

ANALYSIS OF SLEEP-RELATED SYMPTOMS OF PARKINSON'S PATIENTS BASED ON A SYSTEM OF AMBIENT SENSORS

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Abstract

Parkinson's disease (PD) is a chronic, progressive, disabling neurodegenerative disorder that affects up to 2% of the population over 65 years old. It does not significantly shorten life expectancy, involves both motor and non-motor symptoms for which only symptomatic treatment is currently available.

Sleep disorders experienced by PD patients are still largely unknown and multifactorial. However, PD patients experience a clearly disproportionate number of sleep complaints and a worse health-related quality of life (QoL) than the general population. It is estimated that between 60% and 98% of the PD population will experience sleep-wake pattern disturbances during their illness journey.

This project treats specifically the sleep disorders experienced by PD patients. For the project's purpose, a clinical study was designed to install a system of ambient sensors in the home of 20 participants of a national funded project (Swiss CTI). Apart from the clinical study design, we gathered a data set composed of data collected from a Ballistocardiography-based bed sensor installed in apartments of healthy seniors and PD patients. We then statistically analyzed and exploited the different sleep-related biomarkers the bed sensor measured. We observed significant differences in the two populations evaluated. This report presents the results obtained from a thorough research on the specific PD sleep-related disorders. The report also presents different techniques employed to successfully distinguish the two populations by classifying a night's measurement between the PD and healthy class with accuracy rates over 98%.



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Glossary

Ballistocardiography Technology enabling the recording of the body motions imparted to it by the heart beat. It is based on piezoelectric sensors and measures mass movements (of circulating blood and to the heart itself during the cardiac cycle of the body). i, 2, 79

Bradykinesia Slowness of initiation of voluntary movement with a progressive reduction in speed and range of repetitive actions. 1, 5, 6, 79

Dysarthria Imperfect articulation of speech due to disturbances of muscular control.. 6

Dyskinesia Involuntary muscle movements. 1, 5

Hypophonia Weak voice due to incoordination of the vocal muscles. 6

Parkinsonism Any condition that causes a combination of the movement abnormalities seen in Parkinson's disease. 1, 10

Sialorrhoea Excessive salivation. 6



Acronyms

ADL Activities of Daily Life. 18

BAI Beck Anxiety Inventory. 8

BDI Beck Depression Inventory. 8

CART Classification and Regression Trees. 63

DBS Deep Brain Stimulation. 7

DTW Dynamic Time Warping. vii, viii, 52, 53, 55–59, 80

ENN Edited Nearest Neighbors. 61, 62

FSS Fatigue Severity Scale. 8

KNN K-Nearest-Neighbors. 52, 53, 57, 58, 60, 68, 73–75, 80

MLP MultiLayer Perceptron. 65

MoCA Montreal Cognitive Assessment. 18

NMS Non-Motor Symptoms. 5, 8, 9

PD Parkinson's Disease. i, iii, v–vii, 1–3, 5–11, 13, 14, 17–19, 21, 23–33, 35–47, 49–52, 58, 61, 66–72, 76, 79, 81

PDQ-39 Parkinson's Disease Questionnaire. 18

PDSS Parkinson's Disease Sleep Scale. 18

PIR Passive Infrared. 13, 15, 18

PSG Polysomnograph. 16, 20

PSQI Pittsburgh Sleep Quality Inventory. 8

QoL Quality of Life. i, 5, 7–9, 79

Acronyms

REM Rapid Eye Movement. 2, 14

SB Sakoe-Chiba band. v, vi, 68–72

SMOTE Synthetic Minority Over-sampling Technique. 61, 62

SMOTEENN SMOTE and Edited Nearest Neighbors. 61, 62, 80

SVM Support Vector Machine. 63, 65, 73

TRAP Tremor at rest, Rigidity, Bradykinesia and Postural instability. 6

UPDRS Unified Parkinson's Disease Rating Scale. 1, 8, 18

1 Introduction

1.1 Motivations

Parkinson's disease (PD) is one of the most common neurodegenerative disorders with more than 10 million people living with the disease worldwide ([3]), including approximately 15'000 patients in Switzerland([4]). PD is a progressive non-curable neurodegenerative disorder, which is associated with the loss of dopaminergic neurons in the substantia nigra. Patients suffering from PD present a combination of several debilitating neurological signs. In particular PD affects movement, presenting with four cardinal motor symptoms: Bradykinesia (slowness of movement), rest tremor, rigidity, and postural and gait impairments such as freezing and shuffling gait. Furthermore, these patients may present with non-motor symptoms, such as decline in cognitive function, emotional and behavioral modifications and most importantly regarding this project, sleep difficulties. As the disease progresses, patients with PD are unable to continue to live autonomously, thus the importance of developing a better understanding of the disease's evolution.

Introducing dopamine agonist therapy alleviates motor dysfunction in Parkinson's Disease (PD). With disease progression, response to anti-parkinsonian therapy fluctuates during the day with reoccurrence of Parkinsonism alternating with appearance of Dyskinesia. This form of therapy loses transiently its effect, also called the "wearing-off" of the medication, and leads to the re-emergence of motor symptoms. Motor fluctuations demand for the physician to alter the patient's treatment schedule. The Unified Parkinson's Disease Rating Scale (UPDRS) is the internationally accepted PD clinical rating scale. The UPDRS mainly measures activities of daily living and objective motor ratings. The use of clinical rating scales is limited by inter-rater variability and does not permit continuous monitoring for symptoms and fluctuations that occur between clinical appointments. Diaries are important additional tools, but patients' regular adherence is quite poor and does not provide a neutral point-of-view, while judging the nature, severity, and time-of-change of the motor symptoms.

Chapter 1. Introduction

As stated previously, PD is known to be strongly associated with motor dysfunctions and an increasing amount of clinical evidence seems to suggest that not only are disturbances in sleep-wake rhythms present, but that they themselves may influence both the pathogenesis and progression of the disease. Nearly all PD patients experience some form of disruption in both daytime alertness and night-time sleeping, and are among the most frequently present non-motor symptoms, even at early onset.

Rapid Eye Movement (REM) sleep behavior disorder, insomnia, nocturnal polyuria (reduced bladder capacity), restless legs syndrome and periodic limb movements, sleep disordered breathing and excessive daytime sleepiness, are part of the most common sleep-related symptoms associated to PD. The prevalence of those symptoms is regular, yet commonly missed due to non-routine screening of the disorder. Over time, sleep deficits can contribute to further decline in a wide-range of symptoms associated to PD, including cognitive performance. Hence, an expert survey concluded that the debilitating nature of sleep disorders points to the need for systematic monitoring of the quantity and quality of sleep in this patient population [5].

From these observations, the project covers the elaboration of an analysis based on the data collected from ambient sensors, including in particular a Ballistocardiography-based bed sensor. Current technological devices such as the bed sensor used can provide us with measures that can inform us on the sleep-related features that constitute a night of sleep. This sensor in particular can record a wide range of sleep-related biomarkers such as movements in the bed, the awakenings of a person or even the number of times a person tosses and turns in the bed.

1.2 Research questions

During the course of the project, we wish to discover how the Parkinson's Disease is affecting the quantity but mostly, the quality of sleep of the patient so that the project can:

- Assess the features of a PD standard night compared to healthy subjects
- Identify sleep-related features particular to the disease
- Provide information to healthcare experts for the adjustment of the patient's medication plan

Thus, this project explores the following questions:

1. What are the relevant biomarkers from the set of collected data that can be of interest to recognize the sleep-related features of the symptoms affecting PD patients?
2. Which PD sleep-related symptoms are we able to monitor and how accurately, with the help of a non-invasive Ballistocardiography-based bed sensor?

1.3 Structure

The report is designed around five main chapters. Following this first chapter of introduction, we present in Chapter 2 the disease with a particular focus on sleep disorders affecting PD patients. We provide the reader with some medical-oriented knowledge to perceive the motivation for the project and support the symptoms analysis.

Then, Chapter 3 discusses the system of sensors that enables us to collect measures of the different biomarkers we need in order to perform a sleep disorders analysis in the sampled population. It presents each sensor intended to be used to monitor PD people, their usage in the context of the field trial, the motivation for using them and their technical specifications.

Following this, Chapter 4 presents the methodology used to explore the data and the extraction of valuable sleep-related features from the available data set. It also describes the study designed for this project, created during the past year. In this chapter, we present how the collected data is matched to the scientific observations in PD sleep disorders.

This leads us to present in Chapter 5 the results of the data analysis performed during this study on the different sets of data collected. The different sleep-related symptoms of the disease are analyzed with different models in order to recognize the key sleep-related features of the disease and highlight the differences between the healthy and PD ill population. It describes the algorithms used to classify a night-time segment from PD patients compared to healthy subjects based on selected biomarkers.

Finally the thesis concludes in Chapter 6 by summarizing the results of the analysis and introducing the outlook and future work planned for the continuity of the project.

1.4 Partners

As mentioned above, this project revolves around a study conducted by different academic and industrial partners:

CHUV Centre Hospitalier Universitaire Vaudois where Prof. Philippe Ryvlin, chief of the Neuroscience department at the CHUV, is leading as a principal investigator of the study, accompanied by the researcher Dr. Ilona Wisniewski with whom we designed the study.

EPFL Ecole Polytechnique Federal de Lausanne where Prof. Matthias Grossglauser, associate professor at the Laboratory for Computer Communications and Applications (LCA) but also director of the Doctoral School in Computer and Communication Sciences (EDIC), is applying his knowledge of the field of machine learning and stochastic models.

DomoSafety SA where Dr. Philipp Bulushek, Chief Technology Officer of the company, is providing its extensive knowledge on the system of sensors used as well as its experience in connected medical devices as part of his Research and Development unit.

2 Sleep disorders in Parkinson's Disease

You've probably read in People that I'm a nice guy - but when the doctor first told me I had Parkinson's, I wanted to kill him.

Michael J. Fox

2.1 Parkinson's Disease

Parkinson's disease affects the way you move and behave. It happens when there is a problem linked to decreased dopamine production in the substantia nigra in the brain by the nerve cells. It is marked especially by tremor of resting muscles (Dyskinesia), rigidity, slowness of movement (Bradykinesia), impaired balance, and a shuffling gait. Normally, these nerve cells make an important amount of dopamine. Concretely, these cells are either dead or dying, which induce the lack of dopamine produced by the brain. Dopamine sends signals to the part of your brain that controls movement but can impact behavior as well. PD has a high incidence of comorbidity, and for which only symptomatic treatment is currently available. The disease is not fatal but can reduce longevity and affect strongly the QoL of the ill person. The disease progresses more quickly in older patients, and may lead to severe incapacity within 10 - 20 years from the illness start.

It is affecting the population globally with a greater susceptibility of having PD in men, with calamitous socioeconomic effects on individuals, their families and society. As for the European economic impact, the costs of PD in 2010 accounted for 13.9 billion euros alone [6].

Concretely, the disease presents itself with different facets in terms of symptoms and impacts on the daily life of the patients. The disease affects them with both motor symptoms impacting their mobility, autonomy and non-motor symptoms (NMS) having effects on their mood, social interactions and quality of life.

Chapter 2. Sleep disorders in Parkinson's Disease

Motor Symptoms	Non-Motor Symptoms
Tremor	Bradyphrenia (thinking difficulties)
Slowed movement (bradykinesia)	Depression and emotional changes
Rigid muscles	Fear and anxiety
Impaired posture and balance	Sleep problems and sleep disorders
Loss of automatic movements	Rapid eye movement sleep behavior disorder
Blood pressure changes	Vivid dreaming
Camptocormia (abnormal forward bending)	Cognitive impairment
Pain in specific areas or throughout their bodies	Apathy
Freezing of gait	Anhedonia (inability to feel pleasure in normally pleasurable activities)
Postural instability	Fatigue
Hypomimia (reduce of facial expression)	Anosmia (smell dysfunction)
Dysarthria (slow speech)	Ageusia (taste dysfunction)
Dysphagia (difficulty swallowing)	Paresthesias (burning or prickling sensation)
Sialorrhoea (inability to control oral secretions)	Dysautonomia (Autonomic Nervous System malfunction)
Micrographia (writing difficulties)	Constipation
Scoliosis	Sexual dysfunction
Glabellar reflex (repetitive tapping on the forehead)	Urinary dysfunction
Striatal deformity (deformity of feet or hands)	Weight loss
Blepharospasm (excessive blinking and spasming of the eyes)	Abnormal sweating
Muscle Cramps	Mood disorders
Impaired fine motor dexterity	Dementia and psychosis
Impaired motor coordination	Sleep disorders (will be detailed later on)

Table 2.1 – The most common motor and non-motor symptoms observed in Parkinson's disease

Table 2.1, page 6 presents the most common motor and non-motor symptoms observed in the disease. The list is not exhaustive but gives to the reader an insight on how PD affects patients. Indeed, PD is usually seen on the "common public representation" as a disease where patients present tremor, but it is not well known the extent of the impact of the disease on many other aspects of the daily life of the PD patient.

The symptoms called "cardinal symptoms" are, like their name suggests, four of them. They have the named "TRAP" to state for Tremor at rest, Rigidity, Akinesia (or Bradykinesia) and Postural instability. Those four cardinal symptoms are usually not the most impairing disorders in the patient's daily life. In fact, symptoms like depression or apathy, which often can be linked to sleep deprivation, do impact severely the quality of life of the PD patients as it has enormous impacts on their social interactions. Other symptoms like Hypophonia, Sialorrhoea, or Dysarthria can be felt as more impairing by PD patient compared to the cardinal symptoms.

When the lack of dopamine in the system is kicking-in, the PD sick person experiences what is called an "off-phase". An off-phase is an upsurge of the symptoms which severely impairs the PD patient. The off-phases can be experienced during the day but are often arising during the night when the medications are wearing out which can trigger difficulties for the person to correctly sleep.

As an example, the on-off phenomenon is significantly impacting the lengthening of movement time or the urinary dysfunction (storage and voiding). Unfortunately, on-off phases can cause motor complication in 50% of the PD patients that were on drug treatment for 5 to 10 years and can cause important advancements in the disease evolution [7]. Being able to observe such phenomenon would be of interest to compute the drug adherence time and thus adapt the treatment.

Treatments

PD currently has two main treatments to address most symptoms experienced by the sick persons. The first is called the Levodopa drug, developed in the late 1960s and is a dopamine precursor that is often coupled with the Carbidopa, a drug helping the Levodopa to reach the brain and prevent nausea. The Levodopa actually transformed by the brain into dopamine to help compensate for the lack of naturally produced chemical.

Unfortunately, the Levodopa treatment is not 100% sufficient to fully reduce the PD symptoms. Indeed, the sick patients still experience off-phases during the day and night when the drug is wearing out and when they start being less responsive to the treatment. Usually the treatment can be adapted, but with time, the patients starts to respond less and less well to the drug.

For this reason, some persons will turn themselves towards an other solution called the Deep Brain Stimulation (DBS), usually when they experience motor symptoms complications. The DBS is a technique which involves a surgical procedure to reduce the motor symptoms of the disease. The technique enables the implantation of wires with electrodes into the brain which are connected to an electronic device that will generate high frequency pulses, similar to a pacemaker, to stimulate the part of the brain controlling the movement. This medical intervention has proven many benefits in improving the physical symptoms, and researched showed that the surgery improves highly the Quality of Life (QoL) of advance Parkinson's which are still responsive or less responsive to the drug treatment.

2.2 Non-motor symptoms

Table 2.1 on page 6 presents in the right column the most common Non-Motor Symptoms (NMS) which can affect PD ill persons. These are among a wide spectrum of NMS linked with the disease. Unfortunately, the NMS are usually, or used to be, disregarded when taking into account the disease progress, evolution and state. The more the disease advance, the more the NMS become prevalent. In 2002, Shulman et al. [8] made an analysis on NMS over a pool of 101 PD patients and found that neurologists following up PD patients were failing half of the time to detect NMS like depression, anxiety and fatigue and that 40% of the time they failed to recognize sleep disturbances as symptoms affecting their patients. The recognition of NMS is still very marginal and requires more tools, insight and knowledge in order to be better taken into account in the treatment of the disease.

Well-known standardized tools exist like the Beck Depression Inventory (BDI), the Beck Anxiety Inventory (BAI), the Fatigue Severity Scale (FSS), the Unified Parkinson's Disease Rating Scale (UPDRS), the Schwab & England Scale (S/E) and the Pittsburgh Sleep Quality Inventory (PSQI) for example, and can help reflect the status of these NMS and their impact on the QoL of the patient. However, there can be biases in many ways when repeated several times (learning effect from the patient for example).

In sum, the NMS of PD are significantly increasing the disability caused by the disease and is critically determinant in the QoL of the persons. They are recognized as major clues in early diagnostic of the disease and identification of at-risk population as they do arise usually years, even decades, before motor symptoms can be identified and linked to PD . Studies like Muzerengi et al. [9] in 2007 or Chaudhuri et al. [10] in 2009, recognize the need of recognition, follow up and treatment of Parkinson's NMS. However, NMS are not much used in clinical practice and are usually missed during routine consultations, which impact highly the proper treatment of the diseases's symptoms.

The project intends to help moving towards the recognition of some of these PD symptoms, the sleep disorders in particular, in order to improve and support the caregivers in the monitoring of their patient's symptoms. With the help of a study designed at DomoSafety in partnership with the CHUV, a system of ambient sensors is developed to monitor the different biosignals generated by the activity of the PD ill person, focusing in this thesis on the sleep disorders in particular.

