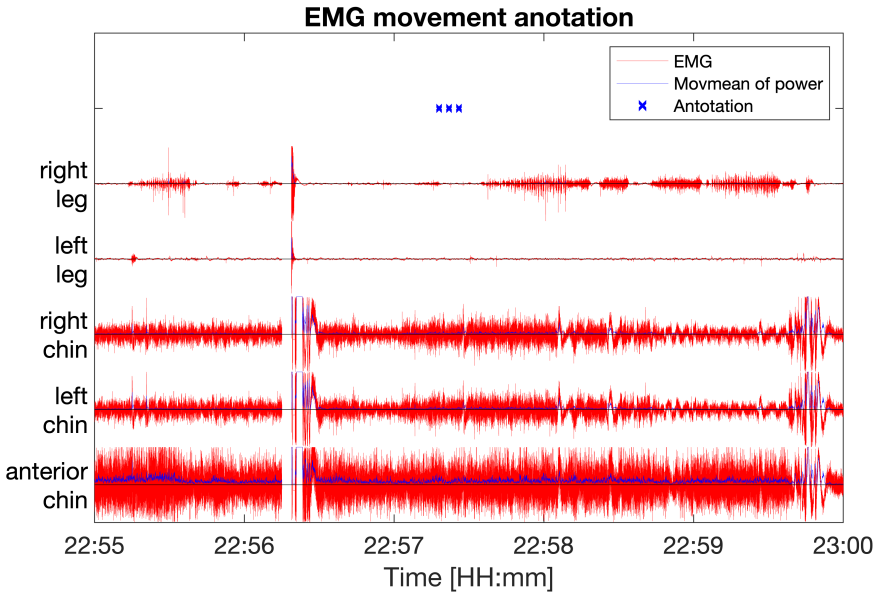

Figure 4.3: Example of EMG event annotation, moving average is computed from symmetrical 30 sample wide window

In the figure 4.3, we can see that some annotated events do not need to match with high power activity in EMG. I could see the same arrangement of activity in multiple channels of EMG and annotation from neurologist nearby on many occasions. Multiple annotations meant longer duration.

Definition of EMG event

I decided to define motor event as an activity, that ocures in all chin channels and at least in one leg channel and beginning of all motor activities are within 5 seconds from each other.

4.4 LFP activity

As discussed in 3.2.2 beta band of 13-33 Hz is most likely to be associated with pathological motor activity. Based on this I extracted beta band from spectrogram. This provided me with power in beta frequency of the original BSTD signal. I divided the signal into 2 bands:

- Upper beta: 21-33 Hz
- Lower beta: 13-21 Hz

To define what is an event in beta, I got inspired from literature [14].

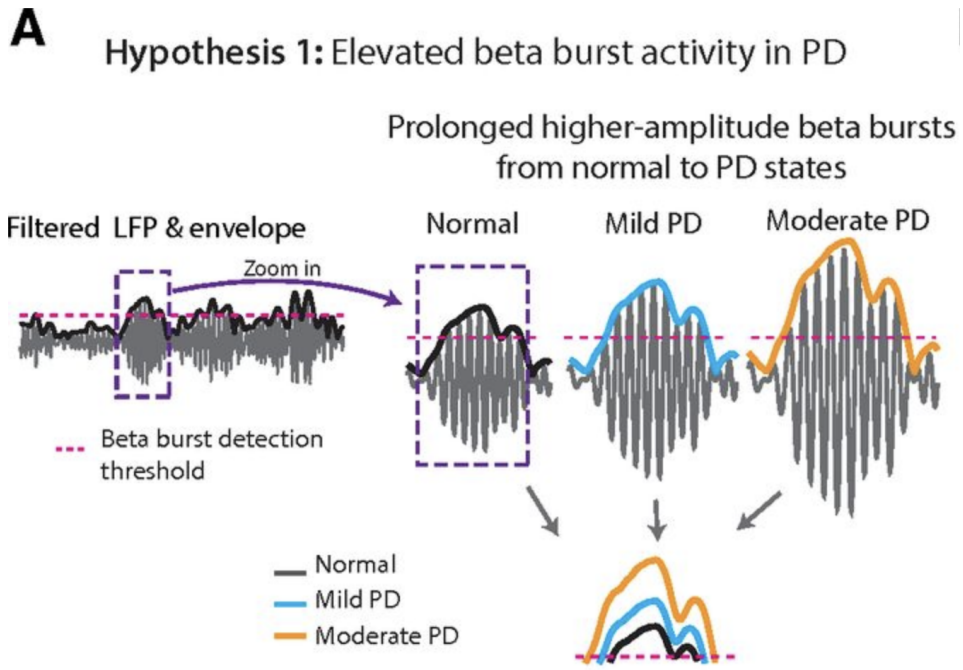

Figure 4.4: Inspiration on beta activity interpretation [14]

My definition of event is based on, that the activity in STN has burst-like character. It means, that solitary peak has no effect, but cumulation of peaks with short time distances between then can cause pathological motor activity. To represent such nature of the power in beta band I used moving average, to be precise I used moving average twice with 50 samples wide symmetrical window.

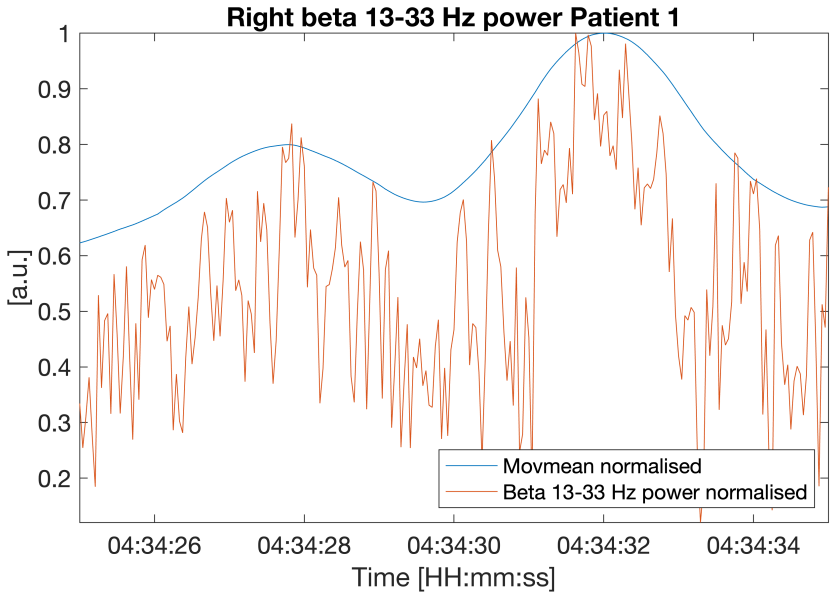

Figure 4.5: Example of right beta 13-33 Hz power Patient 1 and moving mean with symmetrical window 50 samples wide, applied twice. Movmean normalised refers to dividing the movmean signal with its largest values in analysed segment.

4.5 Activity detection

There are many ways of detecting activity. One that comes to mind is detecting peaks in a signal. A peak can be detected multiple in ways with each having its benefits and downsides.

First method than came to mind was to decide, if current sample is peak or not, based on percentile of its value related to the whole signal or analysed segment. This method can work well for signal, that does not change basal activity over time. In my case both EMG and LFP beta power changed basal activity. So I chose the option to compare each sample to its local neighborhood.

Also comparing samples to their neighborhood can be done in multiple ways. I chose to set the time window only before the analysed sample. This approach has one important aspect, that is very beneficial for my data. It detects increases in amplitude. It means, that even if the analysed sample has lower than average value in symmetrical time window around it, the sample can still be detected.

To make the test more robust I added, that the detected sample has to be higher than moving average increased by a variable number of standard deviations of the moving set. The number of standard deviations was set for EMG and LFP beta power separately.

$$X[n] > average(X[n-w,\dots,n]) + k \cdot std(X[n-w,\dots,n]) \qquad (4.4)$$

$X[n]$ is current analysed sample, w is number of samples in the time window

before analysed sample, k is number of standard deviations, std is standard deviation. The Truth is, that this method does not detect a real peak, but a beginning of the peak.

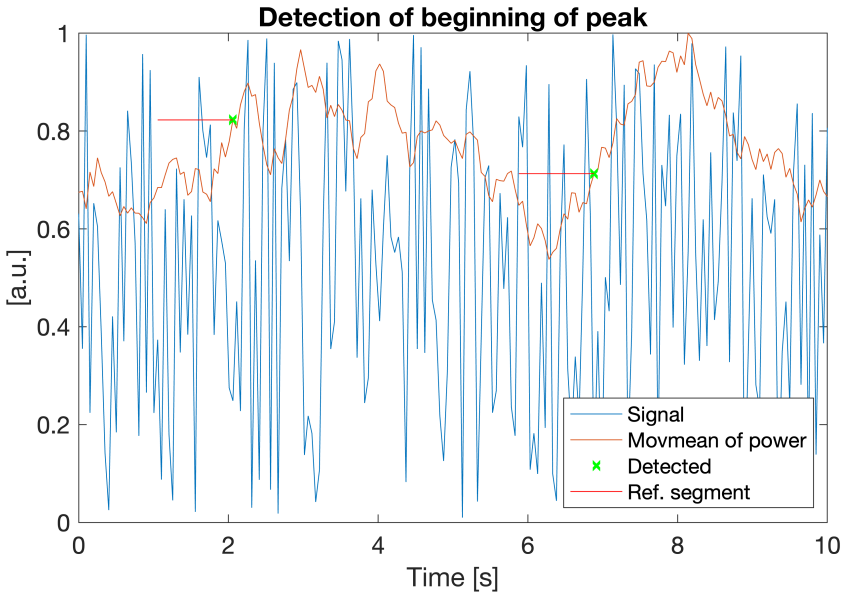

Figure 4.6: Example of detection of the beginning of peaks, referential time window is set to 1 s, averaging window is symmetrical and 30 samples wide and sampling frequency of the signal is 20 Hz.

After observing the signals and possible events I found out, that events are usually solitary in time and consist of a lot of peaks. Therefore only detecting peaks would lead to detection of excessive number of false events. This finding led me to applying moving average, which caused visual smoothing of the signal and the new curve hovered over the low values in between peaks.

Another conclusion I made after observing the signals was, that the events have variable length, and not always have the highest amplitude in the beginning. Based on this finding I decided to detect the beginnings of peaks instead of real local peaks, I expected the parallel modality to have a linkage rather to the beginning of the peaks than to the highest value. I also added, that peaks can not repeat for certain amount of time.

4.6 Statistics

4.6.1 Normal distribution

Normal distribution is one of the most important models of nature in statistics and probability. It can be observed almost everywhere and also is used in almost every field of engineering. It serves as one of the most important standards of what we should expect from the distribution of measured data.

$$f(x) = \frac{1}{\sigma\sqrt{2\pi}} e^{-\frac{1}{2}(\frac{x-\mu}{\sigma})^2} \tag{4.5}$$

f(x) is probability density function, σ is sample variance, μ is sample mean.

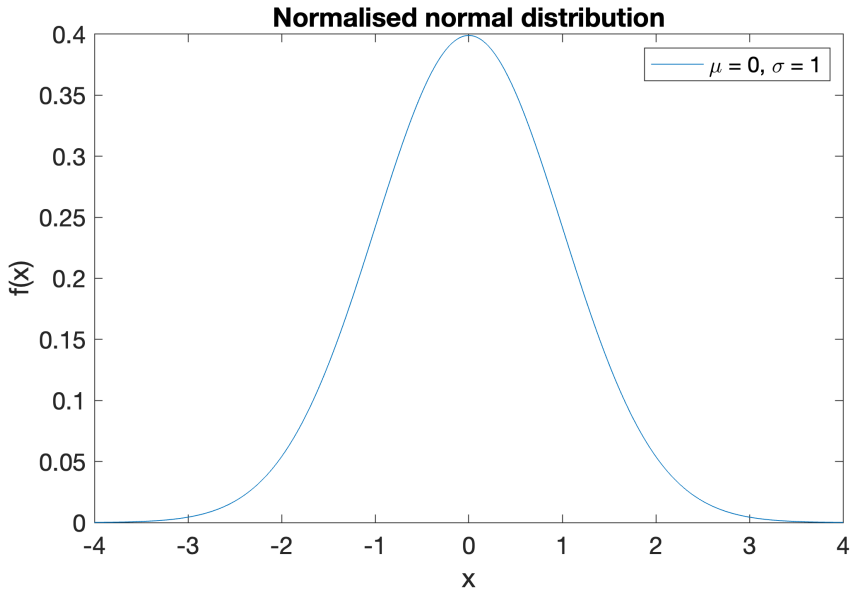

Figure 4.7: Example of normalised normal distribution and p value.

Scaling

Sometimes scaling needs to be performed to make the distribution of measured data closer to the normal distribution.

Functions I used to to scale the data:

- log(x)
- log(log(x))
- square root

4.6.2 Hypothesis testing

At the beginning of hypothesis testing we specify the alternative hypothesis, which is the proclamation which we want to prove. Then we specify the null hypothesis, so that it is a negation of alternative hypothesis. When the null hypothesis is rejected, we accept the alternative hypothesis. When the null hypothesis is not rejected, we reject the alternative hypothesis.

To decide if we reject the null hypothesis we use statistical tests. Based on our decision there can be 2 types of error:

- Type I error: the tested null hypothesis is true, but we reject the null hypothesis
- Type II error: the tested null hypothesis is false, but failed to reject it

4.6.3 Significance level

Significance level, is a value belonging to interval $\langle 0, 1\rangle$. It sets the limits of how strict we are when finding arguments, that go against our null hypothesis. With increasing significance level we increase the chance of type I error, with decreasing significance level we increase the chance of type II error.

4.6.4 P-value

P-value belongs to interval $\langle 0, 1\rangle$. It is the largest significance level for which our test rejects the null hypothesis and accepts the alternative hypothesis. If the p-value is smaller than the significance level we set, then we decide to reject the null hypothesis in favour of the alternative hypothesis.

4.6.5 T-test

T-test is a statistical test, that uses Student's distribution to decide, if sample mean of our data $\bar{X}$ is equal to mean μ_0.

$$T_0 = \frac{\bar{X} - \mu_0}{S_n}\sqrt{n} \tag{4.6}$$

$\bar{X}$ is sample mean of the tested data, μ_0 is mean towards which we test our hypothesis, S_n is sample standard deviation of the tested data, n is number of samples. To obtain valid decision from applying the t-test, we need the distribution of analysed data to be close to normal distribution. Based on what is the percentile of the T values in Student's distribution, we decide on, if we reject our null hypothesis.

In my thesis I used t-test to decide, if the mean of samples in a given time is equal to the mean across of the whole segment. I set the alternative hypothesis, so that mean value of signals in given time is not equal to μ_0.

4.7 Layering

This method is used when we want to compare same length segments of the same signal and to observe if the segments contain some common pattern. We need a set of time events, around which we create the segments. The time events can come from the analysed signal, for example when we want to see, if there is some similarity in peak shape. Or the events can come from another signal, in this case we are observing, if there is a linkage between the signals.

So to realise such visualisation we need to create a 2D array, that contains all the segments around events. Then we create average segment. This gives us basic idea of the shape of the patterns, if there are any. To differ significant and insignificant increases and decreases, we use a statistical tests, for example t-test. But at first we need to subtract the average value of all the segments from each sample in the 2D array, this way we set the whole

segment average to 0. Then we calculate the t-test on each column of our 2D array, in other words we apply it on each set of samples from the given time.

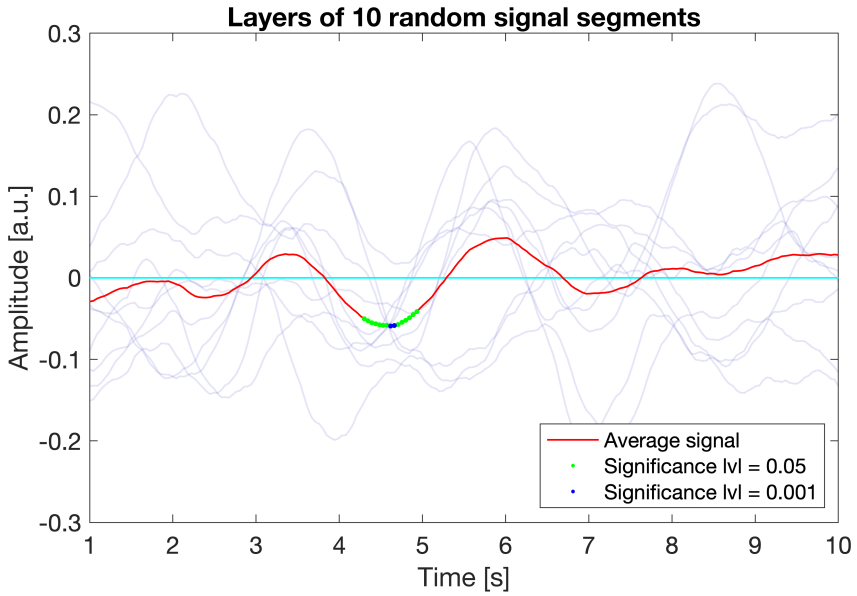

Figure 4.8: Example of layering of segments of signal. T-test was applied with different significance levels.