2.3 Sleep-disorders in Parkinson's Disease

PD patients experience a disproportionate number of sleep complaints and worse health-related quality of life than the general population. Sleep disturbances are amongst the most frequent NMS experienced by PD patients, and can sometimes lead to nocturnal symptoms. The sleep-related disorders specific to PD occur usually early and even before the diagnosis of the disease. However, they are generally more frequent and more severe in patients with advanced PD. They do extend on a wide spectrum and can arise differently in each person, which makes them difficult to identify. As an example, a common sleep disorder is linked to the rigidity of the muscles, when the person gets frozen in bed and thus can not move his body. In this case, this can lead to urinary issues when the person can not get to the bathroom. However, in other cases, PD patients experience vivid dreaming, periodic limb movement and restless legs, where the body moves involuntary by enacting a dream due to a the lack of inhibition of the brain part controlling movement.

In general, PD patients do report a poor quality of sleep (40 to 90% of prevalence [11]) and sleep disorders are one of the most common reported by patient. They are also important early disorders on the onset of the disease. The following tables 2.2 and 2.3 enumerates specific PD sleep-related disorders with their description and linked statistics. Chapter 5 goes in more details with some particular symptoms that the sensors system designed can monitor.

As mentioned, the appearance of NMS is predating the motor dysfunction, years, even decades before. It is thus of high importance to acknowledge the sleep-related symptoms that can appear in the course of the disease evolution. Later on, if proper recognition and monitoring of those symptoms can be established, predicting the pace of the certain symptoms' evolution based on the evolution of recognizable features with an ambient sensors systems could be feasible. This would help provide the necessary information to adjust and apprehend the disease treatment and improve the sleep quality of the patients. Furthermore, it was shown that sleep disturbance is an important predictor of poor QoL [12], which can be leveraged with proper recognition of the symptoms to enact on it.

The PD population is heterogeneous regarding the disease severity, onset and duration. It is also heterogenous regarding the presence of sleep-disorders, cognitive issues, depression, and other motor and non-motor symptoms. All these are significant factors to a poor experienced and perceived overnight seep quality. However, sleep disturbance remains under-diagnosed by clinicians and under-reported by patients. The purpose of this project is to explore the possibilities offered with non invasive and connected systems installed at the homes of PD sick persons who will benefit in their treatment by a close monitoring.

In Chapter 4 is presented the system designed to record and exploit the data in PD patient's home.

Sleep-related symptom	Description	Statistics
Daytime somnolence / excessive daytime sleepiness / Napping	Inappropriate and/or undesirable sleepiness during waking hours of the day.	In about 30% to 50% of patients with PD. [13]
Depression leading to morning headache	Depression, anxiety are often correlated with headaches experienced after awakening.	A study [14] found approximately that it is highly correlated with depression and affects 40% the study IDP patients.
Awakenings with shortness of breath (SOB)	A symptom induced by a wearing-off of the drug treatment inducing a return of muscle rigidity.	Infrequent and if identified, can be improved with entacapone. [15]. For now, no study assures us of a prevalence of this symptom in PD. [16]
Sleep initiation disturbance / Sleep-onset insomnia (primary insomnia)	When the patient can not find sleep when going to bed, even fatigued.	Together, they occur in more than 30% of PD sick patients. [17].
Obstructive sleep apnea (OSA)	Caused by a weakness of the muscles around the upper airway leading to partial or complete airways collapse.	Stewart et al. (18) reported on their PD pool of patients around 66.6% had sleep initiation disturbance. However, Oerlemans found only 16% experiencing this issue. [19]
Rapid Eye Movement Sleep Behavior Disorder (REMSBD)	It causes the loss of the normal skeletal muscle atonia which enables patients to enact their dreams during REM sleep (vocalizations, abnormal movements, assaults, etc.). REMSBD can precede by more than a decade the emergence of motor symptoms.	This is three more times more common in PD patients and may occur in up to 50% of the patients. [19]
		Postuma et al. in 2009 showed that after patients without Parkinsonism but diagnosed with REMSBD were having 17.7% chance to develop PD after 5-year and 40.6% chance after 10 year. [20]

Table 2.2 – The sleep-disorders experienced in PD, their description and linked statistics - Part 1

2.3. Sleep-disorders in Parkinson's Disease

Sleep-related symptom	Description	Statistics
Insomnia (sleep maintenance) / Sleep fragmentation (secondary insomnia)	Insufficient amount of sleep due to awakenings.	Many studies shows that it is affecting up to 77-88% of PD patients [11]. In 1990, Stewart et al. reported that 88.5% of their PD (n=78) experienced sleep maintenance issues. [18]
Incontinence due to lack of mobility / Night-time urge incontinence (Nocturia)	Waking up during the sleep period for voiding. It is often related to wearing-off of the medication.	79% of PD patients exhibited two or more episodes of nocturia during Lees et al. 1988 study (n=220) [21]. A more recent study from Martínez-Martín et al. in 2011, reported 68.4% of their sample of PD patients experienced nocturia.
Restless Legs Syndrome (RLS)	Uncomfortable or unpleasant sensations in the limbs (worse when periods of inactivity) and sometimes accompanied by periodic limb movements during sleep.	The generally accepted frequency of RLS symptoms with PD is 10 to 20%.
Sleep Disordered Breathing (SDB)	Breathing difficulties during sleep (rigidity of muscles).	Varies from 20 to 60% in PD ([22])
Frequent napping	Napping ensued by sleepiness and fatigue.	Oerlemans found 44% being subject to frequent napping (mean of 35min/d). [19]
Body stiffness	Rigidity is experienced when the medicine is wearing-off due to a resurgence of hypokinesia.	Number of stiffness symptoms are explained by wearing-off of the medicine as demonstrated by Chaudhuri et al. in 2009. ([10]). It is for example demonstrated that 65% of the PD population experiences difficulties in turning over in bed ([23]).
Alterations to total sleep time in bed	In combination with sleep fragmentation, a significant decrease of total amount of sleep develops.	Usually, the actual sleep per night is less important in PD patients. Wailke et al reported that a significantly decreased total sleep time where found in PD patients stopping the Levodopa medication after noon. [24]
Alterations of the circadian rhythm disturbances	Dysfunction of the sleep-wake cycle. The timing of physiological rhythms may be altered, leading to changes in the phase relationship of rhythms to each other, which can cause internal desynchronization.	The circadian rhythm in PD and its influence on sleep has been studied very few in the past. Increasing evidence suggest disruptions of the circadian system in PD. However, we do know that PD can have effects on the duration of sleep. Long sleep can be observed with 26.2% occurrence in the study "Sleeping difficulties and health-related quality of life in Parkinson's disease", from Ylikoski, having >= 9 hours of sleep. Short sleep is also common with 32.5% occurrence in this same study. [25]
Sleep deprivation	Sleep deprivation is usually computed as the difference between the need of sleep of the person minus the total sleep time they actually get.	33.8% occurrence of sleep deprivation is observed in Ylikoski et al. study [25].

Table 2.3 – The sleep-disorders experienced in PD, their description and linked statistics - Part 2

3 Data collection: a system of ambient sensors

During the course of this project, an observational study was designed to be proposed to 20 PD ill persons to participate in. The primary goal of the study was to monitor the participants' activity biosignals obtained from different ambient sensors placed at strategic locations in their apartment. During the course of this thesis, an observational study was designed with a set of different ambient sensors. The signals and sensors are detailed along this chapter in Section 3.1 as well as Section 3.2. Then we discuss in Section 3.3 the particular bio-markers investigated according to the possibilities enabled by the ambient sensors' system regarding the long-term monitoring of the PD sleep-related symptoms.

3.1 A non-invasive approach: the system in details

The study designed during the course of the project had for primary goal to put in place a system that would record as much as possible the day and night activity data of Parkinson's patients in their homes, in the less invasive way possible. For that matter, the study uses both motion and bed sensors. The first device is an Emfit QS bed sensor manufactured in Finland by Emfit Ltd. The second is a set of Passive Infrared (PIR) activity sensors and magnetic door sensors manufactured by DomoSafety SA. The combination of both allows us to record the activity of the patient in the apartment as well as his micro-movements triggered in its sleeps. The sensors are detailed in the subsections below.

**Chapter 3. Data collection:
a system of ambient sensors**

Emfit QS system:



The Emfit QS sensor is a ballistocardiography-based sensor, a device supported by a strong scientific research with near a hundred of publications to its credit [26]. It is unfortunately implementing some high-end algorithms still under industry trade secrets, maintaining their lead position in the domain. More particularly, publications on sleep disorders and medical applications retained our interest for selecting this sensor, being the most accurate non-invasive device for sleep-monitoring at home. The Emfit QS (Quantified-Sleep) houses in a strip, an electromechanical film (EMFi) using a quasi-piezoelectric material sensitive to changes in mattress pressure. These changes consists in pressure variations outputting electrical charges, which are then amplified and filtered.

In details, the data set available through the sensor is the following:

Device	Measure	Unit
Emfit QS's System	Heart rate measurements during sleep	Beats/min
	Respiration rate measurements during sleep	Beats/min
	Activity measurements during sleep	Points
	Duration in bed	Time
	Duration in sleep	Time
	Duration awake	Time
	Duration outside bed during sleep period	Time
	Duration in REM, Deep and Light sleep	Time
	Sleep states (REM, Deep, Light, awake) timestamps	Time
	Number of awakenings	Number
	Toss and Turns count	Number
	Bed exits count	Number

Table 3.1 – The available measures and collected data through Emfit QS's system

Chapter 4 details the parameters in more details and those chosen for the sleep-related analysis of a selection of PD symptoms.

3.1. A non-invasive approach: the system in details

DomoSafety's system:



DomoSafety's system includes two different sensors: Passive Infrared (PIR) motion sensors and magnetic door sensors. They are both sending the data collected to a base unit connected to the 3G GSM network to the DomoSafety's storage servers. The motion sensors are working with PIR technology which measures light radiating from heating objects and thus detecting motion. The motion sensors have a range of 6 meters, a conic view of 120 degrees, 2 years of autonomy and have a resolution of two seconds. The sensor captures five minutes batches of motion (or inactivity) and sends them through ZigBee to the system's base unit that consequently sends it back to our servers. The system can thus detect the presence in a room in particular which we induce in the utilization of the room's faculties. For the project, toilet usage detection being rather important, a sensor is discretely installed across the toilet to detect this event. On top of that, simple magnetic sensors are used for door opening and closing detection, sending directly their events (open, close) to the DomoSafety's base unit, then re-transmitted to the storage servers.

Within the study setup, one sensor is installed in every major room, to cover most of the daily activities of the monitored person, with at the least minimum the following locations covered:

- Living Room
- Kitchen
- Bedroom
- Entrance
- Toilet
- Bathroom (or only Toilet if both are one and the same)

During the study, a magnetic sensor is positioned on the entrance door in order for the system to detect if the person is inside or outside of the home (no motion in the flat when paired event (open/close) happens indicates a leave of the person).

In details, the data set available through the sensor is the following:

Chapter 3. Data collection: a system of ambient sensors

Device	Measure	Unit
DomoSafety's System	Duration of motion in a location	Timestamp
	Duration of no motion detected	Timestamp
	Duration outside	Timestamp
	Number of outings	Number
	Timestamp of outings	Timestamp
	Number of entrance door openings	Number

Table 3.2 – The available measures and collected data through DomoSafety's system

The system introduced above and in usage during the project is non-invasive for the participant considering the sensors are placed in discrete locations (ceiling, top of the doors, under the mattress) in their apartment. Discretion allowed us to elaborate a study for long-term monitoring of the daily and nightly activity of the persons.

3.1.1 Limitations

The limitations encountered by using such a system can come from the granularity obtained from the data as well as hardware issues (i.e. connectivity, stability and reliability of the devices). On one hand, when recording data from a system of ambient sensors, it cannot be obtained the same quality of input as wearables sensors do regarding the activity detection and labelization. Indeed, it can not be asked from these sensors (which are used in this context for their long battery life in long-term monitoring studies) to distinguish motion in an apartment room and the activity related to this motion.

On the other hand, with such a system, it can be experienced discontinuities in the recording of data, due to reliability in the wireless connections involved. The system relying on technologies such as ZigBee and 3G GSM, are not a 100% reliable on long-term use and connectivity happens to get lost from time to time as it has been observed in past research projects.

Finally, a non-invasive bed sensor like Emfit QS cannot provide a perfect recording of the participant's vitals or sleep biosignals such as the heart rate, the respiration rate, the sleep stages or even the detection of presence in the bed as would a Polysomnograph (PSG) do. A PSG is a medical device used to record the biosignals from the brain, the eyes, the heart and the muscles to identify the specifications of the circadian rhythm of a person. It can, with absolute accuracy, provide traces for each biosignal as Emfit does with complete reliability. Many studies with Emfit QS coupled with polysomnography allowed the manufacturer to fine-tune their algorithms of measure and provide a good thread-off between perfect accuracy and compliance with the user.

For instance, combination of heart-beat interval and movement measurement by the Emfit sensor shows 79% accuracy in determining sleep architecture [27]. A more recent study, unfortunately not released for industry secrecy, (though algorithms are deployed on the processing

of the sensors data), detects for up to 85 to 90% the sleep architecture (variability induced by the individuals). Emfit sensor has also been validated for sleep-disordered breathing detection [28] as increased respiratory resistance, snoring and increased respiratory efforts induces characteristic respiratory-related spikes in Emfit ([29]).

The principal limitation in the context of this project (based on an observational study), is the lack of accurate ground-truth. The study has to rely on the available data provided by sensors in home settings without labelization possible. However, with a larger data set, unusual behavior or trends will be more easily detectable when weighted against the norm. A further validation study shall enable us to validate assumptions made in this project.

3.1.2 Opportunities

On the bright side, the practicalness of the system in terms of its setup can be emphasized. The system of sensors is composed by few sensors which can be let alone for months recording data continuously. Their position in the apartment allow us to not interfere with the everyday life of the participants and to not rely on their willingness to interact with the system.

An advantage is also the possibility to study the behavior and the sleep-quality of a PD person without having to bring this person to a medical facility. The system also offers a better overview of the sleep biosignals on a daily basis when caregivers only have short sleep monitoring or patient-caregiver discussion during medical visits.

Finally, sleep architecture detection including the sleep-stages (REM, Light, Deep and Awake) is not 100% accurate but still accurate to a much better rate compared to other devices that can be found on the market. With such accuracy, it is considered exploitable on long-term monitoring and already in usage in structures for athletes (for recovery monitoring) and elderly (medication altering sleep-architecture monitoring).

With the experience of this project and the end-to-end tests organized with the hardware, it became an evidence that a 3G enabled version of the device Emfit QS (recently released on the market) should have been used for the data recording in order to improve the reliability of the connectivity. Indeed, the usage of WIFI access points to connect the Emfit QS included a weak link, relying on access points poorly made for long-term connectivity. There is thus matter to improve the setup in a following study.

3.2 Other data inputs

The study is based on the fact that participants are living their life at home with no way to make sure that a recorded event is reality. Thus, the study designed during the project selected different medical questionnaires and self-assessment tools (diaries) to correlate with the collected data.

Chapter 3. Data collection: a system of ambient sensors

At the moment of the system's installation, the patient answers a questionnaire evaluating its daily activities and living environment. Throughout the recording period, the patient keeps a daily diary which documents the missed drug intakes as well as particular changes in health in an unstructured manner (fall recording, illness, etc.). After three and six months of study onset, the patient will present himself to the service of neurodegenerative diseases where he will be examined medically and presented with standardized clinical scales and questionnaires.

These clinical scales and questionnaires are presented below:

- Unified Parkinson's Disease Rating Scale (UPDRS) [30]: is used to follow up progression of PD. The scale contains subparts that evaluate behavior and mood, a self-evaluation of the Activities of Daily Life (ADL), a clinician-scored monitored motor evaluation, complications of therapy, as well as staging of severity in Parkinson's Disease.
- Parkinson's Disease Questionnaire (PDQ-39) [31]: asks the patient to consider their health and general well-being on a Likert-like scale. The questionnaire considers mobility, activities of daily living, emotional well-being, cognition; social dimensions; communication and bodily discomfort.
- Montreal Cognitive Assessment (MoCA) [32]: a short cognitive test designed to screen for mild cognitive impairment.
- Parkinson's Disease Sleep Scale (PDSS) [33]: a scale that quantifies divers aspects of sleep while addressing 15 commonly encountered sleep-related disorders in PD.

3.3 Symptoms against the data

From the previously mentioned data sets, it can be distinguished which symptoms can potentially be of interest in this project with respect to Chapter 2 detailing the symptoms occurring in PD. The system collects two principal categories of signals. The first category can be described as the daily and nightly activity biosignals, acquired through the PIR sensors and the door entrance sensor. The second category is the sleep-related biosignals acquired through the ballistocardiography-based bed sensor. These two categories of biosignals do not allow us to fully cover the symptoms experienced by Parkinson patients. Also, not all biomarkers can be exploited to discover features of sleep-related symptoms. Below is a description of which symptoms can present interest and which are possible to monitor by the system to be further analyzed. A selection is made between the biomarkers of use and the one that are not be taken into account for this project.