The same can be done with the whole spectrogram. To highlight where the deviation is significant we can use the t-test too. Only difficulty is in creating 3D array, because spectrogram of a single segment is already is a 2D array. Then for visualisation of significant increases and decreases we can plot only the values in which we reject the null hypothesis.

Chapter 5

Results

Most of my result are visual to easily demonstrate region of significant changes of amplitude of the signal in time. To fulfill this task the detecting methods are crucial for obtaining relevant results.

5.1 LFP activity detection

I did not know, how high the amplitude of burst should be and I did not want to miss any bursts. Because of this I tried to detect almost every visually notable burst. To achieve it I set the following parameters:

- Time window for calculation of local average before each sample: **10 s**.
- Time window of forbidden sample detection after each detected beginning of peak: **1 s**.
- Number of standard deviation added to local average: **1**.

For more parameter description see section 4.5.

In the figure 5.1 we can see two detected bursts. The second one is the ideal burst, that I would like my method to detect. But in the case of the first peak the detection could be rightfully doubted.

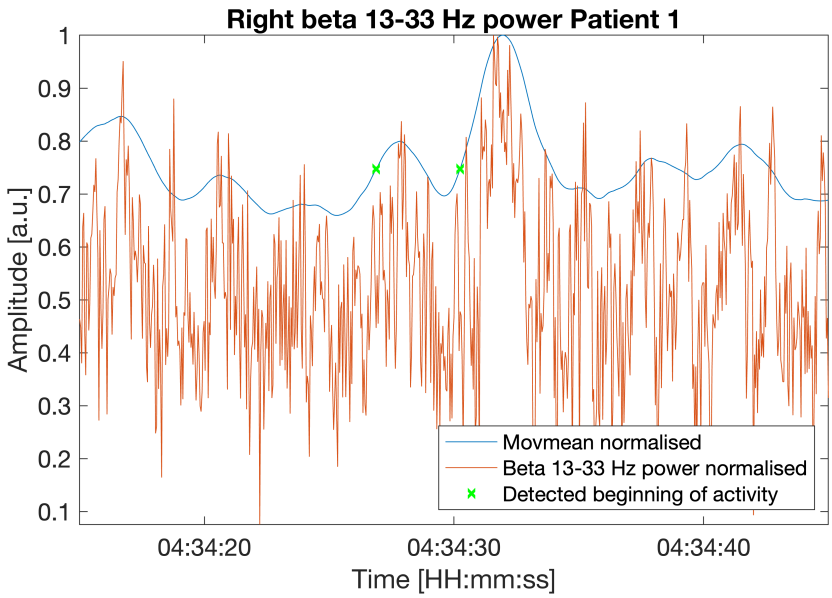

Figure 5.1: Example of results of my LFP beta power activity detecting method, referential window is 10 second before each sample.

5.2 EMG event detection

I tried to detect only the most pronounced EMG activities. To achieve that, I focused more on the actual relative increase in amplitude of each channel than on synchronisation. The setting of parameters for obtaining my results:

- Time window for calculation of local average before each sample: **30 s**.
- Time window of forbidden sample detection after each detected beginning of peak: **3 s**.
- Number of standard deviation added to local average: **5**.
- Tolerance of time distance between two detected samples: **5 s**.

For more parameter description see section 4.5.

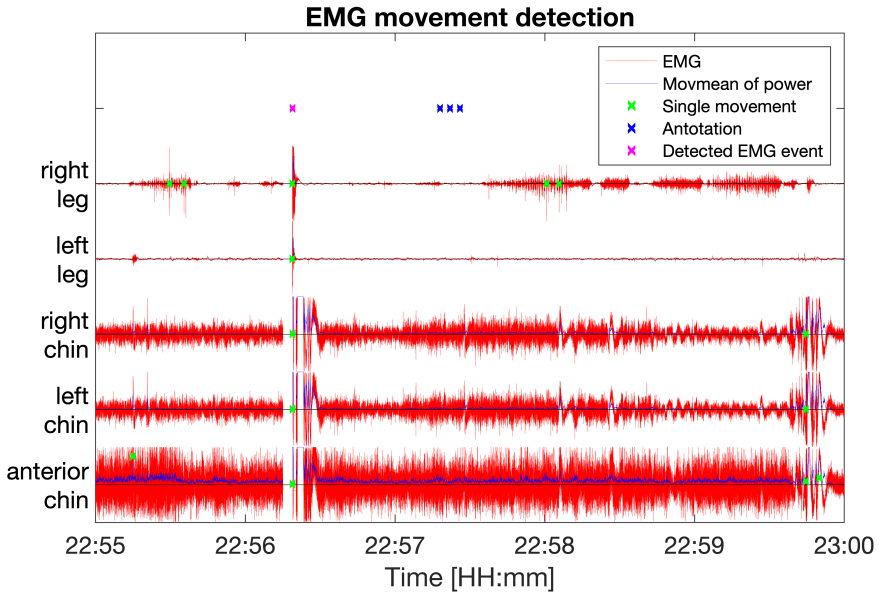

Figure 5.2: Example of results of my EMG event detecting method.

In the figure 5.2 we can see one perfect example of the functionality at 22:56:20. EMG activity is detected in each channel and the EMG event is set, so that it marks the beginning of all EMG channel activities. In the case of detection at 22:59:50 the activity is registered in all the chin EMG channels, in the left leg EMG channel is correctly not registered, but the registration in the right leg EMG channel is questionable.

5.3 Sleep stages summary

5.3.1 Hypnograms

To see what sleep stages are available I created a hypnogram for each patient.

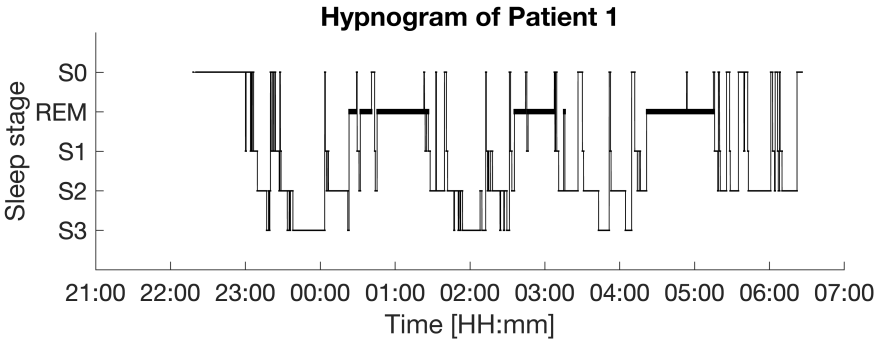

Figure 5.3: Hypnogram of Patient 1, we can see mostly segments of constant annotation, that are usually shorter than 30 minutes.

5.3.2 Patient 1

I possessed with only 3 usable sleep stages, because I had to accept only the segments of sleep that had constant sleep stage annotation. So to get a segment of 10 minutes in length, I had to find segment of 30 minutes in length with constant stage annotation.

Sleep stage	S3	REM #1	REM #2
Duration [mm:ss]	05:29	17:25	11:59
PSG actions count	23	7	5
LFP burst count right (13-33 Hz)	30	89	13
LFP burst count left (13-33 Hz)	29	82	15
LFP burst count right (13-21 Hz)	27	84	19
LFP burst count left (13-21 Hz)	27	69	14
LFP burst count right (21-33 Hz)	22	38	9
LFP burst count left (21-33 Hz)	24	40	1
Average right LFP power(13-33 Hz)	0.3169	0.4760	0.4809
Average left LFP power(13-33 Hz)	0.1515	0.2092	0.2591

Table 5.1: Summary of sleep stages Patient of 1.

Large amount of EMG events detected in S3 is caused by a limitation of my EMG activity detection. I detected relative increases in amplitude, if the amplitude on EMG channel was consistently very low in the whole segment, I detected excessive number of increases.

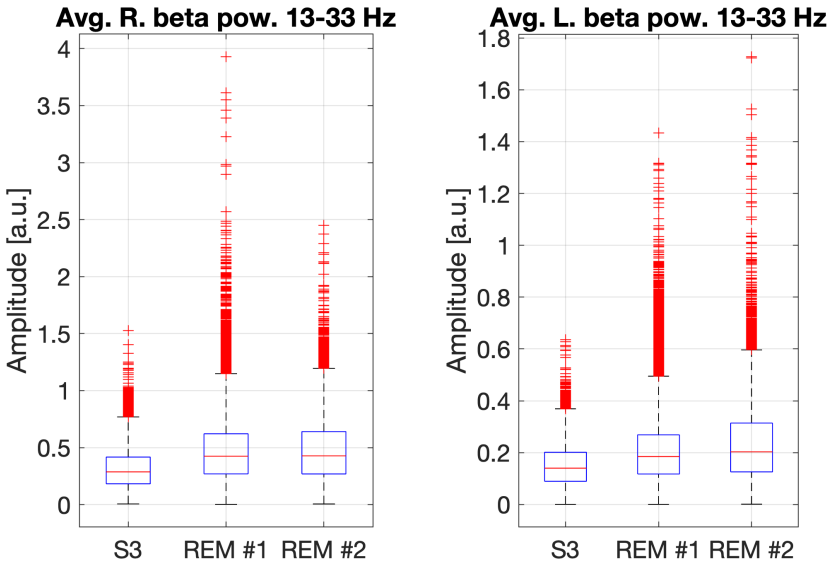

Figure 5.4: Boxplot showing average beta power for each sleep stage of Patient 1.

In figure 5.4 we can see, that median power in beta frequency is higher in both REM stages than in S3 stage.

5.3.3 Patient 2

Again with the Patient 2 i possessed with only 3 sleep stages from the same reason as in case of Patient 1. In case of Patient 2 the absence of REM stages was caused by continuous waking up reactions (this claim is based on annotation from neurologist), which is one of the symptom of sleep disruption in patients suffering from PD.

Sleep stage	**S3 #1**	**S2**	**S3 #2**
Duration [mm:ss]	10:28	03:55	19:29
PSG actions count	0	3	4
LFP burst count right (13-33 Hz)	54	21	104
LFP burst count left (13-33 Hz)	54	21	98
LFP burst count right(13-21 Hz)	52	20	104
LFP burst count left (13-21 Hz)	57	23	99
LFP burst count right (21-33 Hz)	58	20	113
LFP burst count left (21-33 Hz)	59	23	111
Average right LFP power(13-33 Hz)	1.5843	3.4073	3.1314
Average left LFP power(13-33 Hz)	0.7623	1.9836	1.9380

Table 5.2: Summary of sleep stages of Patient 2.

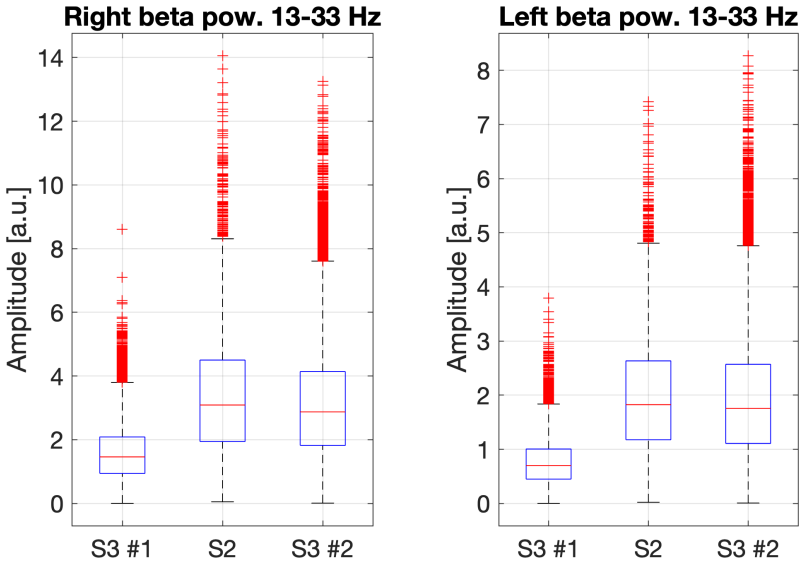

Figure 5.5: Boxplot showing average beta power for each sleep stage of Patient 2.

In figure 5.5 we can see, that the median of power in beta frequency of S3 #1 stage is lower than in other stages. In table 5.1 and in table 5.2 we can observe that, in the NREM sleep stages the LFP burst count does not decrease in higher beta (21-33 Hz) compared to lower beta (13-21 Hz), but such decrease can be observed in the REM sleep stages.

5.4 LFP signal around EMG events

I focused on both ipsilateral and contralateral possible relations of increases or decreases in LFP from both electrodes and EMG events. EMG event is defined in subsubsection 4.3. I used second root to scale the LFP power to bring the distribution of the data closer to the normal distribution. This is important for the validity of the t-test.

5.4.1 Patient 1

REM #1

The LFP activity around EMG events in REM #1 is shown in figure 5.6. In REM #1 I found 2 decreased regions in LFP power on 0.05 significance level in the right beta (13-33 Hz). The first decrease could be found also in the right lower beta (13-21 Hz) and the second decreased region could be observed in the right upper beta (21-33 Hz). I could observe very small significant region in spectrogram, see figure 5.7 and 5.8. When observing the left beta I did see only single very small decreased region on 0.05 significance level in the left beta (13-33 Hz) at -00:05, and even smaller one in left upper beta (21-33 Hz) at 00:00.

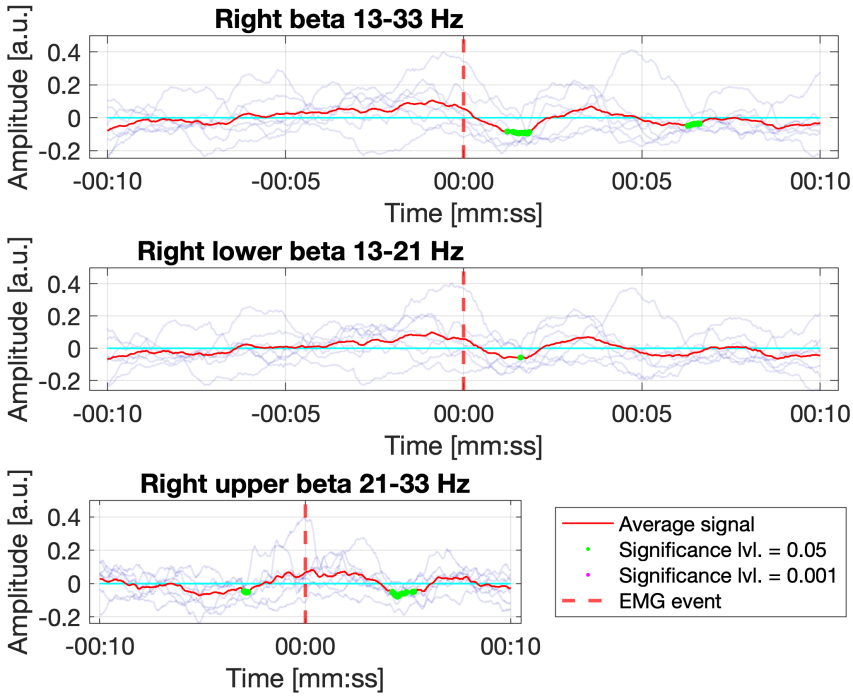

Figure 5.6: Layering of right beta LFP power around EMG event in REM #1, Patient 1.

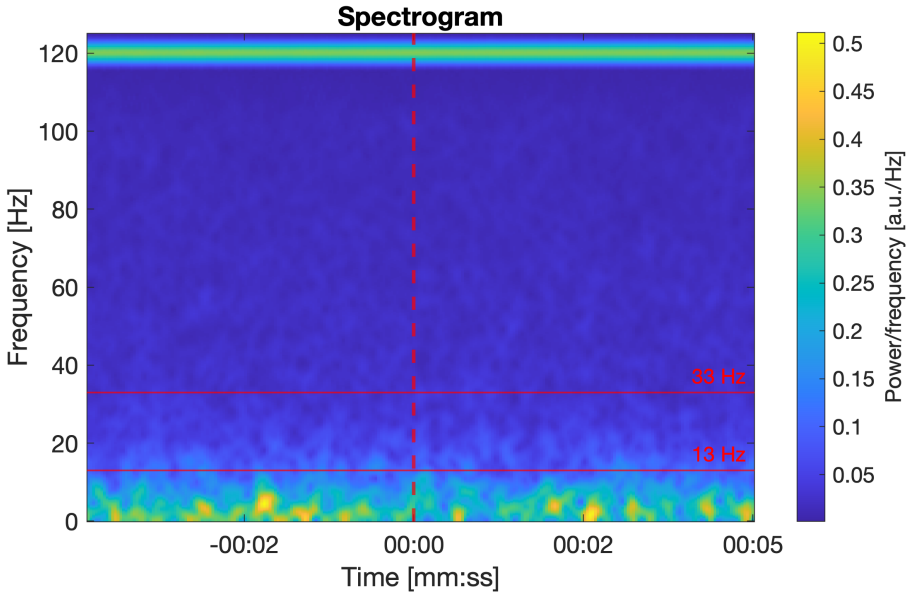

Figure 5.7: Spectrogram of right beta LFP signal around EMG event in REM #1, Patient 1. We can see small region of high power at -00:02 on 10 Hz frequency.