3.3. Symptoms against the data

In Chapter 2, tables 2.2 and 2.3 presented a number of nightly symptoms that can affect PD patients. By linking the medical knowledge of Parkinson's sleep-related symptoms with the possibilities the system offers, this list is reduced to a shorter list of symptoms detectable and/or monitorable by the system. In the following tables 3.3 and 3.4, a selection is made regarding the symptoms and data of interest. The selection was made by matching the features available in the expected data set against the sleep-related disorders of PD.

Sleep-related Symptom	Sensors key features for symptom recognition
Daytime somnolence / excessive daytime sleepiness	Impossible due to lack of data on the patient state at a moment in time
Depression leading to morning headache	The system can not detect neither depression or morning headaches. It can only expose bad sleep quality and the impact on the mood the patient.
Awakenings with shortness of breath (SOB)	The bed sensor could detect an acceleration in the respiration rate in the awakening period. Features: Respiration rate, end of sleep period.
Sleep initiation disturbance/ Sleep-onset insomnia (primary insomnia)	The system can detect the duration of the awake state before the patient falls into sleep. Features: Sleep-onset duration.
Obstructive sleep apnea (OSA)	Obstructive Sleep apnea would require a professional of the sleep to analyze the respiration rate.
Rapid Eye Movement Sleep Behavior Disorder (REMSBD)	This symptom would require a polysomnograph as well as video recordings to be accurate in the diagnostic. Indeed, patients can not reliably report their movement during the night as they are not fully conscious.
Insomnia (sleep maintenance) / Sleep fragmentation (secondary insomnia)	Features: Number of awakenings, number of bed exits, awake duration during the night.
Incontinence due to lack of mobility / Night-time urge incontinence (Nocturia)	This symptom can be monitored with a wide granularity. The system can record the number of toilet usages during the night and make them correspond to bed exits for a more accurate correlation. Features: Number of bed exits, timestamps of toilet usage during the night.

Table 3.3 – Mapping between the sleep-related symptoms observable in Parkinson's patients and the data features matching such symptoms - Part 1

**Chapter 3. Data collection:
a system of ambient sensors**

Sleep-related Symptom	Sensors key features for symptom recognition
Restless Legs Syndrome (RLS)	Similarly to REMSBD, RLS can be difficult to recognize due to a lack of ground-truth data and the impossibility for a patient to self-assess his own sleep.
Sleep Disordered Breathing (SDB)	Similarly to SOB, a specialist should evaluate case by case the full night respiration rate of the Parkinson's patient. The differences on a trace of respiration rate can be too subtle for a system like this to detect SDB. We would also need ground-truth data from already detected events of SDB with the bed sensor device as well as a ground-truth support (video and practitioner diagnostic).
Frequent napping	Frequent napping is often due to sleepiness of the Parkinson's patient. This could be detected in the event a patient regularly naps onto his or her bed, which yet unknown. Features: sleeping periods during the day.
Alterations to total sleep time in bed	A simple way to recognize a change in the total sleep duration is the monitoring on the long-term of the duration in sleep during the night. Features: duration in sleep over time (longer or shorter).
Alterations of the circadian rhythm disturbances	Internal desynchronization can be detected with the computation of a shift in the sleep periods over time.
Sleep deprivation	The data concerning the need of sleep from the patient is not available unfortunately in this study.

Table 3.4 – Mapping between the sleep-related symptoms observable in Parkinson's patients and the data features matching such symptoms - Part 2

From tables 3.3 and 3.4, the symptoms can be separated between the ones which are involving the unfolding of the night with particular events such as movement, bed exits, sleep duration, from the ones involving the state of mind of the patient such as depression or sleepiness. Moreover, some symptoms require more medicalized devices of signal acquisition and means to confirm events such as SOB, SDB, RLS or REMSDB artifacts, for example with a camera, PSGs or polygraphs, as patients can not report objectively these kind of events and their timestamp in a diary to be correlated with the recorded signals.

3.3. Symptoms against the data

Finally, we do not explore the symptom of sleepiness with naps during the day as relying only on naps inside the bed can be unreliable (most persons nap on their sofas for example). The project does not explore the nocturia neither as data sets with PD do not supply the motion activity at night for the moment. Consequently, the project focuses mostly on the Emfit QS data set and on the detection of the activity at night and its unfolding with the following symptoms in mind:

- **Sleep Initiation disturbance:** the symptom can be studied through the duration it takes PD patients to fall asleep against our data from healthy subjects.
- **Insomnia:** the fragmentation of the night can be studied through the awakenings and the bed exits occurring during the unfolding of the night in PD patients against data from healthy subjects.
- **Alterations to total sleep time in bed:** the duration of sleep can be studied and compared to already known measures from the literature in PD [25].
- **Body stiffness:** The bed sensor allows to record the activity in bed, thus enabling the system to quantify the movement the body generates during sleep.

Finally, selecting these four symptoms enables us to focus on exploring potential markers of wearing-off of the medicine at night or degradation of the illness over time. The summary of the selected parameters and matching symptoms is presented below in Figure 3.1:

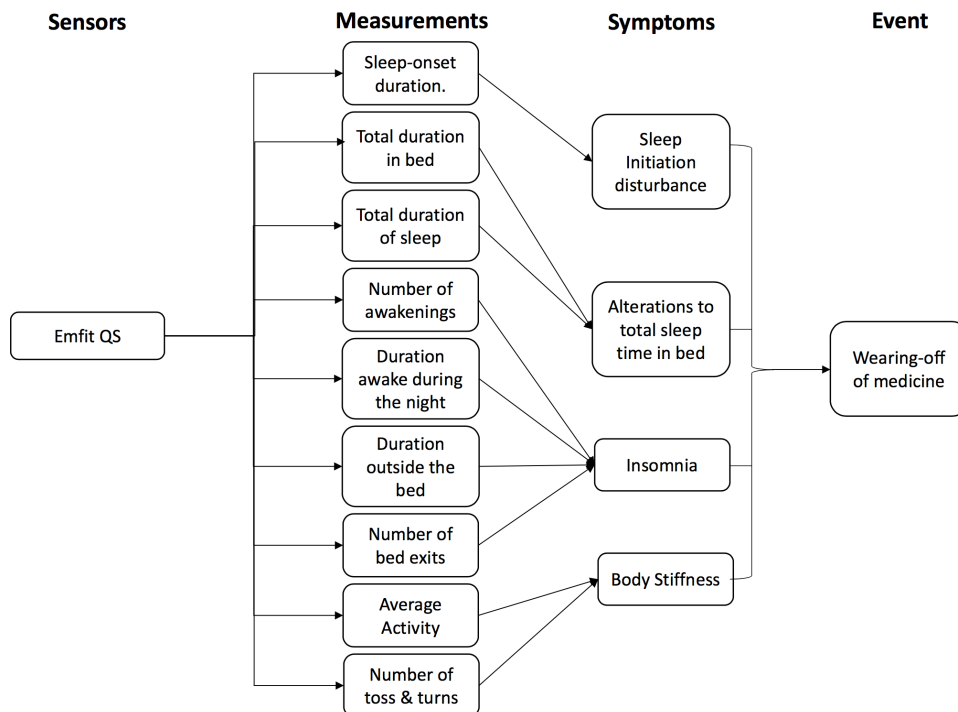


Figure 3.1 – Summary of the selected symptoms and data features from the available setup.

Chapter 3. Data collection: a system of ambient sensors

The next two chapters present the results of the exploratory analysis achieved on our available data sets and the analysis of the stated chosen symptoms resulting from the data exploration.

4 Methodology

This Chapter explores the methodology employed to analyze the data sets obtained during the duration of the project according to the symptoms presented in Chapter 2 and 3. Section 4.1 presents the designed study developed during the project to collect the needed data set for further analysis. Afterwards, Section 4.2 presents the data set used for the sleep-related symptoms analysis and its preparation. Finally, Section 4.3 presents the results of the exploration made upon the available data.

4.1 Study design

During the course of this project, the goal was to create a study designed to provide us with insights on the occurrence and evolution of sleep-disorders in the Parkinson's Disease with the help of non-invasive technologies. In fact, symptoms related to sleep can provide valuable information to caregivers about the QoL of their patients and thus their analysis can be used as a tool to take more informed decisions onto their patient's treatment. This observational study prospectively assesses a small sample of 20 PD patients. This study is observing the changes in patients' sleep behavior, as inherent to the disease or in response to missed drug intakes at the patient's home for a duration of six months. During the course of this project, recruitment started lately and thus it was impossible to get all the necessary input data. Still, we were able to extract a large data set for healthy participants of an elderly age, similar to an other small data set of PD patients that are detailed in the next section.

The study is designed around the the collection of data sets from ambient sensors as well as gathering of medical questionnaires completed by a full medical background. In a first phase, screening and recruitment of the patients are done. Then in a second phase, a medical visit with the caregiver is planned to obtain demographic and clinical data as well as to complete the four medical questionnaires planned (UPDRSS, PDQ-39, MoCA, PDSS). Following this, the installation of the system of sensors is done at the patient's house. From this time up to the middle of the study (3 months), the patient fills a diary indicating if he missed his medication or if its health has deteriorated. At the middle of the study, a new medical visits assesses again

Chapter 4. Methodology

the four questionnaires as well as at the end (6 months). It is important that even with only three assessments of the questionnaires during the study it is ensured that data is scientifically valid, compared to more frequent assessments, as it can be less valuable impacted by an effect of "learning the correct answers".

The study is not interventional but has for purpose to collect on the long-term as many biosignals with references in time (medical questionnaires) to observe the sleep-related symptoms of PD.

Inclusion criteria

In partnership with the University Hospital of Lausanne, the following criteria were established to include the patients into the study.

- Probable PD according to UK Parkinson 's Disease Society Brain Bank (UKPDSBB) diagnostic criteria
- Presence of motor fluctuations
- Aged from 30 to 80 years
- Willing to wear a wearable device during the day
- Willing to keep a daily diary

The recruitment is done by a professional of neuropathologies and expert in the Parkinson's Disease from the University Hospital of Lausanne.

Sample size

Several primary endpoints are correlated during this project. These endpoints rely on previously conducted validation studies. Correlation of sensor endpoints, with the UPRS sub-scores were previously obtained by studying patients groups with Parkinson's Disease as small as ten patients for changes in positions [34], twelve patients for activity parameters [35], ten patients for the quantification of tremor and bradykinesia [36], as well as the assessment of gait parameters respectively [37]. The study by Aran et al. (2016) [38], relied on the analysis of 40 patients for the anomaly detection method. To our knowledge there was no indications about an appropriate number of patients in the literature for this novel approach of long-term monitoring with connected objects. Therefore we considered that a study based on a sample of 20 patients would allow more insight into sample calculations for a subsequent clinical trial and would be acceptable to obtain a significant amount of data to perform the desired analysis.

4.2 Ambient sensors data set

The design of the study was made during the course of this project. However, the recruitment was not completed before the deadline and thus, the data sets available is more restricted than expected. During the course of the project though, we were able to successfully collect the following data sets:

- A data set of 2356 night periods (before data pre-processing) recorded with Emfit QS bed sensors from 20 elderly persons.
- A data set of 93 night periods (before data pre-processing) recorded with Emfit QS bed sensors from 13 PD ill persons.

These data sets represent approximately 60Go of data with different parameters to investigate that are introduced in the next subsection. The treatment of this data set is detailed below. From those, we had to remove 33 invalid night segments in the healthy night segments (1.4% corrupted) and 3 in the PD night segments (2.2% corrupted) which provided us with 2323 uncorrupted healthy night segments and 90 uncorrupted PD night segments. In order to base the analysis on the same type of night, we removed segments shorter than five hours to eliminate the possibilities of included naps. This provided us finally with a total of 1717 healthy night segments and 82 PD night segments.

Additionally to the key measures of each night (number of bed exits, number of toss and turns, average activity, etc.), the data set provides the time series of the activity measurements sampled every two seconds. Considering that Chapter 4 proved the value of the activity at night as an important measure of distinction between the two analyzed populations, these time series are also considered in the further developed algorithms. In the next section is presented how we can distinguish a night segment from a person with Parkinson's and a healthy person.

The healthy elderly population is composed of 10 female and 10 male persons, with average age of 69.1 years old whereas the PD population is composed of 7 males and 6 females persons averaging 66.8 years old. The age difference between the two populations allows us to have the same comorbidity risks linked to aging and make a more plausible analysis. The populations are also split equally considering the gender of the participants, avoiding gender bias. Chapter 4 provides more details on the pre-processing of the data set.

Parameters analyzed

Among these data sets, only certain features are kept for the further symptoms analysis. From these key features, vitals such as respiration rate or heart rate are discarded as well as the sleep architecture (REM, Deep, Light). They are not supporting the investigation of the symptoms described in Chapter 3. In the following table, a summary of the parameters returned from

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the devices that are explored in this chapter, excluding those of no interest for the symptoms analysis:

Sensor	Parameters	Name
Emfit QS	Duration of the night period	duration
	Duration of the presence in bed	duration_in_bed
	Duration of sleep	duration_in_sleep
	Duration awake (with bed exits duration)	duration_away
	Duration of sleep onset	duration_sleep_onset
	Duration of bed exits	bedexit_duration
	Timestamp from which period started	from, from_string
	Timestamp from which period started	to, to_string
	Number of bed exits	bedexit_count
	Number of toss and turns	tossnturn_count
	Average movement	avg_act
	Number of awakenings	awakenings
	Timestamps of bed exits	start_at, end_at
	Timestamps of toss and turns	timestamp
	Timestamp of generated movement	timestamp
Value of generated movement at "timestamp"	act	

Table 4.1 – Summary of all data variables obtained from the bed sensor

In the next section, the approach employed to explore the promises of the key sleep-related features of our data sets is presented. Section 4.3 presents the results of the statistical analysis performed on the previous stated data features.

4.3 Data exploration

The purpose of this thesis is to explore whether or not the data obtained from non-invasive sensors can highlight the artifacts of PD sleep-related symptoms. This section develops the different statistical tests and visualizations employed to explore the relevant parameters establishing a potential difference between healthy persons and PD sick patients.

4.3.1 Primary exploration comparing the PD population with the healthy population

According to Chapter 3, four symptoms were selected to focus on. The related parameters of the night were thus used to compute different statistics in order to provide a first feeling on the existence of differences between the two populations. In a first phase, a standard statistical analysis was made on the sensors features selected and compared to one another. In the following table 4.2 are presented the means, medians and standard deviations of the

parameters against each other.

Variables	Healthy Population ($n = 20$)			PD Population ($n = 13$)		
	Mean	Median	Std	Mean	Median	Std
Bed Exits counts	1.97	1	4.01	3.09	2	6.65
Awakenings counts	1.52	1	1.40	1.98	2	1.66
Toss and turns	26.12	18	28.25	13.23	10	13
Duration of sleep onset	22.6 *	19.5 *	15.3 *	25 *	22.5 *	14 *
Duration in Bed	434.4 *	472.9 *	181.5 *	496.5 *	514.6 *	144.1 *
Duration of awake time in bed	66.7 *	61.5 *	36 *	71.7 *	63 *	38.4 *
Duration in Sleep	367 *	408 *	173.7 *	435.3 *	445 *	147.3 *
Duration outside bed	12.5 *	8.3 *	13.4 *	16 *	19.9 *	19.9 *
Average Activity	89.23	56	98.19	38.88	35	23.95

* in minutes

Table 4.2 – Statistics on the different Emfit QS features

From this primary exploration, a few important conclusions can be made. The most important information to extract from this table concerns the movement activity in bed during sleep. The average activity is much higher, with on average more than twice the activity in the healthy population. An other indicator of unusual movement during sleep is the number of toss and turns at night, almost twice lower in PD persons compared to healthy persons. According to the scientific knowledge on sleep in Parkinson's patients as mentioned in Chapter 2, it is known that wearing-off of the medicine is inducing body stiffness. During the night, there is no opportunity for the patients to take their medicine unless they wake up for that purpose. Thus it is assumed as a biomarker of possible wearing-off of the Levodopa medicine during the night. Indeed, Levodopa is generating a peak in concentration at about one hour and is maintained for about 4 to 5 hours ([39]) before declining. Secondly, we can notice indicators of insomnia with a number of awakenings and a number of bed exits higher, as well as a slightly longer period awaken or outside the bed at night for the PD population. As we saw in Chapter 3, these markers are valuable clues for the detection of insomnia in PD patients.

Based on that we calculated the percentage of persons affected by frequent awakenings. The threshold of 5 awakenings is based on Factor et al. and their study "Sleep Disorders and Sleep Effect in Parkinson's Disease" in 1990 ([18]), where they find that at least 5 awakenings or bed exits is considered sufficiently frequent to be unusual. A high number of awakenings is slightly more common in the PD population with 2.2% against 0.9% for healthy persons. Bed exits are also more common for PD patients with 18.3% having more than 5 bed exits per night against only 5.7% in the healthy population. This difference indicates that a more important portion of the PD population experiences disturbances at night and suffer more frequently of

sleep fragmentation (or insomnia).

An other important marker is the total duration in sleep which is on average greater than an hour more for PD patients. An hour asleep is sufficiently important to be considered as a strong clue in the alteration of the sleep for PD persons. The sample of PD patients is spending more time asleep and in bed compared to the healthy sample according to the data.

Finally, the duration of sleep-onset is not considerably higher in PD compared to healthy persons. We can thus not rely this result to make any valuable conclusion.

4.3.2 Secondary exploration with data visualization and statistical tests

In this subsection is presented the different data visualization made to apprehend the bed sensor data set. Statistical tests used to validate our hypothesis of potential symptoms biomarkers are then presented based on the discoveries of the primary data exploration.