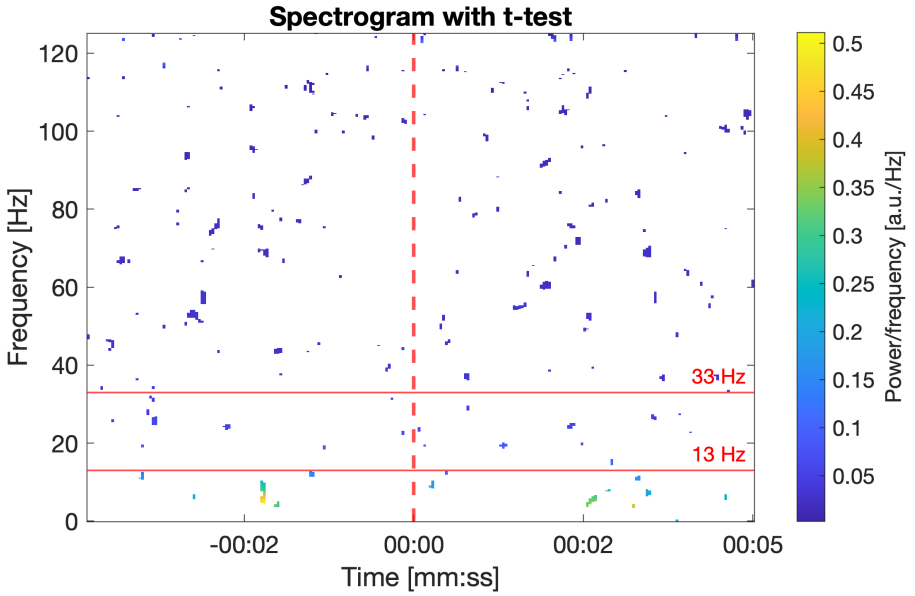

Figure 5.8: Spectrogram of right beta LFP signal around EMG event with t-test in REM #1, Patient 1, t-test (0.05 significance level) applied on spectrogram (5.7) was calculated from differences between spectrogram of 10 second segment around EMG event and spectrogram of 10 second segment before the analysed segment. We can see small region of significance at -00:02 on 10 Hz frequency.

REM #2

The LFP activity around EMG events in REM #2 is shown in figure 5.9. In REM #2 I found 1 increased region in LFP power on 0.001 significance level in the right beta (13-33 Hz). I did not observe any region of significance in spectrogram. I did not observe any decrease or increase of at least 0.05 significance level in any left beta frequency band.

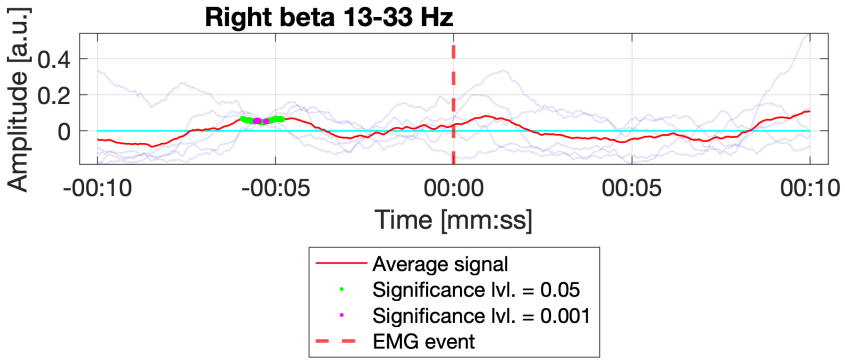

Figure 5.9: Layering of right beta LFP signal around EMG event in REM #2, Patient 1.

S3

The LFP activity around EMG events in S3 is shown in figure 5.10. In S3 I found 1 decreased region in LFP power on 0.05 significance level in right beta (13-33 Hz). The decreased region could be observed also in right lower beta (13-21 Hz). I could observe a small region of significance in spectrogram. I observed 1 decreased region in LFP power on 0.05 significance level in left beta (13-33 Hz) at -00:05, the region was much smaller compared to the region in right beta (13-33 Hz).

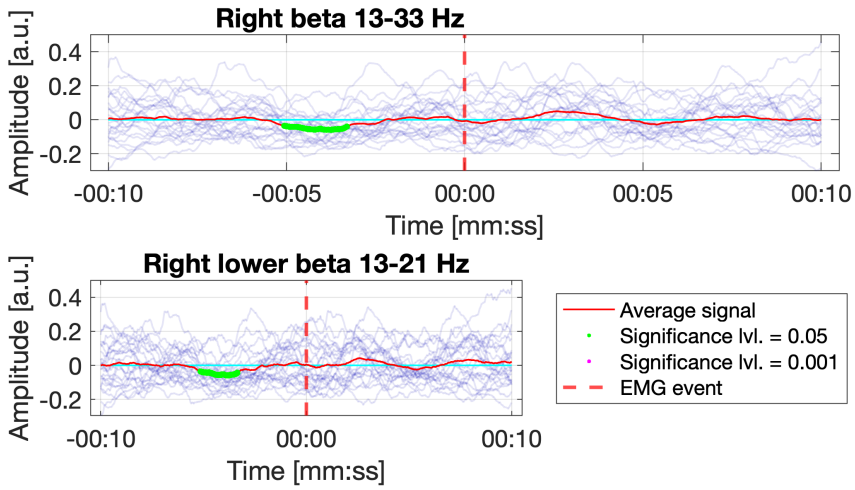

Figure 5.10: Layering of right beta LFP power around EMG event in S3, Patient 1.

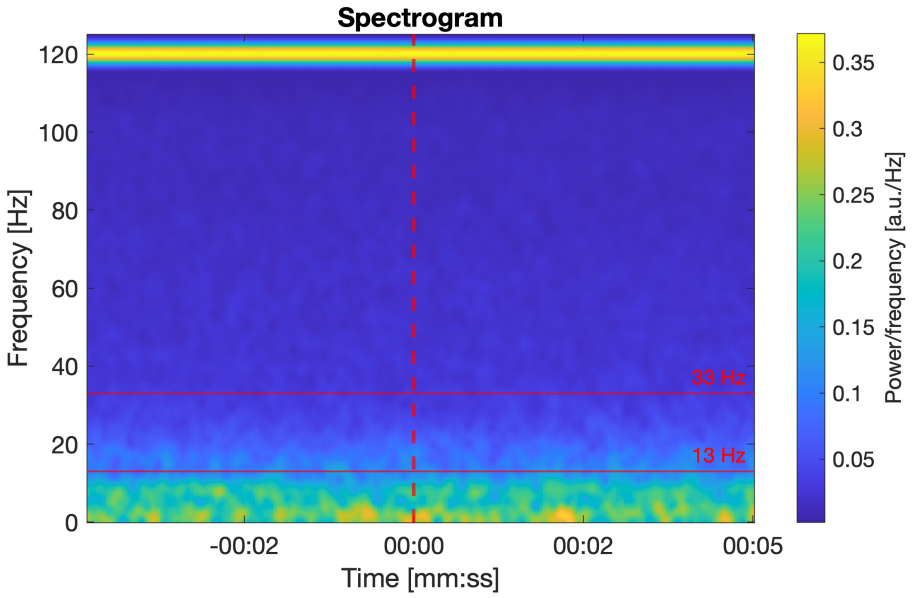

Figure 5.11: Spectrogram of right beta LFP signal around EMG event in S3, Patient 1.

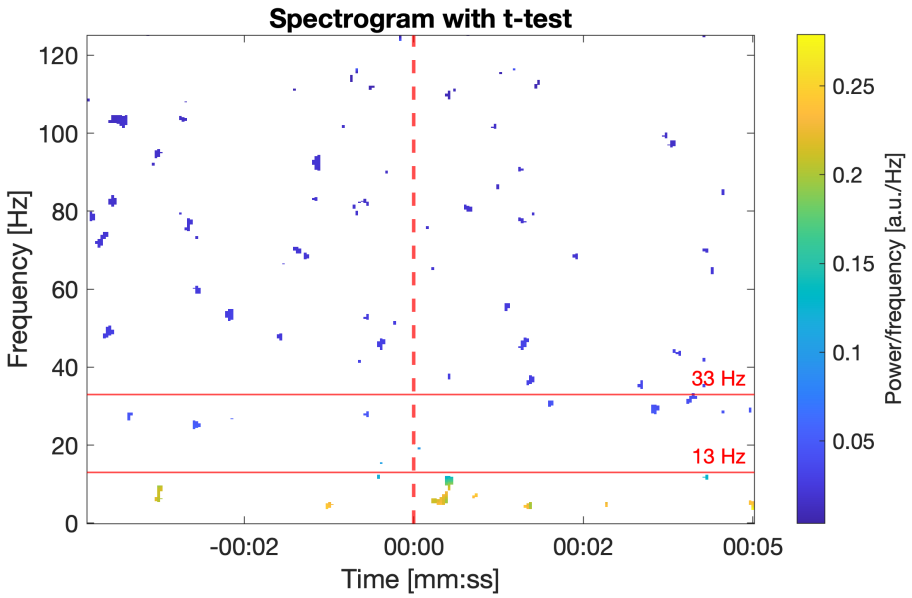

Figure 5.12: Spectrogram of right beta LFP signal around EMG event in S3, Patient 1, t-test (0.05 significance level) applied on spectrogram (5.11) was calculated from differences between spectrogram of 10 second segment around EMG event and spectrogram of 10 second segment before the analysed segment. We can see small region of significance at 00:00 on 10 Hz frequency.

5.4.2 Patient 2

S3 #1

Because I did not detect any EMG event in S3 #1 could not observe any LFP power segment.

S2

The LFP activity around EMG events in S2 is shown in figure 5.13. In S2 I found 1 decreased region in LFP power on 0.001 significance level in the left beta (13-33 Hz). Similar decrease could be observed in in the left lower beta (13-21 Hz). The decreased region was located at -00:01. The pattern in the LFP power has a slight resemblance to two consecutive peaks surrounding a decrease centered to the time of EMG event. I did not observe any significant region in spectrogram. I did not observe any decrease or increase of at least 0.05 significance level in any left beta frequency band.

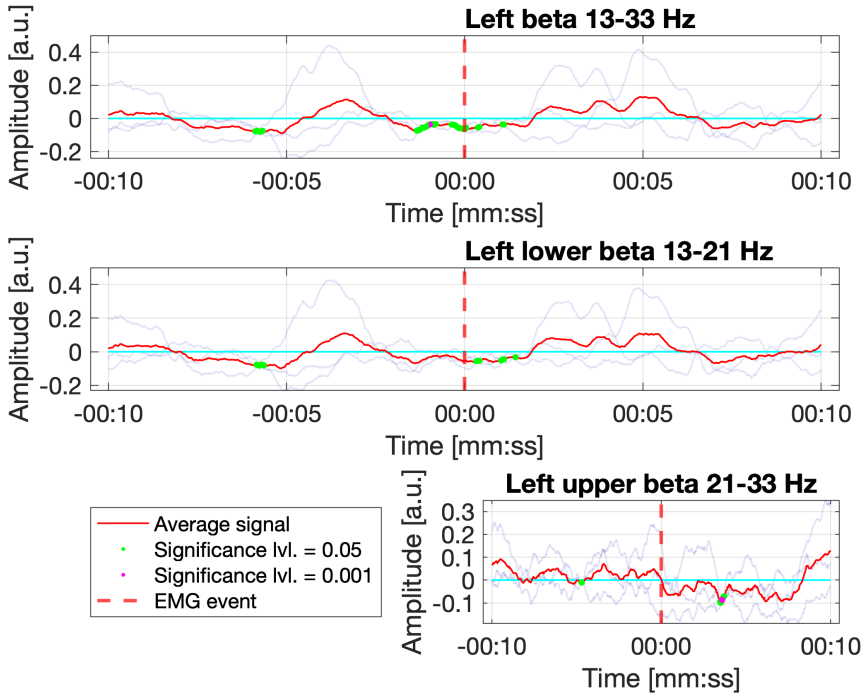

Figure 5.13: Layering of right beta LFP signal around EMG event in S2, Patient 2.

S3 #2

The LFP activity around EMG events in S3 #2 is shown in figure 5.14. In S3 #2 I found 1 decreased region in LFP power on 0.05 significance level in teh right beta (13-33 Hz), the right lower beta (13-21 Hz) and the right upper beta (21-33 Hz). The decreased region was located at 00:00. I also found an increased region in all right beta bands, that was located after the previously discussed decreased region. The decreased region could be observed also in the right lower beta (13-21 Hz). The pattern in the LFP power has a slight resemblance to two consecutive peaks surrounding a decrease centered to the time of the EMG events. I did not observe any significant region in spectrogram. Similar patter but with smaller amplitudes could be seen in left beta bands too.

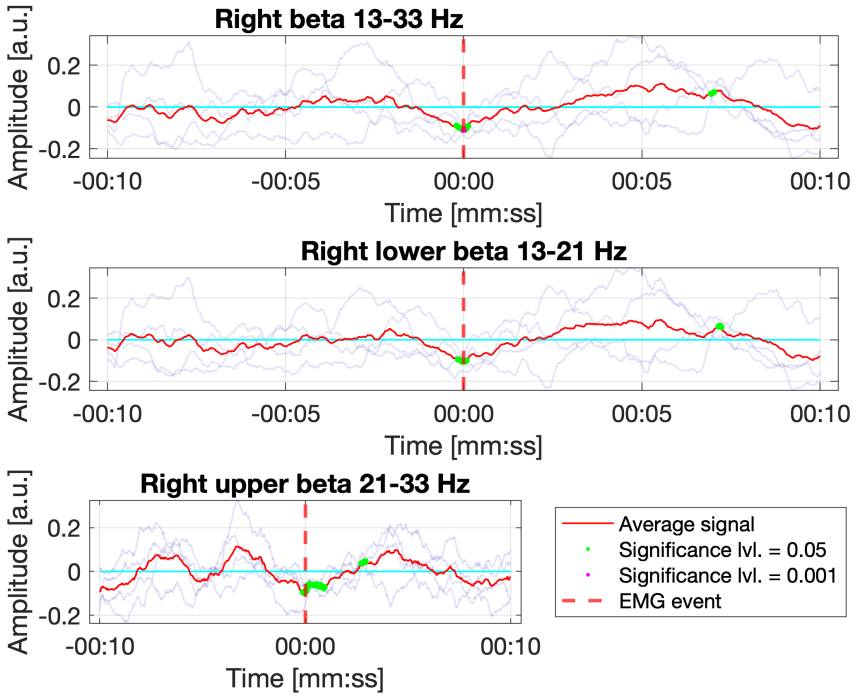

Figure 5.14: Layering of right beta LFP signal around EMG event in S3 #2, Patient 2.

5.4.3 Summary of LFP power around EMG event

- In REM stages of Patient 1 I found, that in both cases the right STN had more power and formed more burst-like shape around the EMG event.
- In NREM stages of Patient 2 I found a decrease in power in the right STN on beta frequency at the time of EMG event.

5.5 EMG signal around LFP bursts

I focused on both ipsilateral and contralateral possible relation of LFP bursts from both electrodes and increases or decreases in EMG activity in all EMG channels. I used log twice to scale the EMG signals, again to bring the distribution of the data closer to the normal distribution.

5.5.1 Patient 1

REM #1

The EMG activity around LFP bursts in REM #1 is shown in figure 5.15. In REM #1 I found a decreased region on 0.001 significance level. The region

was about 5 seconds long and located right before the left beta (13-33 Hz) burst times. In case of layering around the right beta (13-33 Hz) bursts I found similar but much less pronounced and shorter decrease and I also found very small decreased region on 0.001 significant level in chin channels.

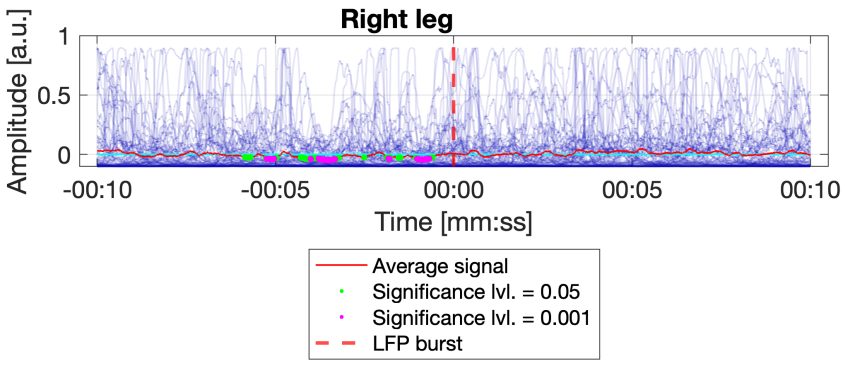

Figure 5.15: Layering of both legs EMG channels around left beta LFP bursts in REM #1, Patient 1.