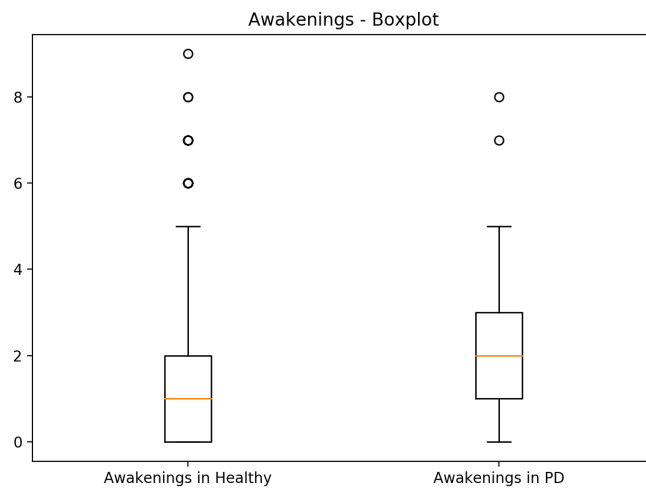
Because the PD population's data is sparse, the next step is to visualize the data in order to apprehend if some features are not representing the population and if there are outliers too important to take certain features into consideration. The next figures presents the different representations of the data distributions and statistics.

Box plots

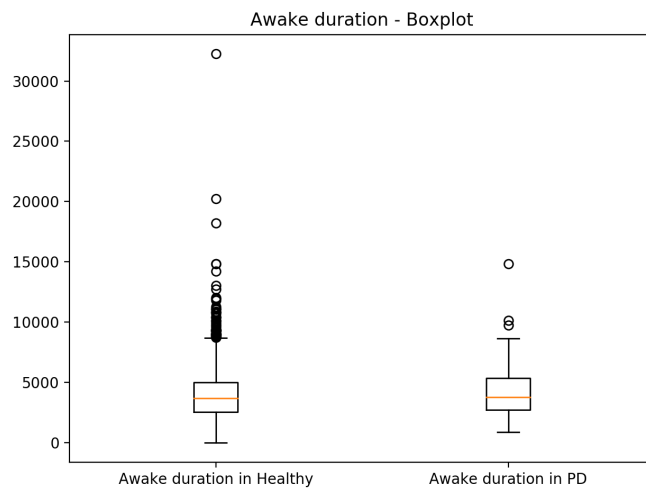
In order to check the variation information in our data sets and get a good overview of the 9 selected data features distribution we use box plots which allows us to compare the two different groups of PD and healthy populations. Below in Figure 4.1 can be found the features distributions represented with box plots:



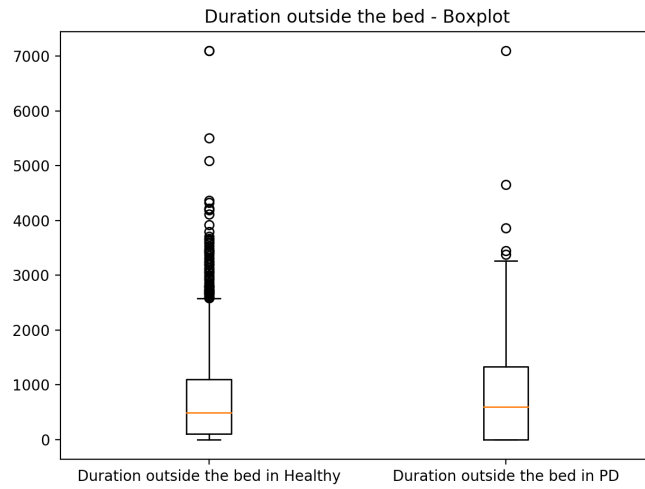
(a) Box plot of the number of bed exits per night. The median of the number of bed exits in PD is higher and the upper quartile shows more exits at night in general.



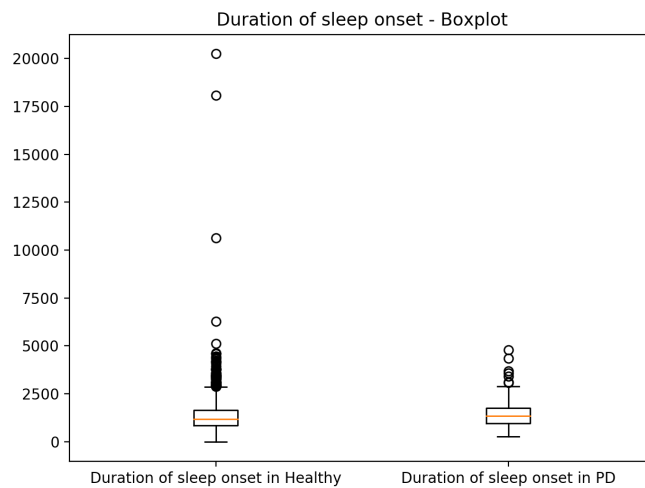
(b) Box plot of the number of awakenings per night. The box plot is much higher in PD, showing a tendency to awake more during the night.



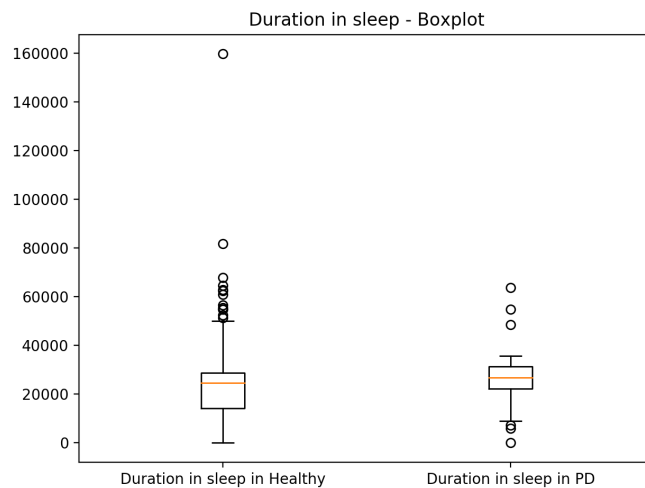
(c) Box plot of the duration awake in bed at night. The awake duration at night does not seem higher in PD.



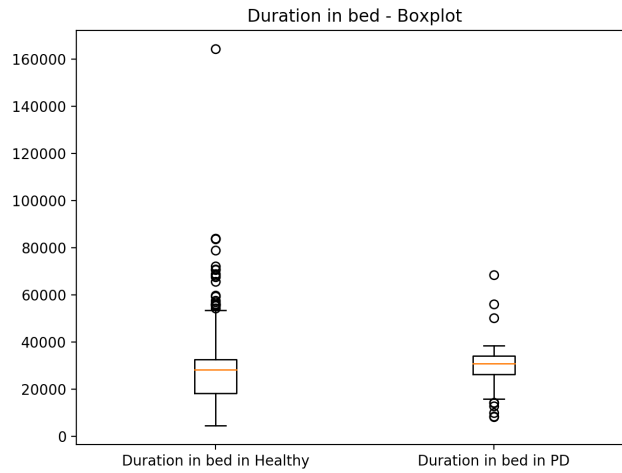
(d) Box plot of the duration outside the bed during the night. The duration outside the bed is generally slightly higher in the PD population, though the medians are close together.



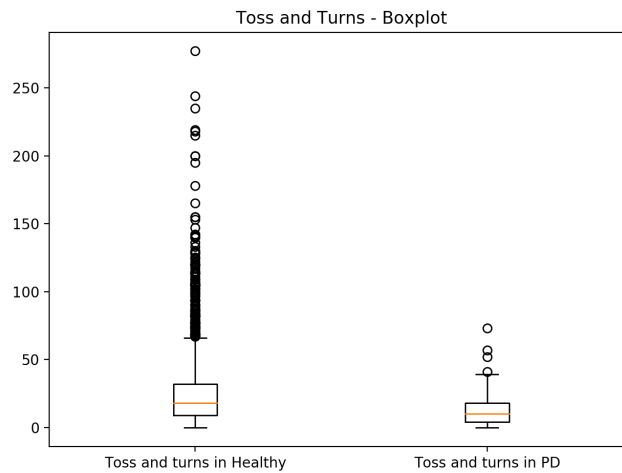
(e) Box plot of the sleep onset duration. The sleep onset duration are similar in both populations.



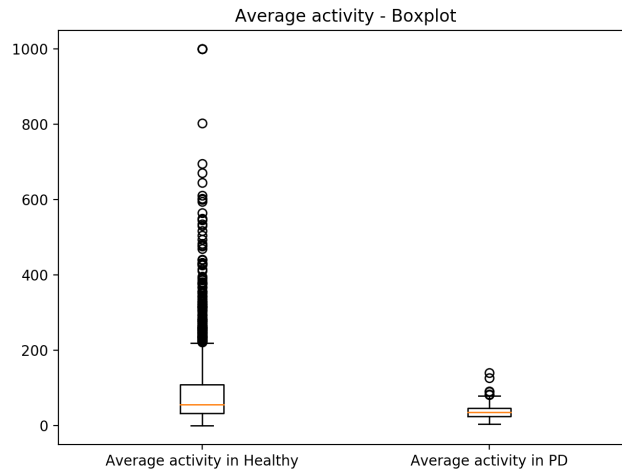
(f) Box plot of the duration asleep at night. The healthy population sleeps less in general while the PD population tends to invariably sleep more.



(g) Box plot of the duration in bed at night. The PD population spends more time in bed and shows less variance compared to the healthy population.



(h) Box plot of the number of toss and turns per night. Toss and turns are less frequent at night for the PD population.



(i) Box plot of the average activity per night. In general, the PD population present much lower values of activity during the night compared to the healthy population.

Figure 4.1 – Distributions of the nine bed sensors features displayed with boxplots.

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The box plots are interesting to visualize rapidly the noticeable differences or similarities between the two groups. The Figures 4.1(a) and 4.1(b) are biomarkers of insomnia, presenting a significant difference with a right skew for the PD population. It indicates a higher incidence of awakenings and bed exits during the night for the PD population. These two markers can indicate a much more fragmented night for Parkinson's patients, thus a worst quality of sleep compared to the healthy population. Figures 4.1(c), 4.1(d) and 4.1(e), do not enable any sure interpretation, which may be due to the lack of data for measures of long duration, inducing too much variability. Finally, we can clearly distinguish a low variance in the movement (average activity and number of toss and turns), clearly showing that PD patients are suffering from a certain body stiffness in bed.

In conclusion, we can observe the following from the primary exploration:

- The PD population present less movement during their sleep with less activity and less toss and turns.
- The fragmentation of the nights is more important in the PD population with more frequent bed exits and awakenings.
- The PD population seems to sleep and stay in bed longer than the healthy population.
- The sleep onset seems similar in both populations though statistics are showing a slight difference with longer periods of sleep onset for the PD population.
- The PD population spends generally more time outside their bed during the night.

These remains observations and no proof. In the next section, we validate (or invalidate) the above hypothesis and if the observed tendencies of the selected measures are proved to be true.

Statistical analysis

To validate the hypotheses made based on the primary data exploration in the above subsections, it is important to validate statistically that such impressions are not up to luck. For each feature was made a null hypothesis H_0 and an alternative hypothesis H_1 based on the simple statistics made in Section 4.3.1 and the visualizations of the data distribution in the section above. The purpose of testing our hypotheses is to validate that the research question upon which we wish to show that certain features of the night can indicate a poor quality of sleep and symptoms experienced by the Parkinson's patients. The hypotheses are described in Table 4.3, page 33.

4.3. Data exploration

Feature	Hypothesis
Bed Exits counts	<p>H_0: There is no difference between the number of bed exits during the night between our two populations.</p> <p>H_1: The number of bed exits during the night experienced by PD patients is higher compared to healthy persons.</p>
Awakenings counts	<p>H_0: There is no difference between the number of awakenings during the night between our two populations.</p> <p>H_1: The number of awakenings during the night experienced by PD patients is higher compared to healthy persons.</p>
Toss and turns counts	<p>H_0: There is no difference between the number of toss and turns during the night between our two populations.</p> <p>H_1: The number of toss and turns during the night experienced by PD patients is lower compared to healthy persons.</p>
Duration of sleep onset	<p>H_0: The duration of sleep onset is the same in PD patients and in healthy persons.</p> <p>H_1: The sleep onset duration in PD patients is longer compared to healthy persons.</p>
Duration in Bed	<p>H_0: The duration in bed is the same in PD patients and in healthy persons.</p> <p>H_1: The duration in bed during the night in PD patients is longer compared to healthy persons.</p>
Duration of awake time in bed	<p>H_0: The awake time in bed is the same in PD patients and in healthy persons.</p> <p>H_1: The awake time in bed during the night in PD patients is longer compared to healthy persons.</p>
Duration in Sleep	<p>H_0: The duration asleep during the night is the same in PD patients and in healthy persons.</p> <p>H_1: The duration asleep during the night in PD patients is longer compared to healthy persons.</p>
Duration outside the bed	<p>H_0: The time outside the bed during the night is the same in PD patients and in healthy persons.</p> <p>H_1: The time outside the bed during the night in PD patients is longer compared to healthy persons.</p>
Average Activity	<p>H_0: The average activity at night in PD patients is the same in PD patients and in healthy persons.</p> <p>H_1: The average activity at night in PD patients is lower compared to healthy persons</p>

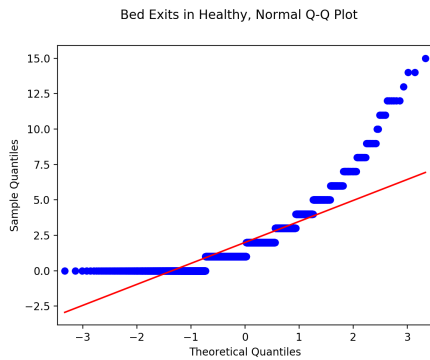
Table 4.3 – Statistical hypotheses based on primary data exploration for the nine selected bed sensor features.

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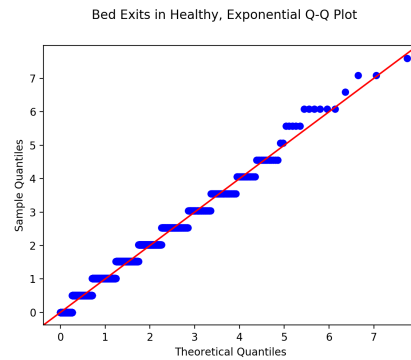
Based on Fisher's "Statistical methods for research worker" ([40]), and the numerous biomedical and bioengineering research studies achieved in the past, this statistical analysis chooses a level of significance p-value of 0.05. This means that there is only a 5% probability of obtaining a result at least as extreme as the one observed when the null hypothesis is considered true.

The choice of statistical tests is made based on the nature of the data and the hypothesis. The hypotheses made here compare numerical values. The choice however needs to be made on what to compare for each feature (mean, variance, distributions, etc.) and how the data is distributed (parametric if following the parameters of the normal or normal distribution curve). With our data, we assess with Q-Q plots (Quantile-Quantile plots) our data's distribution against the normal distribution so to discover if our it is normally distributed and then against other fitting distribution. This tool enable us to graphically evaluate the shapes of a distribution. It is simply the representation of the two sets of quantiles against each other (x axis being the theoretical distribution, y axis being the feature's distribution). The Q-Q plots display the features' distributions against a normal distribution and then against a non parametric distribution. The closer the points lie on the line $x = y$, the closer the data follows the distribution against which it is plot. The distributions are presented and discussed in the following figures from page 35 to page 42.

4.3. Data exploration



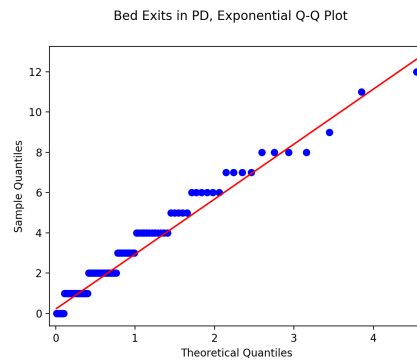
(a) The healthy population with a normal distribution



(b) The healthy population with an exponential distribution



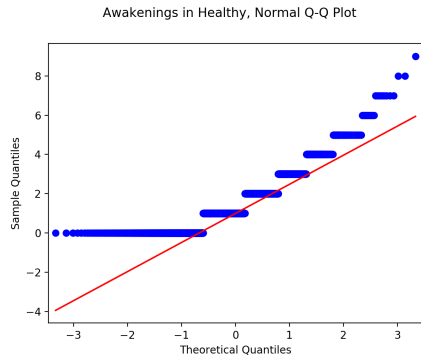
(c) The PD population with a normal distribution



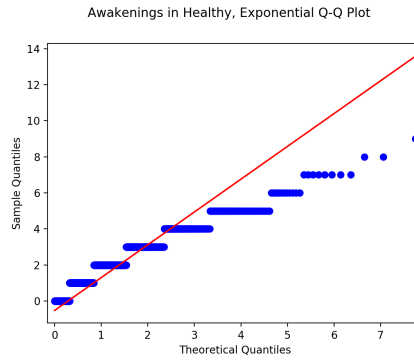
(d) The PD population with an exponential distribution

Figure 4.2 – Q-Q plots of the number of bed exits at night in the healthy and PD populations against a normal and an exponential distribution

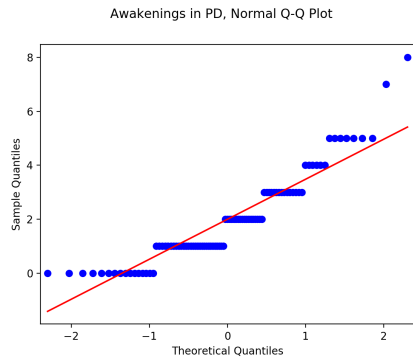
It is distinctly visible that the distribution of the number of bed exits is highly exponential in both the PD and healthy population as can be seen in Figures 4.2(a) and 4.2(c). This is confirmed by the Figures 4.2(b) and 4.2(d) which plot the distributions against the normal distribution. Both distributions are close to the $x = y$ line.



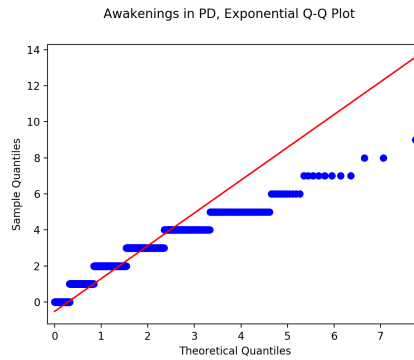
(a) The healthy population with a normal distribution



(b) The healthy population with an exponential distribution



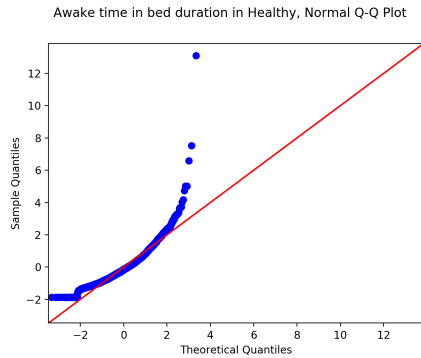
(c) The PD population with a normal distribution



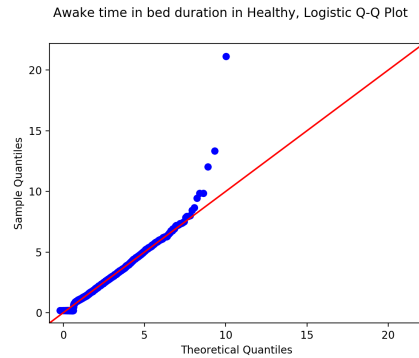
(d) The PD population with an exponential distribution

Figure 4.3 – Q-Q plots of the number of awakenings at night in the healthy and PD populations against a normal and an exponential distribution

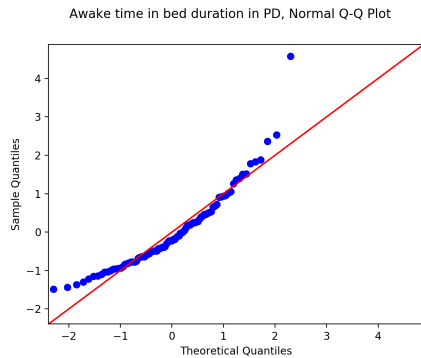
Similarly here, we observe an exponential distribution for the number of awakenings during the night both the elderly and PD population.



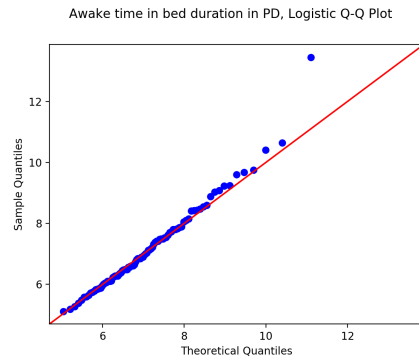
(a) The healthy population with a normal distribution



(b) The healthy population with a logistic distribution



(c) The PD population with a normal distribution



(d) The PD population with a logistic distribution

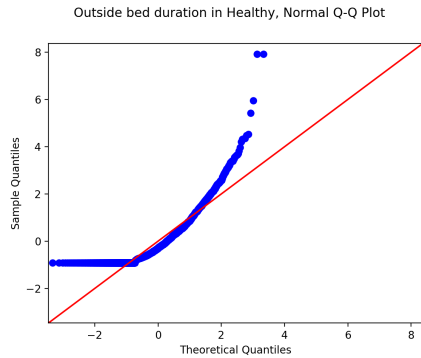
Figure 4.4 – Q-Q plots of the duration awake at night in the healthy and PD populations against a normal and a generalized logistic distribution

The duration awake at night can not totally be fitted to an exponential distribution in both populations, thus it was necessary to find a better match. The distribution can actually be fitted to a generalized logistic distribution, similar to the normal distribution but with heavier tails. The generalized logistic density distribution (Type I, also known as "skew-logistic" distribution) has the following:

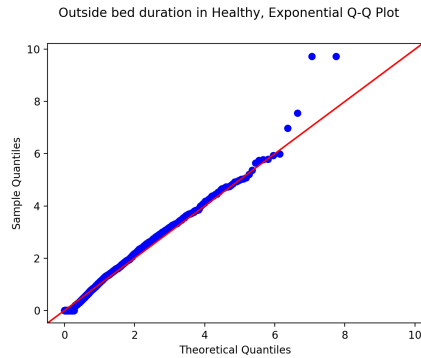
$$f(x, c) = c \cdot \frac{\exp(-x)}{(1 + \exp(-x))^{c+1}}$$

with $x > 0, c > 0$. c is a shape parameter.

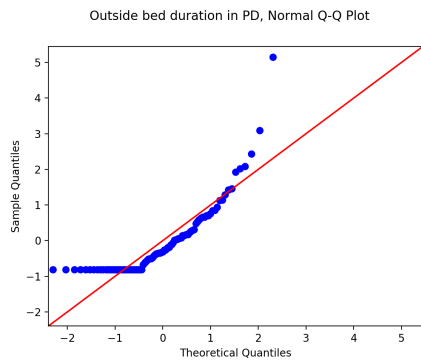
Both populations data do fit to the generalized logistic distribution, so it is impossible to attribute a normal behavior to the distributions, and thus it is not possible to apply standard parametric statistical tests to the data.



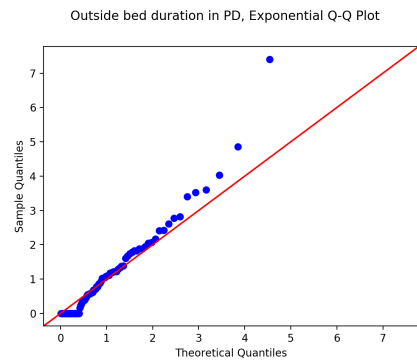
(a) The healthy population with a normal distribution



(b) The healthy population with an exponential distribution



(c) The PD population with a normal distribution

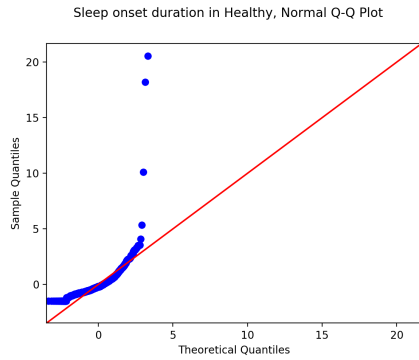


(d) The PD population with an exponential distribution

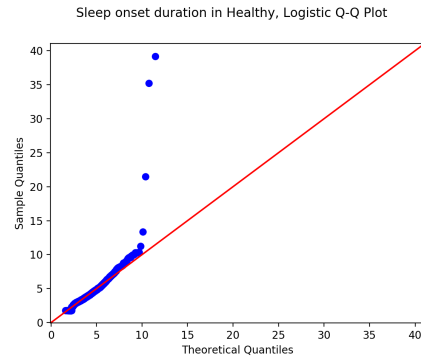
Figure 4.5 – Q-Q plots of the duration outside the bed during the night in the healthy and PD populations against a normal and an exponential distribution

Similarly to the number of bed exits and awakenings, the distribution of the bed exits during the night follow strongly an exponential distribution as can be seen in the Figures 4.5(b) and 4.5(d) where the quantiles are closely distributed on the $x = y$ line based on the standard exponential distribution.

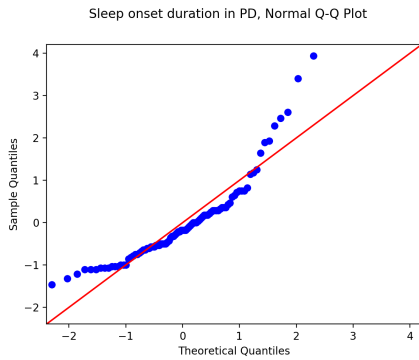
4.3. Data exploration



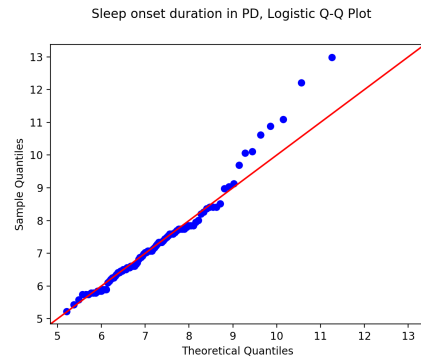
(a) The healthy population with a normal distribution



(b) The healthy population with a generalized logistic distribution



(c) The PD population with a normal distribution

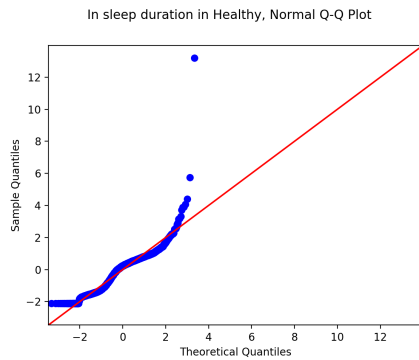


(d) The PD population with a generalized logistic distribution

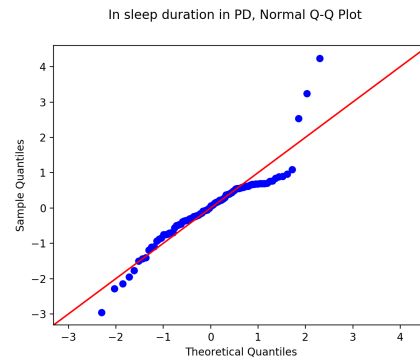
Figure 4.6 – Q-Q plots of sleep onset duration in the healthy and PD populations against a normal and a generalized logistic distribution

Similarly to the duration awake at night, we can see that both PD and healthy sleep onset duration data follow a generalized logistic distribution, which can be instinctively observed on figures 4.6(b) and 4.6(d).

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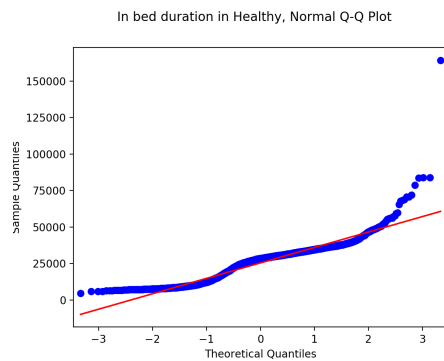
(a) The healthy population with a normal distribution



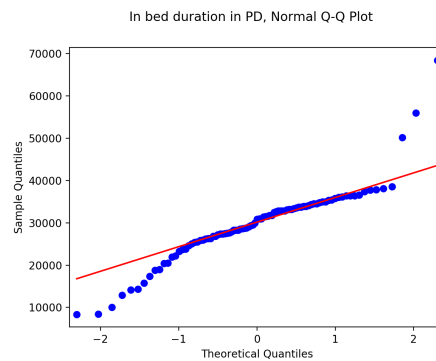
(b) The PD population with a normal distribution

Figure 4.7 – Q-Q plots of the duration in sleep in the healthy and PD populations against a normal distribution

These Q-Q plots with normal distributions are already sufficient to determine their features. The Figure 4.7(a) shows a bimodal behavior with two gaussians. The Figure 4.7(b) presents a left skew with heavy tails but rather close to the $x = y$ line. Both distributions are considered non-parametric as the first is not normal and the second presents strong left skew.



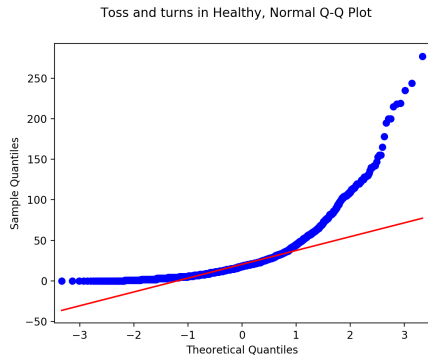
(a) The healthy population with a normal distribution



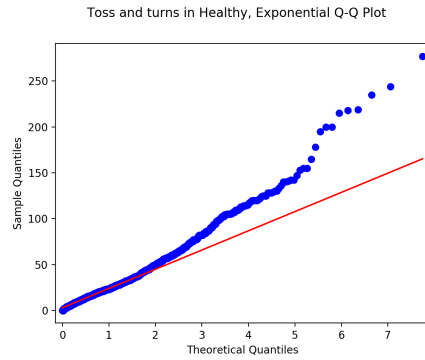
(b) The PD population with a normal distribution

Figure 4.8 – Q-Q plots of duration in bed in the healthy and PD populations against a normal and an exponential distribution

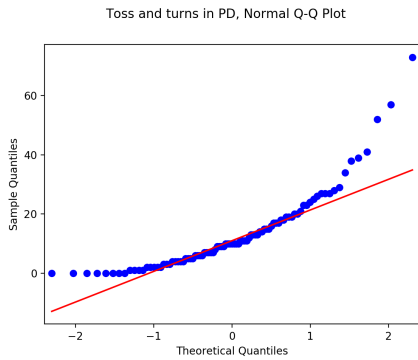
Similarly to the duration in sleep, we observe bimodality in Figure 4.8(a) and a left skew in Figure 4.8(b). Applying parametric statistical tests is therefore not ideal.



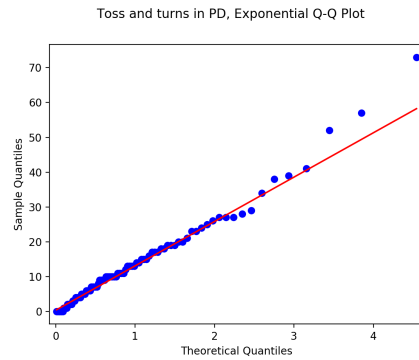
(a) The healthy population with a normal distribution



(b) The healthy population with an exponential distribution



(c) The PD population with a normal distribution

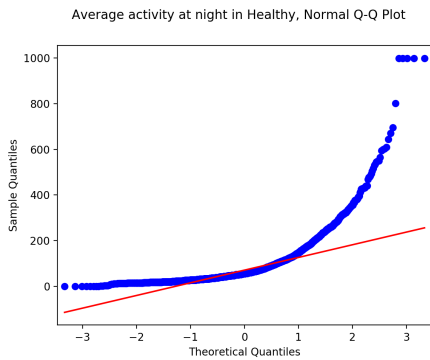


(d) The PD population with an exponential distribution

Figure 4.9 – Q-Q plots of the number of toss and turns during the night in the healthy and PD populations against a normal and an exponential distribution

Both distributions in the PD and healthy population present exponential behavior, though we can observe in Figure 4.9(b) that the highest value do not lie on the $x = y$ line, while most of the values fall on the line. We can thus not consider these distributions as parametric.

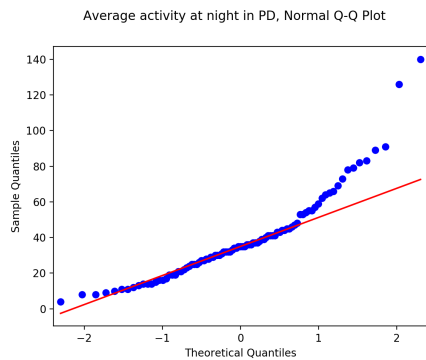
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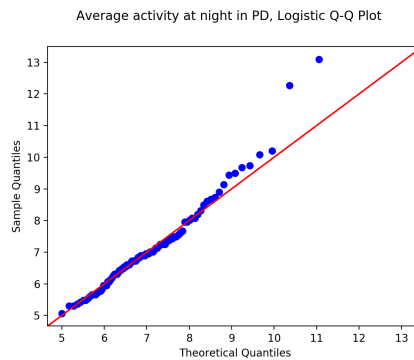
(a) The healthy population with a normal distribution



(b) The healthy population with an exponential distribution



(c) The PD population with a normal distribution



(d) The PD population with a generalized logistic distribution

Figure 4.10 – Q-Q plots of the average activity at night in the healthy and PD populations. The healthy data is compared against a normal and an exponential distribution and the PD data is compared against a generalized logistic distribution.

The above distributions show significant differences. First, the Figure 4.10(c) shows a more spread distribution and a totally different behavior (exponential for the healthy population while logistic for the PD population). Secondly, the Figure 4.10(b) show deviance from the $x = y$ line, which shows an exponential behavior with a strong right skew.

The distributions presented in the above Figures show apparent non-parametric behavior (mostly exponential, generalized logistic or bimodal), it is not suitable to use parametric tests to validate our hypotheses and thus we need a test following the below requirements:

- Suitable for non-parametric
- Suitable for numerical data
- Suitable for unpaired groups (data is not derived by repeated measurements)
- Suitable for independent groups

The Mann-Whitney U (also known as Wilcoxon rank-sum test) is a test assuming the above requirements. In case the distributions are presenting significant differences such that if we draw a sample from one group, there is at most 5% chance that this sample could have been drawn from the other group. This test present the advantage to be more widely applicable to independent samples and more robust to the presence of outliers.