REM #2

The EMG activity around LFP bursts in REM #2 is shown in figure 5.16. In REM #2 I found a decreased region on 0.001 significance level. The region was about 6 seconds long and located about 1.5 seconds before the left beta (13-33 Hz) burst time. In the other EMG channels the decreases very evenly distributed, some occasionally on 0.001 significance level. In case of the right beta (13-21 Hz) bursts I found even distribution of decreases in all the EMG channels, some were on 0.001 significance level.

left beta

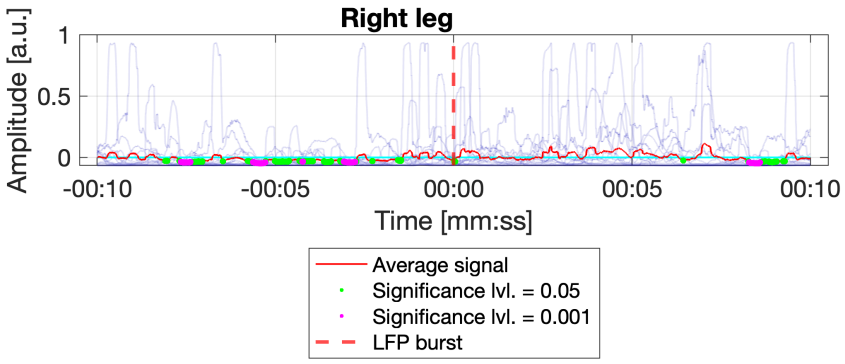

Figure 5.16: Layering of right leg EMG channels around left beta LFP bursts in REM #2, Patient 1.

S3

The EMG activity around LFP bursts in S3 is shown in figure 5.17. In S3 I found in all chin EMG channels a decreased region on 0.001 significance level. The decrease was located about 4 seconds before the right beta (13-33 Hz) burst times. I also observed slight increases in all the EMG chin channels located about 3 seconds after the right beta burst times. In other EMG channels the decreases were evenly distributed, mostly on 0.05 significance level. In case of left beta (13-33 Hz) bursts, there were decreases, that were again scattered evenly in every EMG channel.

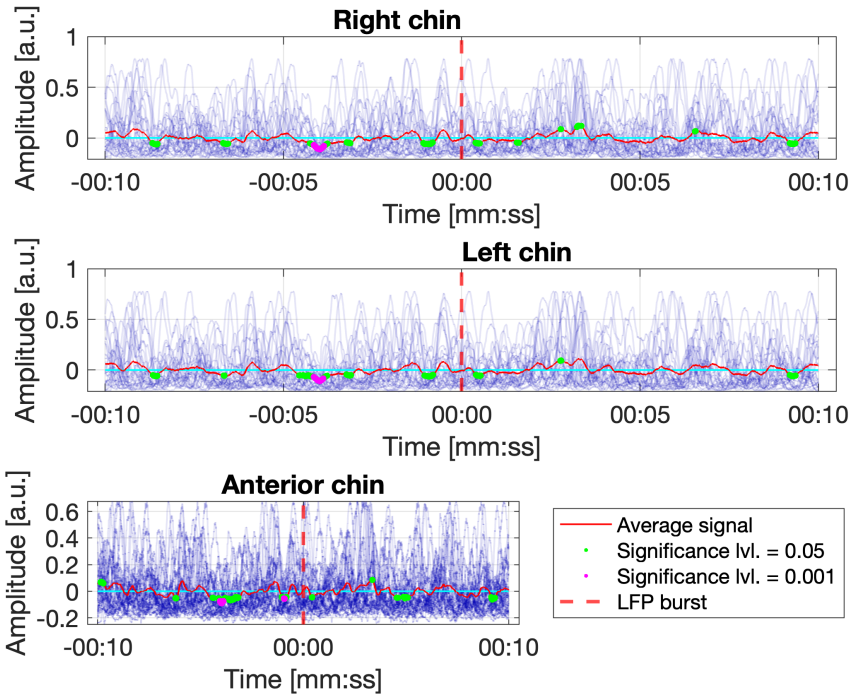

Figure 5.17: Layering of all chin EMG channels around right beta LFP bursts in S3, Patient 1.

5.5.2 Patient 2

S3 #1

In S3 #1 I did not find any specific increases or decreases on 0.05 significance level, only some scattered ones.

S2

The EMG activity around LFP bursts in S2 is shown in figure 5.18. In S2 I found periodic activity in all chin EMG channels. The activity had a period

of approximately 1 s and started about 5 seconds before the LFP right beta (13-33 Hz) burst. In leg EMG channels I observed only small regions of both increase and decrease on 0.05 significance level. In case of teh left beta (13-33 Hz) bursts similar pattern in chin EMG channels could be recognised, but with lesser amount of significant regions and the start of periodical activity was less pronounced.

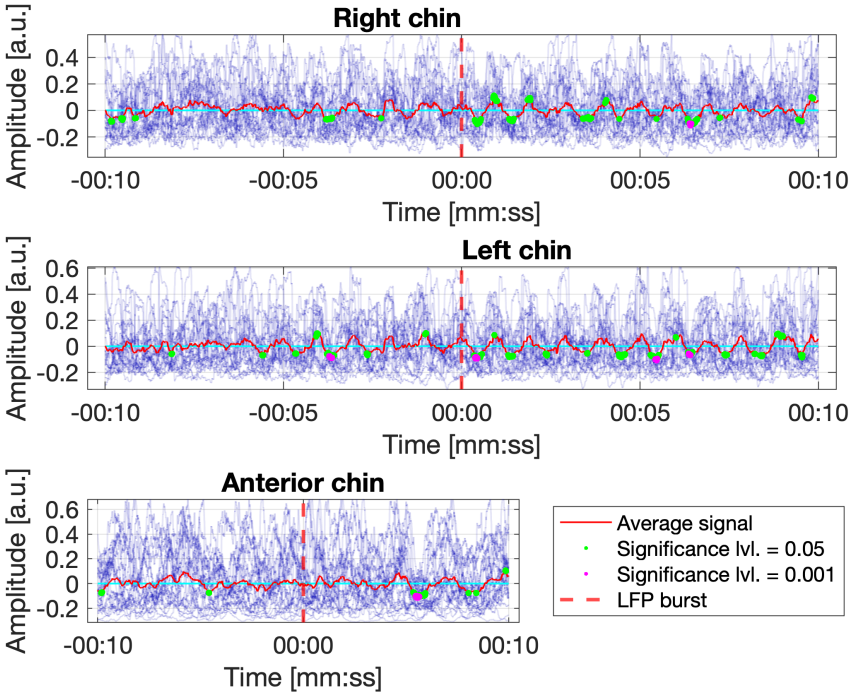

Figure 5.18: Layering of all chin EMG channels around right beta LFP bursts in S2, Patient 2.

S3 #2

In S3 #2 I did not find any specific increases or decreases on 0.05 significance level, only some scattered ones.

5.5.3 Summary of EMG signal around LFP bursts

- In REM stages I observed connection between the bursts in LFP and the contralateral leg EMG channel activity. This connection was observed only for the left hemisphere of Patient 1.
- In NREM stages I observed connection between bursts in LFP and all the chin EMG channels.

Chapter 6

Summary

DBS is a method of invasive treatment of PD. Patients suffering from PD frequently develop sleep disruption, which include but are not limited to pathological motor activity. I took part in obtaining overnight sleep recordings of these patients. The parallel recordings were of two types. The first type was LFP from DBS in STN. The second type was EMG recording containing channels from both legs and three chin channels.

The aim of this thesis was to estimate the relation between LFP and motor activity and, if there was any, to estimate, if it was specific to REM and NREM sleep stages. I explored the signals with use of frequency analysis and visual representation. Based on my exploration and literature I designed two methods for examinations of possible relation between LFP and motor activity. One was focused on burst-like activity in STN, the other on synchronised activity in channels of EMG.

After statistical evaluation I found relation between LFP in STN and motor activity in sleep in patients suffering from PD. It consisted in burst-like activity in STN linked to increase in motor activity. The relation between LFP and motor activity was specific for REM an NREM sleep stages. In REM the effect of STN activity was seen predominantly on leg EMG channels, while in NREM it was seen predominantly in chin EMG channels. The effect in REM was contralateral, in NREM I could not evaluated the laterality due to close location of chin electrodes. I also observed, that LFP activity showed both increases and decreases both before and after EMG event, but EMG activity showed mostly only decreases before the LFP burst.

Main problem I had to face was, that I had not enough data. I had only sleep recording of two patients and one of them did not have any REM sleep stage. Another limiting factor was, that my detection methods were relatively simple and in some cases did not yield optimal outcomes.

All the limitations of this thesis open new possibilities for future research. Even though the data I was working on are rare, more such data exist and are regularly recorded. Methods can be improved and tested on more patients. Better statistical evaluation can be done.