Mann-Whitney U Test

Let's assume we have the following:

- PD population sample data: x_1, x_2, \dots, x_n
- Healthy population sample data: y_1, y_2, \dots, y_m

Where x_i and y_i are the sample's values for the two groups (i.e. average activity values, asleep durations, etc.). The Mann-Whitney U test compares each observation x_i from the first sample to each observation y_j in the other sample. The number of pairwise comparisons is $n \cdot m$. Any given observation is either strictly less than or strictly greater than any observation. Having a data set of 1717 nights from the healthy population and 82 nights from the PD population, we have: $n = 1717$ and $m = 82$. What the Mann Whitney test does is first to merge the data from the two populations into a single data set and then order them in ascending order ranked from 1 to n where n is the total number of observations (in our case, $n = 1799$). Then it adds up the ranks from the first sample and we call it R_1 and do the same with the second sample to obtain R_2 . Then the test calculates for both samples the following:

$$U_1 = n_1 \cdot n_2 + \frac{n_1(n_1 + 1)}{1} - R_1$$

$$U_2 = n_1 \cdot n_2 + \frac{n_2(n_2 + 1)}{1} - R_2$$

From these two, we choose $U = \min(U_1, U_2)$, and U is our "statistic". Then to make a decision upon the acceptance or rejection of our hypotheses, we need to compute the level of significance of the statistic. For sample sizes under 10, we can use the "Mann-Whitney table" (Jacobson, J. E., Journal. of the Amer. Stat. Ass., 1963, 1086), however here, we need to approximate U as a normal distribution, or in other words, as: $Z = \frac{U - \mu}{\sigma}$ where $\mu = \frac{n_1 \cdot n_2}{2}$ and

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$\sigma = \sqrt{\frac{\sqrt{n_1 n_2 (n_1 + n_2 + 1)}}{12}}$ and U is the Mann Whitney U statistic calculated above. For a two-tailed test (the comparison of two "new" populations) the value of $|Z_{\alpha/2}|$ where α is the significance level (5%), giving us a 97.5% distribution is a value of 1.96. Thus, the Z obtained shall reject the hypothesis if $|Z| > 1.96$. The p-value is obtained by taking the probability that the observed values of a standard normal distribution distribution is less than or equal to Z .

The Mann Whitney test is overall much more robust in providing significant results compared to parametric tests and thus we can apply it to our data set. If the dataset were to scale but keep non-parametric distributions, the results would only get more precise. If the data set scales and data becomes more and more parametric, we recommend to use the powerful Student test. In the Table 4.4, page 45, is presented the summary of the Mann Whitney U test performed on the samples of the nine sleep-related measures studied.

Discussion

From Table 4.4, we observe that two of the nine hypotheses are rejected. The duration awake at night in the bed is not considered different enough between the populations to confirm the alternative hypothesis H_1 which state the difference between the two sets (p-value of 0.148731). Similarly, the duration outside the bed is not significantly different between the healthy and PD populations (p-value of 0.210558). Both these hypotheses are showing that the duration awake or outside the bed are not good parameters to identify unordinary behavior at night in a person. These can thus not be taken into account when considering insomnia features.

At the contrary, some measures present strong differences with very small p-values such as the average activity (p-value of $1.69695e^{-12}$) at night or the number of toss and turns (p-value of $1.08702e^{-8}$) during the night. This indeed confirms the assumptions that Parkinson's patients do generate less movement compared to the healthy persons during the night, and thus might present inconvenient body stiffness.

Finally, these statistical tests shows that the number of bed exits (p-value of $2.67332e^{-6}$) and awakenings (p-value of 0.00447857) are significantly higher in the PD population. Moreover, the duration of onset sleep that was considered at first as very similar between the two populations, presents still important difference (p-value of 0.0348875). This confirms the hypothesis that PD patients experience more difficulty to fall asleep compared to healthy persons. The durations asleep (p-value of 0.000107093) and in bed (p-value of 0.000336718) do also present similar results and are considered different between the two populations. This confirms that PD patients tend to have more sleep and overall, be in bed longer than the healthy persons.

Feature	Hypothesis	H_0 Result	H_1 Result	p-value	U Statistic
Bed Exits counts	H_0 : There is no difference between the number of bed exits during the night between our two populations. H_1 : The number of bed exits during the night experienced by PD patients is higher compared to healthy persons.	Rejected	Accepted	2.67332e-06	78376
Awakenings counts	H_0 : There is no difference between the number of awakenings during the night between our two populations. H_1 : The number of awakenings during the night experienced by PD patients is higher compared to healthy persons.	Rejected	Accepted	0.00447857	90965
Toss and turns counts	H_0 : There is no difference between the number of toss and turns during the night between our two populations. H_1 : The number of toss and turns during the night experienced by PD patients is lower compared to healthy persons.	Rejected	Accepted	1.08702e-08	144438
Duration of sleep onset	H_0 : The duration of sleep onset is the same in PD patients and in healthy persons. H_1 : The sleep onset duration in PD patients is longer compared to healthy persons.	Rejected	Accepted	0.0348875	95727.5
Duration in Bed	H_0 : The duration in bed is the same in PD patients and in healthy persons. H_1 : The duration in bed during the night in PD patients is longer compared to healthy persons.	Rejected	Accepted	0.000336718	85293.5
Duration of awake time in bed	H_0 : The awake time in bed is the same in PD patients and in healthy persons. H_1 : The awake time in bed during the night in PD patients is longer compared to healthy persons.	Accepted	Rejected	0.148731	100798
Duration in Sleep	H_0 : The duration asleep during the night is the same in PD patients and in healthy persons. H_1 : The duration asleep during the night in PD patients is longer compared to healthy persons.	Rejected	Accepted	0.000107093	83311.5
Duration outside the bed	H_0 : The time outside the bed during the night is the same in PD patients and in healthy persons. H_1 : The time outside the bed during the night in PD patients is longer compared to healthy persons.	Accepted	Rejected	0.210558	102394
Average Activity	H_0 : The average activity at night in PD patients is the same in PD patients and in healthy persons. H_1 : The average activity at night in PD patients is lower compared to healthy persons	Rejected	Accepted	1.69695e-12	153405

Table 4.4 – The Mann Whitney U test applied to the nine different sleep-related measures and the results of the statistical test at accepting or rejecting the hypotheses of Table 4.3.

4.3.3 Results of the statistical analysis

In this section we presented the consolidation of the observations made in Section 4.3. The primary and secondary analyses made allowed to deeply look into the sleep biosignals divergences between both the PD population and the healthy population.

The primary analysis performed in the Section 4.3.1 showed the following:

- The number of bed exits and awakenings during the night is higher in general in the PD population compared to the healthy population. We suspected thus a more fragmented night induced by insomnia symptoms.
- The number of toss and turns during the night and the average activity is much lower for PD patients compared to the healthy persons. We suspected thus that PD persons show less movement in bed due to body stiffness which can be triggered by the wearing-off of the dopamine medication.
- The duration in bed and asleep is longer for PD persons and thus can be induced by the alteration of total sleep time in bed experienced by the PD persons as the disease gets advanced.
- The sleep onset duration is only slightly more important in the PD population but has no major difference with the healthy population. The difficulties of falling asleep at night is not suspected to be detectable with this measure.
- The duration of the bed exits during the night for PD persons is more important compared to the healthy persons. The fragmentation of the night in PD can be reinforced by this observation.
- The duration awake at night, though more frequent in PD, does not present major differences with the healthy population.

Overall, the comparison of the PD population against the healthy population present differences, mostly in the movement detected by the bed sensor, the number of awakenings and the duration spent in bed. This conclusions though needed to be supported by a statistical evaluation of the two data sets. In the Section 4.3.2 was showed visually the data distributions and their non-parametric behavior. It was also presented the results of the statistical analysis performed with the non-parametric robust test "Mann-Whitney U" to establish the correctness of the hypotheses made in the primary observation. The statistical test performed enabled the following conclusions:

- The number of bed exits and awakenings during the night is indeed having evident differences.
- The number of toss and turns during the night and the average activity is indeed much lower in the PD population.
- The duration in bed and asleep is indeed longer for the PD population.
- The sleep onset duration is however presenting difference which were not particularly visible at first sight.
- The duration awake at night and outside the bed is actually not representative of a difference between the population.

From these observations derive the direction of the further analysis in Chapter 5. The body stiffness is a symptom that do seem to be quite apparent in the PD population, with a large observable difference with the healthy subjects. The fragmentation of the night, the most important marker of insomnia, seems also to present enough difference to be noticeable statistically. Chapter 5 explores in more details the patterns of movement in bed during the night and the patterns of the course of the night in PD compared to the patterns of the healthy population.

5 Data analysis: recognition of Parkinson's disease sleep-related symptoms

Performing data analysis on ambient Parkinson's related data rather than standard laboratory polysomnograph is a novel approach brought by the rise of new medical-oriented devices coming to the market. The problem at hand, recognizing markers of Parkinson during sleep, has thus not been studied before. This thesis presents novel results obtained from a data analysis made with ambient bed sensors installed at a set of healthy seniors and Parkinson's ill patients. Chapter 5 will present the different classification algorithms built during the project towards recognizing the symptoms of wearing-off of the dopamine medication for PD patients during their sleep. Section 5.1 will detail the strategy employed to handle the available imbalanced data set and present solutions to overcome such issue. It will also address the features selected to work with in the algorithms presented along the Chapter. Section 5.2 will detail the algorithms implemented and Section 5.3 will be presenting the performance results of the built sleep-related symptoms recognition algorithms.

5.1 Software tools

In order to achieve the further analysis was used the following tools.

Python 3.6: Python is a powerful programming language offering a performant and wide environment to perform data analysis. From the built-in libraries were used *os*, *math*, *csv*, *time*, *json*, *random* and *re*.

NumPy: NumPy is comprehensive Python library offering support for data structures like matrices, data frames or simply arrays. It provides functionalities to ease the manipulation of data.

Pandas: Pandas is a library built on top of NumPy and offers much wider functionalities at a higher level to enclose and manipulate large data sets.

Matplotlib: Matplotlib is a plotting libraries offering functionalities to visualize data.

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Seaborn: Seaborn is a plotting library based on matplotlib and offers more attractive designs to the produced graphs.

Statsmodels: Statsmodels provides statistical models and functions helping the conduction of statistical tests.

SciPy: SciPy provides tools used for scientific computing and offers a wide range of mathematical functions.

Scikit-learn: Scikit-learn is a library built on top of NumPy, SciPy, and matplotlib providing tools to perform data mining and data analysis as well as visualization of learning models. It also provides tools to compute learning models performances.

Imbalanced-learn: Imbalanced-learn is a library that offers re-sampling techniques used for strongly imbalanced data sets.

On top of that, homemade libraries were built during the project in order to mine and process the bed sensor data. In the next section we present the algorithms built based on the data sets described above and the leads provided in Chapter 4.

5.2 Implementation and experiments

This section provides insight in the implementation work achieved on top of the available data gathered during the thesis. Section 5.2.1 presents a classifier based on the activity time series of the two populations. The Section ?? presents on the other hand a more holistic classifier based on the seven key biomarkers that were selected in Chapter 4.

5.2.1 Activity time series classifier

In Chapter 4, we presented a set of 14 available parameters measured by the Emfit QS, in table 4.1 page 26, and we performed an exploratory data analysis on the quantitative measures described in table 4.2 page 4.2. From these measures was highlighted that the most relevant ones as to differentiate PD persons from healthy persons were the average activity, the number of toss and turns, the number of bed exits and awakenings as well as the duration spent in bed. The first noticed, the activity in bed, was thus considered as a good lead to start digging in the features differentiating the two populations.

The challenge in analyzing time series is first the dimensionality. Night segments are different in size and length which implies normalization or truncation and dimensionality reduction for performance issues. A second issue is to keep the order in the values as their are time dependent. In this section will thus be presented the purpose and idea behind the built activity time series classifier.

Idea

The idea behind the construction of a classifier based on the activity segments of the healthy and PD persons is first to ensure that their behavior during the night is similar from a class to another and that these two populations do not present the same patterns at night. This idea is driven by the fact that in the future, potential PD customers using such bed devices could be monitored with this algorithm and observe the effects of an adaptation of drug treatment on the quality of their night. We know that PD patients tend to move less during the night due to the wearing-off of their medicine. Currently, doctors try to adjust dosages, time of intake and mix of drugs in order to better cover the symptoms 24/7 and prevent symptoms such as the body stiffness at night.

When looking into the healthy activity segments compared to the PD ones, it can be definitely observed differences in patterns and amplitude of movement over night between the two populations. The healthy population presents spikes of activity much higher and more frequent over night compared to the PD subjects. Examples are shown in the following Figures 5.1 and 5.2 page 51:

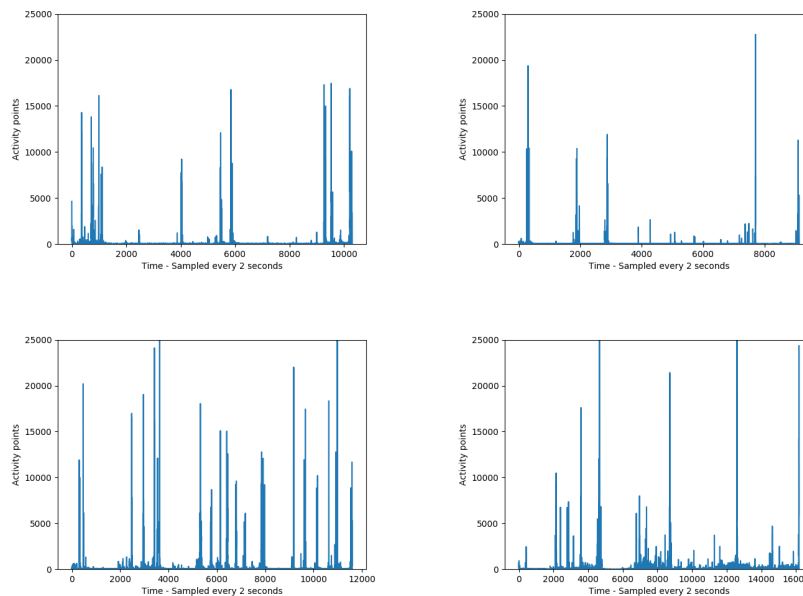


Figure 5.1 – Examples of segments of activity at night for four nights taken from healthy senior subjects. The y-axis represents the scale of activity between 0 and 25000 points and the x-axis represents the time.

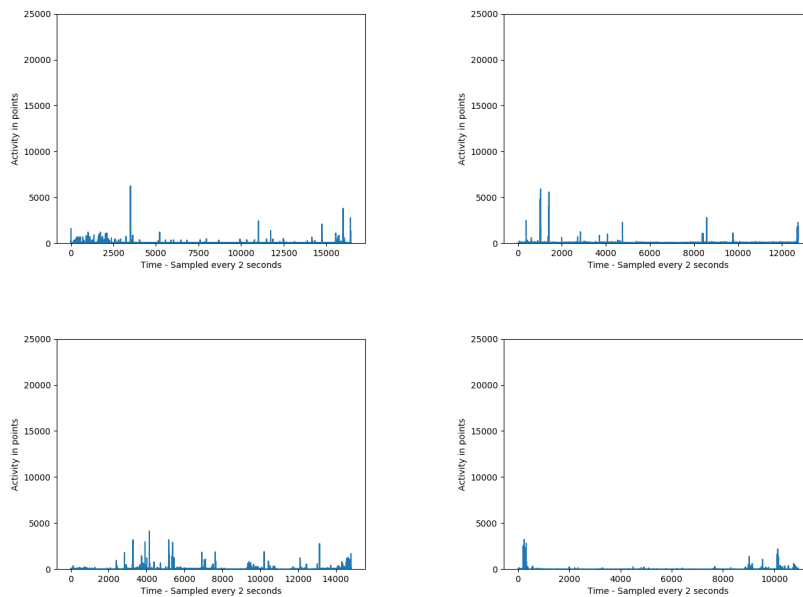


Figure 5.2 – Examples of segments of activity at night for four nights taken from PD ill study participants. The y-axis represents the scale of activity between 0 and 25000 points and the x-axis represents the time

Time series similarity

Based on the differences observed in the night segments, it was clear that the segments could be potentially classified in two distinct classes. In order to do such classification, it is needed to know how different the night segments are between the two populations. Instinctively, the night segments of healthy persons should be closer together and similarly for the PD patients. Thus, in order to quantify this distance it was important to choose cautiously the distance between the two time series analyzed.

The choice of metric measured between segments of temporal data was made based on Teophano Mitsa's work on "Temporal Data Mining" (2010) ([41]) where he evokes the technique of K-Nearest-Neighbors (KNN) combined with Dynamic Time Warping as the golden standard for time series classification. Dynamic Time Warping (DTW) is a nonlinear distance measure or more accurately, a similarity metric between time series. Misaligned but similar segments can be recognize as close with this metric. This metric is an improvement to the standard Euclidean distance. It is also interesting to highlight that DTW produces higher accuracy rates for small data sets compared to the Euclidean distance. The downside of DTW is that it is computationally expensive is the segments are long and the data set large though techniques can help in improving the computational complexity (see next section).

On top of the distance metric to distinguish the different segments, a K-Nearest-Neighbors

(KNN) approach was used. Xi et al. in their Fast time Series Classification Using Numerosity Reduction, 2006 ([42]), proved that a 1NN approach using DTW was highly difficult to beat in the domain of time series classification.

The problem at hand finally resolves itself to a binary classifier based on time series of the activity of the persons monitored. The challenges here to overcome are thus the noisy data (similar data in both groups though from different populations) and the large sizes of the time-series issuing performance issues for the DTW computations. It will be presented the implementation section the chosen approach to obtain an accurate classifier.

Dynamic Time Warping

As mentioned, DTW enables to compute the similarity between two time series. As opposed to the Euclidean distance aligning the time series in time, the DTW distance enables to elastically shift the time axis to accommodate the similarity computation between time series. It enables to find similar patterns though both sequences can be out of phase or non-linearly aligned. Below is showed the difference between the Euclidean distance commonly used and the DTW distance we will be using in this algorithm.

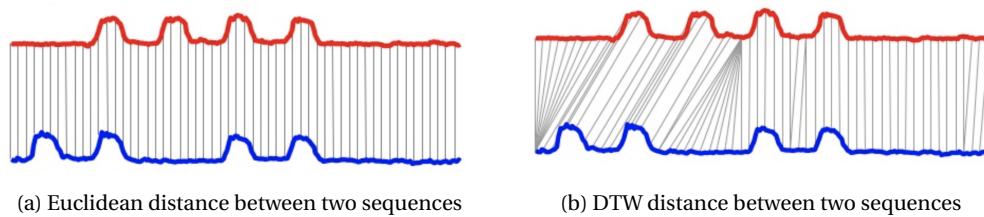


Figure 5.3 – Distance between two time series with the Euclidean distance and the DTW distance. [2]

The DTW distance is calculated as the minimum cost path of all the possible warpings between the two time series compared. The calculation is creating a matrix with all the distances between two points in time on both sequences and the minimum distance is called the warping path.

For two sequences Q and C of size n :

$$Q = q_1, q_2, \dots, q_n$$

and

$$C = c_1, c_2, \dots, c_n$$

We derive the DTW matrix ($n \times n$) with element $(i, j) = d(q_i, c_j) = (q_i - c_j)^2$ for $i, j \in [1, n]$. The (i, j) element corresponds to the alignment between the points q_i and c_j . The warping

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path is a set of these matrix elements that defines the best mapping between the two sequences. This path W is a set of elements and defined as follow: $w_k = (i, j)_k$ so that $W = w_1, w_2, \dots, w_K$ with $N \leq K < 2N - 1$. This path is subject to three constraints:

- **Continuity:** The path should not have any jumps: if $w_k = (i, j)$ and $w_{k-1} = (i', j')$ then $i - i' \leq 1$ and $j - j' \leq 1$.
- **Monotonicity:** The path should not go back in time: if $w_k = (i, j)$ and $w_{k-1} = (i', j')$ then $i - i' \geq 0$ and $j - j' \geq 0$.
- **Boundary conditions:** The path should have a beginning and ending: $w_1 = (1, 1)$, $w_k = (n, n)$.

The warping path of interest is the path minimizing the warping cost:

$$DTW(Q, C) = \min \sqrt{\sum_{k=1}^K w_k}$$

There are $O(n^n)$ possible paths to compute. The minimum cost path can be found by using the cumulative distance recursively in $O(n^2)$:

$$\gamma(i, j) = d(q_i, c_j) + \min\{\gamma(i-1, j-1), \gamma(i-1, j), \gamma(i, j-1)\}$$

where $d(q_i, c_j)$ is the Euclidean distance $d(q_i, c_j) = (q_i - c_j)^2$. The highly expensive computational complexity can be reduced thanks to a global constraint called the "Sakoe-Chiba band" which limits the scope of the warping path [46]. The Sakoe-Chiba band constrains the warping path by restricting the matrix indices in time: $w_k = (i, j)_k$ such that $j - r \leq i \leq j + r$ where r is called the reach and is the allowed range of warping for a given point in a sequence. Below is represented in Figure 5.4 the warping path and the Sakoe-Chiba band that constrains it:

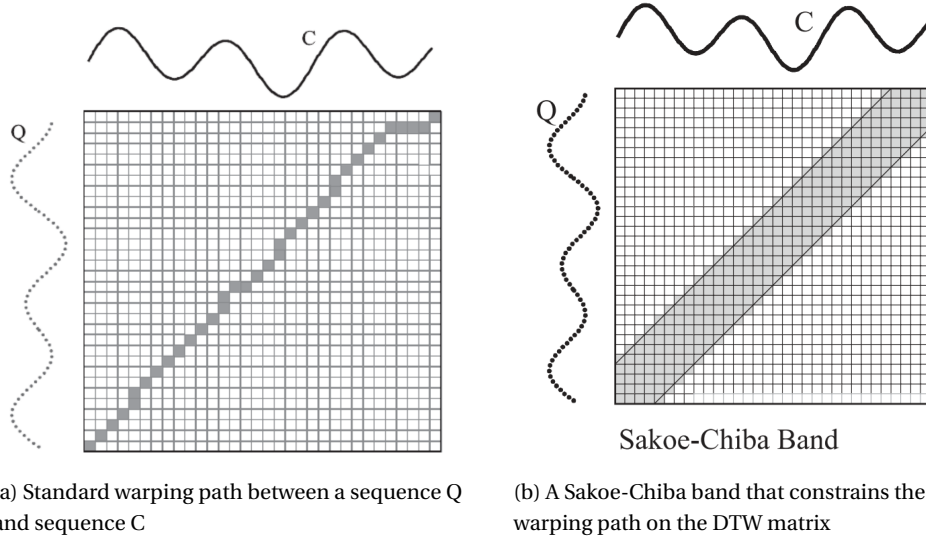


Figure 5.4 – 5.4(a) is a representation of the DTW matrix between the sequences Q and C and 5.4(b) shows the application of the Sakoe-Chiba global constraint on the warping path.

Finally, an additional technique to speed up the computation of the DTW distance, introduced by Dr. Eamonn Keogh, is the lower bounding. The lower bounding is a technique that uses lower and upper boundaries (called L and U) to envelope the sequence that is being compared (Q) and is of constant width, defined by the reach r :

$$U_i = \max(q_{i-r} : q_{i+r})$$

and

$$L_i = \min(q_{i-r} : q_{i+r})$$

with $\forall i, U_i \geq q_i \geq L_i$.

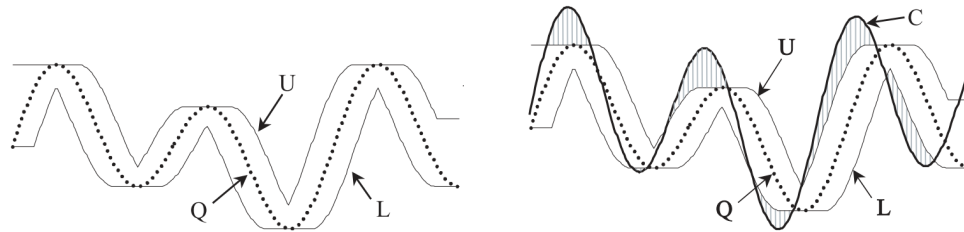
From this envelope is defined a lower bounding measure for the DTW distance called LB_Keogh :

$$LB_Keogh = \sqrt{\sum_{k=1}^n \begin{cases} (c_i - U_i)^2 & \text{if } c_i > U_i \\ (c_i - L_i)^2 & \text{if } c_i < L_i \\ 0 & \text{otherwise} \end{cases}}$$

The $LB_Keogh(Q, C)$ measure the Euclidean distance between any part of the candidate matching sequence of C not falling within the envelope and the nearest (orthogonal) corresponding section of the envelope. The calculation of the LB_Keogh lower bounding function is linear and runs in $O(n)$. Keogh et al. proved that the following inequality holds [43]:

$$LB_Keogh(Q, C) \leq DTW(Q, C)$$

The lower bounding is illustrated in Figure 5.5 as well as the LB_Keogh distance function.



(a) The lower bounding envelope with the Sakoe-Chiba band illustrated

(b) The LB_Keogh distance function illustrated

Figure 5.5 – 5.5(a) is a representation of the lower bounding envelope around the sequence Q with reach r and 5.5(b) is the $LB_Keogh(Q, C)$ distance function between Q and C which is the squared sum of the distances from every part of the sequence C not falling within the envelope around Q .

The Keogh lower bounding enables us to drastically speed up the computation of the DTW distance. An other technique we used to reduce the time of computation is the numerosity reduction of our segments. From the night segments selected, we truncated the first five hours of the night which gave us segments of size 9000. From this segments we performed the DTW algorithm which was taking too much time to feasibly be considered as a possibility. Thus we reduced the size of our segment by taking the maximum value over a fixed sized window. The size of the window was chosen empirically between [10, 20, 30]. We were able to witness that though the segments are drastically reduced in size, the peaks and profile were still conserved by the numerosity reduction as can be seen in Figure 5.6:

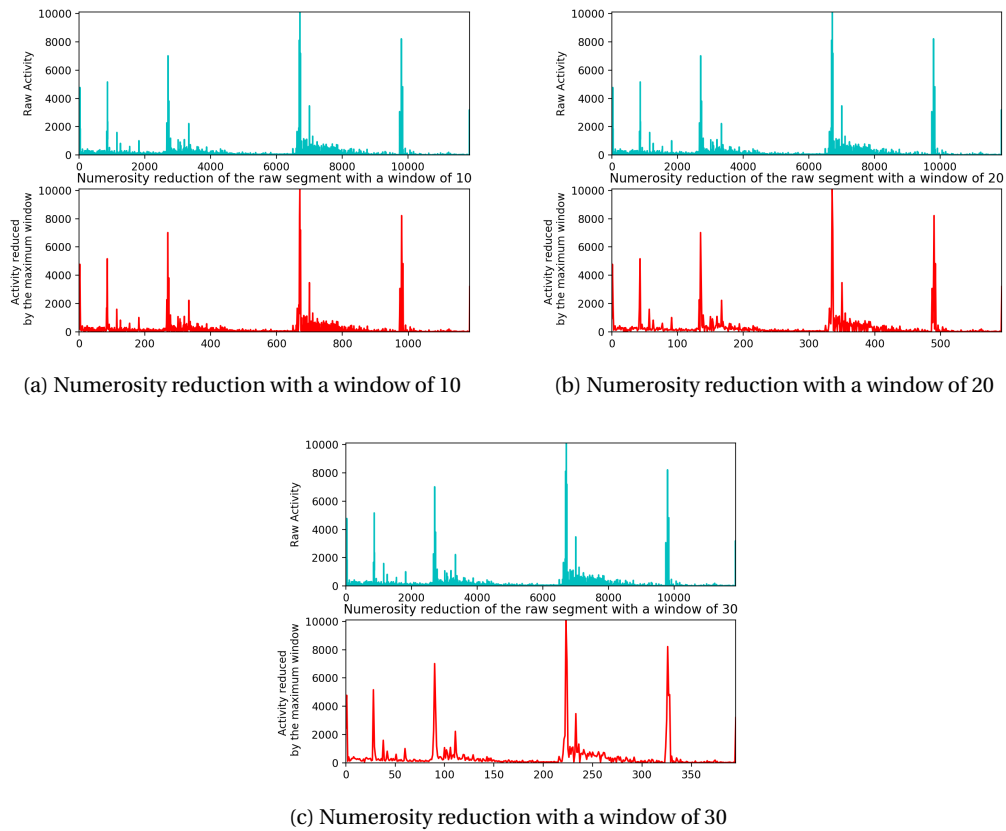


Figure 5.6 – A segment reduced by a maximum window of: 5.6(a) a window of 10, 5.6(b) a window of 20 and 5.6(c) a window of 30.

The DTW distance with numerosity reduction and lower bounding will be used as a similarity measure in the KNN classifier describe below.

K-Nearest-Neighbors

The K-Nearest-Neighbors (KNN) classification method is a classic in the domain of supervised classification as it is quite robust with enough data and doesn't require any probability distributions on the input data. The algorithm classifies instances based on the distance of its neighbors, it classifies an input by a majority vote of its neighbors. The classification happens in three steps:

Training phase: a model is constructed from a set of training instances which creates a model.

Testing phase: the model is tested on test instances for which we know the labels but which are not used as part of the model.

Usage phase: the model is put to use on new date for which we don't know the labels. This

phase will not be made here as no new unknown data is available.

The algorithm is as follow:

1. Initialize a training set and K the number of neighbors to vote.
2. Initialize a testing set on which the model is tested against.
3. Compute the distance for a test instance against each instance of the training set.
4. Sort the distances.
5. Take the K shortest distances (the K nearest neighbors).
6. Apply a majority vote of the K shortest distance.

The model created by the KNN classifier is the training labeled data placed in a metric space to which our testing instances are compared to. In order to select the proper parameters (K , sizes of training and testing sets, numerosity reduction, DTW reach window, etc.), we performed cross-validation by taking random subsets of different sizes of the segments available to create our training and testing sets and tested our algorithm to obtain a good approximation of the performance of our algorithm.

The solution we are proposing is using a 1NN approach based on empirical testing as we will see in Section 5.3. As a distance of choice, the algorithm presented is using the DTW distance which provides us with the similarity of the night segments. Below is presented the implementation of the combination of KNN and DTW to classify nights of healthy seniors from PD patients.

Implementation

The algorithm was implemented from scratch in order to properly insert the DTW distance and lower bounding method. The following algorithm describes in pseudo-code the flow of the algorithm.

Algorithm 1 KNN-DTW-LB_Keogh Classifier Algorithm

```

1: procedure KNN-DTW-LB_KEOGH(training_set, testing_set, reach)
2:   predictions  $\leftarrow$  [] ▷ Predictions of the testing set
3:   for testing_sample in testing_set do ▷ Looping over the testing set
4:     distances  $\leftarrow$  [] ▷ Distances of the testing instance to the training instances
5:     dtw_min_distance  $\leftarrow$   $\infty$  ▷ Minimum distance of the DTW measure for the
testing instance
6:     for training_sample in training_set do
7:       if LB_Keogh(testing_sample, training_sample, reach) <
dtw_min_distance then
8:         current_dist  $\leftarrow$  DTWDistance(testing_sample, training_sample, reach)
9:         distances  $\leftarrow$  current_dist
10:      end if
11:    end for
12:    sorted_distance  $\leftarrow$  distances.sort(smallest first) ▷ Sort the distances from
smallest to greatest
13:    nearest_neighbors  $\leftarrow$  sorted_distance[1 : k] ▷ Take the first closest K
neighbors
14:    if nearest_neighbors.labels(count(-1)) > nearest_neighbors.labels(count(1))
then
15:      predictions  $\leftarrow$  (-1)
16:    else if nearest_neighbors.labels(count(-1)) = nearest_neighbors.labels(count(1))
then
17:      predictions  $\leftarrow$  sorted_distance[k + 1].label ▷ If there is a tie, add one
neighbor and take its label for classification
18:    else
19:      predictions  $\leftarrow$  (1)
20:    end if
21:  end for
22:  return predictions ▷ Return the array of testing set labels and predicted labels for
those
23: end procedure

```

The algorithm will return the predictions it has made of the testing set. From these predictions, we can compute the precision, recall, accuracy and F1_score enabling us to measure the performance of the classifier. In the Algorithm 1, we use the lower bounding *LB_Keogh* and the DTW distance. Therefore, below is presented the two algorithms to compute the two different measures.

Algorithm 2 LB_Keogh Lower bounding Algorithm

```

1: procedure LB_KEOGH(sequence1, sequence2, reach)
2:   LB_sum ← 0                                     ▷ LB_Keogh distance is initialized
3:   for i, val in sequence1 do                 ▷ Looping over the testing set
4:     lower_bound ← min(sequence2[(i - reach if i - reach >= 0 else 0) : (i + reach)])
     ▷ Lower bound for time index i
5:     upper_bound ← max(sequence2[(i - reach if i - reach >= 0 else 0) : (i + reach)])
     ▷ Upper bound for time index i
6:     if val > upper_bound then
7:       LB_sum ← LB_sum + (val - upper_bound)2
8:     else if val < lower_bound then
9:       LB_sum ← LB_sum + (val - lower_bound)2
10:    end if
11:  end for
12:  return  $\sqrt{LB\_sum}$                              ▷ Return Lower bound measure
13: end procedure

```

The LB_Keogh technique described in Algorithm 2 is to be plugged in Algorithm 1, line 7 and allows to reduce the computation of all the DTW distances as:

$$LB_Keogh(sequence1, sequence2) \leq DTWDistance(sequence1, sequence2)$$

Algorithm 3 DTW distance calculation Algorithm

```

1: procedure DTW-DISTANCE(sequence1, sequence2, reach)
2:   DTWMatrix ← {}                               ▷ Empty  $n \times n$  matrix
3:   for i = 1, i ≤ length(sequence1), i ++ do
4:     for j = 1, max(0, i - reach) ≤ j ≤ min(length(sequence2), i + reach), j ++ do ▷
     Application of the Sakoe-Chiba band.
5:       dist ← (sequence1[i] - sequence2[j])2
6:       DTWMatrix[i, j] ← dist + min(DTWMatrix[(i - 1, j), DTWMatrix[(i, j - 1)], DTWMatrix[(i - 1, j - 1)])
7:     end for
8:   end for
9:   return  $\sqrt{DTWMatrix[n, n]}$                    ▷ Return the minimum DTW distance between
     sequence1 and sequence 2
10: end procedure

```

The DTW distance Algorithm 3 is to be plugged in Algorithm 1, line 8 and computes the similarity between the current training sample and the sample being tested in order to be used by the KNN algorithm to derive the closest neighbor. In Section 5.3 will be presented the results of this classifier on our data set.