Importance if my results for clinical medicine can be seen in adaptive systems, that can detect burst activity and change stimulating regimes, which would result in higher comfort of patients with PD. Also scientific benefit can

be seen, for example in bringing emphasis to neural information transmission principles and to differences between physiological and pathophysiological neural activity.

I think, that this thesis can definitely serve as a good starting point for future students, that would be interested in analysis of signals from brain. It is as fascinating topic centered around one of medicine's least understood organ systems.

Appendix A

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Appendix B

Software documentation

All the software development was done in Matlab 2020b. Matlab functions and scripts can be downloaded from: `https://gitlab.fel.cvut.cz/jerabad1/bakalarka-adam-jerabek`.

B.1 Basic conception

There are 2 main scripts, that run all the functions. Almost every function, that generates new signal creates an extra large PNG file documenting the operation. In general huge emphasis was given to visualisation.

The software is semiautomatic, after you fill the addresses of data to the load script (load_data.m), you can get all the visualisation and data processing without changing the code. But due to possible differences in data format in different patients it is possible, that the code will have to be changed.

B.2 Scripts

load_data.m

Main script, loads JSON DBS recordings, TXT sleep annotation, TXT movement annotations and EDF EMG data.

sleep_stages_1.m

Main script, runs all the function a generates all the images except for boxplots and average beta power computation.

observe_signal_1.m

Script generates extra large PNG image of all emg channels, right and left BSTD, right and left beta power in multiple frequency bands and a spectrogram of right/left BSTD. Time step can be set.

B.3 Functions

B.3.1 Load

get_session.m

Function loads BSTD from all the JSON files in a folder. In single folder are expected to be only the JSON files from one patient from one night recording. Also fills missing values with NaN values based on tick times form JSON file or based on length of signals. Uses get_report.m.
Arguments:

- pathname (string)

Returns:

- session (struct) - contains right and left BSTD signals and times (datetime) of the samples, duration of signal (duration), start of the signals (datetime)

get_report.m

Function load BSTD form single JSON file, fills missing values with NaN values based on tick times form JSON file or based on length of signals. Uses get_segment.m.
Arguments:

- filename (string)
- pathname (string)

Returns:

- report (struct) - contains right and left BSTD signals and times (datetime) of the samples, duration of signal (duration), start of the signals (datetime)

get_segment.m

Function loads BSTD from single TimeDomain struct from JSON file. Missing values between sigals from TimeDomain structs fills with NaN values based on tick times form JSON file or based on length of signals.
Arguments:

- TimeDomain (struct) from JSON file

Returns:

- segment (struct) - contains right and left BSTD signals and times (datetime) of the samples, duration of signal (duration), start of the signals (datetime)

get_lfp_session.m

Function loads BSLFP from all the JSON files in a folder. In single folder are expected to be only the JSON files from one patient from one night recording. Uses get_lfp_report.m. BSLFP is called LFP in JSON files.
Arguments:

- pathname (string)

Returns:

- session (struct) - contains right and left BSLFP signals and times (datetime) of the samples, duration of signal (duration), start of the signals (datetime)

get_lfp_report.m

Function load BSLFP form single JSON file. Uses get_lfp_segment.m. BSLFP is called LFP in JSON files.
Arguments:

- filename (string)
- pathname (string)

Returns:

- report (struct) - contains right and left BSLFP signals and times (datetime) of the samples, duration of signal (duration), start of the signals (datetime)

get_lfp_segment.m

Function loads BSLFP from single TimeDomain struct from JSON file. BSLFP is called LFP in JSON files.
Arguments:

- TimeDomain (struct) from JSON file

Returns:

- segment (struct) - contains right and left BSLFP signals and times (datetime) of the samples, duration of signal (duration), start of the signals (datetime)

B.3.2 Detection

get_sleep_stages.m

Function returns information about available sleep stages.
Arguments:

- sleep_stages_values (int) - values of sleep stage annotations in hypnogram
- sleep_stages_times (datetime) - times of sleep stage annotations
- real_start (datetime) - start of the recording, that can processed (no artifacts, patients already sleeps)
- real_end(datetime) - start of the recording, that can processed (no artifacts, patients already sleeps)

Returns:

- sleep_stage (struct) - struct containing information about times of start of individual sleep stages, their duration and count.

get_lfp_bursts.m

Function detects beginnings of bursts in specified segment and generates PNG image of the signal and the detected marks.
Arguments:

- st, ed (datetime) - start and end of the segment
- session (struct)
- averaging_n (int) - used in moving mean for detection
- step (int) - used in PNG generation for specifying the step in time axis
- sleep_stage_value (int) - number describing sleep stage in hypnogram
- fs_bstd (int) - sampling frequency of BSTD

Returns:

- bursts (struct) - containing containing indexes (01 logical array) and times (datetime) of burst beginnings

get_emg_movements.m

Function detects beginnings of EMG events in specified segment of EMG and generates PNG image of the signal and the detected marks.
Arguments:

- st, ed (datetime) - start and end of the segment
- 5 EMG channels - (double)
- averaging_n (int) - used in moving mean for detection
- step (int) - used in PNG generation for specifying the step in time axis

- sleep_stage_value (int) - number describing sleep stage in hypnogram
- fs_emg (int) - sampling frequency of EMG

Returns:

- movements (datetime) - times of EMG events

detect_peaks.m

Function detects beginnings of peaks, see section 4.5. Arguments:

- sig (double) - signal
- w (int) - window in seconds before the peak
- d (int) - min time range between peak in seconds
- arg - can be array of sampling frequency (int) or array of times of spectrogram (double)
- stdev_multiplier (int) - multiplier of standard deviation

Returns:

- ind (logical) - array of indexes of peaks

combine_peaks.m

Function combines two arrays of times of beginnings of peaks, times from shorter array are used for combined beginnings of peaks. Arguments:

- p1 (datetime) - array of beginning of peaks
- p2 (datetime) - array of beginning of peaks
- dist (double) - max duration between two beginnings of peaks in seconds

Returns:

- peaks_out (datetime) - times of combined beginnings of peaks

B.3.3 Utils

limit_signal.m

Function limits the input signal so that the output signal has all the sample times within the time limits. Arguments:

- sig (double) - input signal
- t (datetime) - times of samples of input signal
- st, ed (datetime) - time limits

Returns:

- signal_out (double) - limited signal
- t_out (datetime) - times of samples of limited signal

val2name.m

Function translates value to name of sleep stage. Arguments:

- val (int) - numerical value of sleep stage used in hypnogram

Returns:

- name (string) - name of sleep stage

logr.m

Function performs logarithmic scaling on the signal, norms the output signal. Arguments:

- sig (double) - input signal

Returns:

- sig_out (double) - output signal

pow.m

Function performs square on the signal, norms the output signal. Arguments:

- sig (double) - input signal

Returns:

- sig_out (double) - output signal

B.3.4 Analysis

lfp_layers.m

Function performs layering of LFP around EMG events and generates PNG image.
Arguments:

- st, ed (datetime) - start and end of the segment
- actions (datetime) - times of EMG events
- session (struct) - contains BSTD signal
- averaging_n (int) - used in moving mean for detection
- step (int) - used in PNG generation for specifying the step in time axis
- sleep_stage_value (int) - number describing sleep stage in hypnogram
- fs_bstd (int) - sampling frequency of bstd

Returns:

- None

emg_layers.m

Function performs layering of EMG around LFP bursts and generates PNG image.
Arguments:

- st, ed (datetime) - start and end of the segment
- actions (datetime) - times of LFP bursts
- 5 EMG channels (double)
- averaging_n (int) - used in moving mean for detection
- step (int) - used in PNG generation for specifying the step in time axis
- sleep_stage_value (int) - number describing sleep stage in hypnogram
- fs_emg (int) - sampling frequency of EMG
- id (string) - string to be included in PNG file name

Returns:

- None

plot_layers.m

Function performs plotting for layering.
Arguments:

- sig (double) - input segments in 2D array
- t (datetime) - 1D array of times of samples
- amp (int) - amplitude multiplier for plotting
- lvl (int) - y axis shif
- leg (logical) - legend on/of

Returns:

- None

spectral.m

Function plots average spectrogram around EMG events, performs t-test on differences between average spectrogram around EMG events and average spectrogram before the segment around EMG events, generates PNG files.
Arguments:

- st, ed (datetime) - start and end of the segment

- actions (datetime) - times of EMG events
- sig (double) - analysed signal
- sig_t (datetime) - times of smaples of analysed signal
- sleep_stage_value (int) - number describing sleep stage in hypnogram
- fs_bstd (int) - sampling frequency of bstd
- id (string) - string to be included in PNG file name

Returns:

- None