5.2.2 Holistic classifier

Section 5.2.1 focused on the physical activity itself of the Parkinson's patients, this section is now focusing a more holistic approach which includes several biomarkers of the night sleep of a person. In Chapter 4, we were able to select seven features of interest that do differ from the healthy senior population to the PD population:

1. The number of bed exits per night
2. The number of awakenings per night
3. The number of toss and turns per night
4. The duration of sleep onset per night
5. The total duration in bed per night
6. The total duration in sleep per night
7. The average activity per night

From these features, we wish to discover if a sample from a PD ill person can be recognize as such. Within Section ?? is presented the different classifiers tested on these features.

Imbalanced to balanced data set

The data set obtained and detailed in Section 5.1 is highly imbalanced with a ratio of roughly 21 : 1 with 1717 healthy night measures and 82 night measures for each of the selected measures. In order to battle this, we had to use oversampling and undersampling techniques to overcome this issue which we could not use with the previous DTW-KNN classifier as values were time-ordered. In this section, we will cover which are the techniques employed.

First empirical test with standard binary classifiers (SVM, KNN, Ensemble classifiers, etc.) showed very poor results with almost a zero accuracy in detecting PD nights from healthy seniors nights. Thus, as a first step, it was needed to bring our imbalanced data set to a synthetically balanced data set in order to obtain accurate performance metrics for the tested classifiers. To do this, we used a combination of over-sampling technique (Synthetic Minority Over-sampling Technique (SMOTE)) and under-sampling technique (Edited Nearest Neighbors (ENN)) that is called SMOTE and Edited Nearest Neighbors (SMOTEENN).

The SMOTE approach is to synthetically create samples for the minority class (called "abnormal"). Instead of randomly adding samples to the minority class, it adds samples which are close to the feature space of the minority class by using the Euclidean distance to its k neighbors (currently implemented with five neighbors) to . The following details the procedure of SMOTE over-sampling:

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1. For each sample in the minority class:
 - (a) Compute its k ($k = 5$) nearest neighbors (Euclidean distance)
 - (b) Randomly choose $r \leq k$ of the neighbors with replacement
 - (c) Choose a random sample along the feature space between p and all the r chosen
 - (d) Add the new sample with the minority class label to the data set

For a more details on the algorithm of SMOTE refer to Appendix A.

Over-sampling enables us to increase our minority class proportion, now the under-sampling technique ENN enables us to under-sample the majority class. ENN removes any sample whose class label differs from the class of at least two of its nearest neighbors. For a sample s in the training data set, from any class, is calculated its three nearest neighbors. If the sample s is from the majority class and the its three nearest neighbors gives a classification in the minority class, then it is removed. If the sample s is from the minority class and its three neighbors classifies it in the majority class, then all neighbors from the majority class are removed.

Finally, the combination of SMOTE and ENN, called SMOTEENN, enables us to obtain an acceptable ratio for our data set and improve drastically the performance of our classifiers as will be presented in Section 5.3.

Classifiers

With our newly resampled data set, we are now ready to test different classifiers. In a first step, we identified the better candidates among the list below which are common classifiers in the medical diagnosis [44]. The following description shows the different classifiers we tested our data set against.

Logistic Regression: Logistic Regression is a technique borrowed from the field of statistics and is usually a go-to method for binary classification. It also require no specific distribution in the data which makes it robust with real world data sets. Logistic regression is a linear classifier (its output can be expressed in terms of the input x). It is based on the logistic function $\frac{1}{1+\exp(-x)}$ and models the probability of one class which is then used to provide predictions and thus classify between the two classes. The objective when using the logistic regression is to maximize the log-likelihood of the prediction by tuning the model parameter w where the prediction is $P(Y = 1|w, X) = \frac{1}{1+\exp(-wX+w_0)}$. To make the prediction, the classifier pick the class that maximizes the probability outputted from the model.

Decision Tree (using CART): Decision Trees are a category of classifiers and is a non-parametric supervised learning technique. A decision tree creates models that predicts an input's label by learning rules inferred from the training data features. Decision trees englobes

many different variations such as ID3, C4.5, C5.0 and Classification and Regression Trees (CART), which differ in their inputs types (categorical, numerical). In this context, we are using the CART variation which can handle numerical values. CART constructs binary trees by using features and thresholds which result in the best prediction at each node. Each node represents a single input variable and split in two leaves depending on a condition upon a certain variable (i.e: average activity is greater or equal to 50? Yes or no will split this node in two leaves). The tree is modeled with the training data and making predictions on a new input is straightforward by traversing the tree. The complexity and performance of the tree depends on the stopping criterion which limits the number of splits the tree makes.

Random Forest: Random Forest belongs to the branch of Ensemble classifiers which combines the predictions from several learning algorithms together to address potential instability of one algorithm and make more accurate predictions. Random forest uses several decision trees to make predictions, thus the term forest. The point of random forest is to prevent overfitting by creating random subsets of the features and constructing smaller trees using each subset and finally combine them. An input for which we want to predict his label will go through each tree and the label is chosen by the majority vote. The Random Forest is a technique which has the advantage of reducing the variance of the classifier though it is slower than standard unique decision trees.

Support Vector Machine: Support Vector Machines are a machine learning technique which searches for the best optimal hyperplane that separate all the classes. The support vectors are actually the points which are the closest to the optimal hyperplane and build it. They are also regarded as the critical elements of the data set and are the building blocks of the SVM. To train such classifier, SVM use what is called an objective function which maximizes the margin in the data (margin: distance from the closest data points to the hyperplane) and minimizes the mistakes made on the training data. The objective function is at the heart of the SVM and contains a loss function also called Hinge loss ($c(x, y, f(x)) = (1 - y * f(x))_+$, c is the loss function, x is the input, y is the true label, $f(x)$ is the predicted label) "regularizer" λ which controls the trade off between low training error and low testing error. It is usually set to $\frac{1}{epochs}$ so that the parameter decreases as the number of epochs increases. The objective function is enunciated as such:

$$\min_w \lambda \|w\|^2 + \sum_{i=1}^n (1 - y_i \langle x_i, w \rangle)_+$$

with w a weight vector, n the number of data points, η the learning rate (too high overshoot the optimal point, too low: never converge), λ the regularizer function (too high: overfitting of the model, too low: underfitting of the model) and w the weights. The objective function the total loss for our data. To optimize the objective function, we have to optimize the terms by using the gradient descent technique. This technique will enable to update the weights of the objective function at each epoch (initial weight vector is usually the zero vector) like so: $w = w + \eta(-2\lambda w)$ if input is correctly classified

$(y_i \langle x_i, w \rangle \geq 1)$ or $w = w + \eta(y_i x_i - 2\lambda w)$ if input is misclassified ($y_i \langle x_i, w \rangle < 1$). Usually, because data sets do not live in a linear space, kernel methods are used to transform the data from non-linear to linear (or when $x \times y$ is impossible). Most common kernel functions are the polynomial kernel ($K(x, y) = (x \times y + 1)^d$) and the Radial Basis Function (RBF) kernel ($K(x, y) = \exp(-\gamma \|x - y\|^2)$). Prediction is thus made depending on which side of the hyperplane a new input is placed.

K-Nearest-Neighbors: K-Nearest-Neighbors was already presented in the above section with the first algorithm we built. Simply putted, K-Nearest-Neighbors are classifiers which classify a data point regarding the class of its neighbors based on the distances between the pairs. The classification is made based on the majority vote of its k neighbors. If there is a tie in the classification vote, the next nearest neighbor makes the vote. Common methods to measure the distances are the Euclidean distance ($\sqrt{\sum(x - y)^2}$) and the Minkowski distance ($(\sum |x - y|^p)^{\frac{1}{p}}$ with $p = 2$).

Multilayer Perceptron: The Multilayer perceptron can solve nonlinear classification problems. It is based on multiple perceptrons which are functions which determines the class of an input combining a set of weights on the feature vector. The output $o(x)$ is computed from the so called "activation function" (hyperbolic, rectifier ($\max(0, x)$) or sigmoid functions are the common ones) and the weights:

$$o(x) = f(b + \sum_{i=1}^n w_i x_i)$$

where x_i are the input values, w_i are the summation weights, f is the activation function and b is a bias term determining the probability that the branch is taken (how the activation function is firing). The weights are values proportional to the probability that the predicted branch agrees with the i^{th} branch in the history. Similarly to the support vector machine, the perceptron defines a hyperplane in the $n+1$ dimensional space. The perceptron learns by modifying the weights w_i by an amount that is proportional to the product of the input x and the difference between the real output y_{true} and actual output y :

$$w_i(t + 1) = w_i(t) + \eta(y - y_{true})x$$

where η is the "gain" (between 0 and 1) and t is the iteration number. The weights vector is fixed once the number of iteration chosen is reached or if a certain user-specified threshold is reached. A multilayer perceptron is when multiple perceptrons are combined with their own weights and activation functions. The multilayer perceptron can have several layers where the output of the previous layer is the input of new perceptrons until the final output is computed. The output of the layer L is thus:

$$o^l = \mathfrak{F}^l(W^l \hat{o}^{l-1})$$

for $l = 1, \dots, L$ and where $o^0 = x$. For this equation, x is the input vector, \mathfrak{F}^l is the activation function matrix (diagonal matrix), W^l is the weights matrix and \hat{o}^{l-1} is the

output of the layer $l - 1$. The bias term of layer l is the first column of W^l . The MLP can match the data from its feature space to the proper classification output space. Evaluating the MLP requires a cost function which is usually using the mean squared error. Similarly to SVM, we minimize the cost function with gradient descent at each epoch in order to better refine the weights.

Parameter tuning and cross-validation

We then implemented a "grid-search" with 10-fold cross-validation in order to tune the parameters of our chosen classifiers as we will see in Section 5.3. The grid-search enable us to choose the best parameters which improve the performance of the tested classifiers by testing our models on different parameters proper to the classifiers. The cross-validation consists in splitting the data set in K ($K = 10$, a value validated by Kohavi's reference studies. [45]) partitions and use for each fold $K - 1$ partitions as training data and the K^{th} part to use as validation set. Kohavi's reference paper "A study of cross-validation and Bootstrap for accuracy estimation and model selection" recommends to use stratified K-fold cross-validation which imply to keep the balance of each class in the training an testing data sets. Moreover, K-fold cross-validation minimizes the chance of overfitting our models by making sure the models behave correctly both on training and unseen testing data.

5.3 Results

5.3.1 Performance of the classification algorithms

Metrics of performance

Several metrics can be used to assess a classifier's performance. Below is listed the metrics analyzed and their description:

Accuracy: Accuracy is an intuitive performance measure of the classification algorithm which simply takes the number of positive class values predicted over the number of total classes observed in the testing set:

$$accuracy = \frac{\#True\ Positives + \#True\ Negatives}{\#True\ Positives + \#True\ Negatives + \#False\ Positives + \#False\ Positives}$$

This measure can be calculated for both negative and positive class.

Precision: Precision indicates the exactness of a classifier. If low, it can indicate a large number of false positive. It is equal to the number of positive predictions divided by the total number of positive class values predicted:

$$precision = \frac{\#True\ Positives}{\#True\ Positives + \#False\ Positives}$$

This measure can be calculated for both negative and positive class.

Recall: Recall indicates the sensitivity of a classifier, or what is called the true positive rate. If low, it indicates a high number of false negatives. It is equal to the number of positive predictions divided by the number of positive class values in the test data:

$$recall = \frac{\#True\ Positives}{\#True\ Positives + \#False\ Negatives}$$

This measure can be calculated for both negative and positive class.

F1 Score: The F1 Score measures the balance between recall and precision and is a good performance measure to have both a balanced precision and recall. It is an harmonic mean of the precision and recall:

$$f1_score = 2 \times \frac{precision \times recall}{precision + recall}$$

Cohen's Kappa score: The Cohen's Kappa score is a measure of agreement between two raters who classify x items into c mutually exclusive classes. It is a good balanced measure which indicates the accuracy normalized by the imbalance of the classes in the data:

$$\kappa = \frac{(p_0 - p_e)}{(1 - p_e)}$$

where p_0 is the empirical probability of agreement on the class assigned to any sample and p_e is the expected agreement when both annotators assign classes randomly. p_e is estimated using a per-annotator empirical prior over the class label. A value above 0.8 ($\kappa \in [0; 1]$) is considered as good performance for a classifier.

Area Under the Receiver Operating Characteristic Curve (ROC AUC): The ROC AUC is a score which compute the area under the ROC curve plotting the false positive rate against the true positive rate. It is a dedicated metric for binary classification. The more the ROC AUC score gets close from 1 (ROC AUC $\in [0; 1]$), the more we reduce the false positive rate and improve the true positive rate and thus reach the perfect classifier.

It is important here to underline that our Positive class is the class of PD and the Negative class is the class of healthy seniors. The true positives are the correctly unknown night segments of PD patients predicted as belonging to the PD class. The true negatives are the correctly unknown night segments of healthy seniors predicted as belonging to the healthy senior class. The false positives are the incorrectly unknown night segments of healthy seniors predicted as belonging to the PD class. The false negatives are the incorrectly unknown night segments of PD patients predicted as belonging to the healthy senior class.

Based on these metrics, we were able to find the better parameters for our algorithms and highlight their performance.

Performance of the KNN-DTW-LB_Keogh algorithm

In order to get better performances from our algorithm, we used a common technique of under-sampling our major class (healthy seniors) which consist in selecting an smaller subset of the available data from the major class to be inserted in the classification model. The algorithm is thus fed with a training set where the ratio of both classes is 1:1. To evaluate the KNN-DTW-LB_Keogh algorithm's performance, we proceeded as follow:

1. Create a training set with X (X being variable depending on the experiment) training samples from the healthy seniors class and 77 (the maximum of available segments if we use five testing segments from PD) training samples from the PD patients class which were picked randomly among the available segments.
2. Create a testing set of size $5 = 10$ with 5 training samples from the healthy seniors class and 5 training samples from the PD patients class which were picked randomly among the available segments.
3. Run an arbitrary number of times, 20 times, the algorithm on the randomly formed subsets (training and testing) to obtain an average performance of the algorithm with fixed parameters (reach, k neighbors, sample size, maximum window, etc.).
4. Average precision, recall, F1_score for each class and average accuracy of the classifier based on the 20 iterations.

The reason that drives the use of random subset is that we can not decide beforehand which training subset of the healthy seniors night segments are worth taking and technically we should not exclude any segment, thus the repetition of the classification upon different testing sets against different training sets. Also, using standard k -fold cross validation would require more samples for our minority class and thus is it more important for us to conserve as many PD segments in our training sets.

For each experiment, we tested our algorithm on five segments of each class, selected randomly from the available data set and unavailable to the training set. The following parameters are tested on the data set:

- The under-sampling window: w
- The number of healthy samples in the training data set
- The number of K neighbors: k
- The global constraint (reach) for the Sakoe-Chiba band: r

The following parameters were kept fixed:

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- The number of iterations: 20. The ratio of 21 : 1 healthy segments compared to PD segments. Knowing that the size of the training set can not be too imbalanced due to the noise effect of an imbalanced ratio, we chose this number of fold to cover most of the healthy segments in the training data set, but keeping the processing time under control.
- The sample size: 9000. 9000 samples sequenced every 2 seconds gives us five hours of sleep from the start of the night. Using fixed and equal length for our segments was not imperative but enabled us to keep the processing time lower. Interpolating each sequence to the largest sequence length would involve interpolating a high number of hours on smaller segments and thus the order of time and provoke issues regarding the time global constraint Sakoe-Band.
- The number of PD samples used in the training data set (77) and the number of PD samples used in the testing data set. Due to the low number of PD samples, we tried to provide as much as possible samples for the training data set to compare against and removed only five segments for testing.
- The number of healthy testing samples: symmetrically to the PD testing set, we kept five segments to compare against the training set.

Firstly, we empirically tested the the first parameters altogether in order to define a direction. We tested the hypothesis that indeed a KNN classifier where $K = 1$ is more powerful to a KNN with a higher K . We tested for $K \in [1, 3, 5, 11]$. Simultaneously, we tested upon the Sakoe-Chiba. Literature recommended a Sakoe-Chiba band of 10% [46], thus, we tested different band size of 3%, 5%, 10%, 20% and 50%. Following this, we tested the same different Sakoe-Chiba band and K neighbors on different sizes for the training sets with: 77 PD segments (the maximum we can take with 82 segments available and 5 in the testing set) and we tested for x healthy seniors segments for $x \in [77, 150]$.

The following tables present the results for the under-sampling window 30 and two training data sets: [77 healthy segment, 77 PD samples] and [150 healthy segment, 77 PD samples] with moving Sakoe-Chiba band and a moving number of k neighbors:

Number of neighbors k	1		3		5		11	
Results	H	PD	H	PD	H	PD	H	PD
Precision	0.568	0.58	0.65	0.6	0.7	0.6	0.68	0.61
Recall	0.55	0.58	0.5	0.71	0.46	0.78	0.52	0.75
F1 score	0.55	0.58	0.55	0.64	0.53	0.67	0.57	0.66
Accuracy	0.56		0.61		0.62		0.63	

Table 5.1 – Results of the DTW-KNN-LBK algorithm with **77:77** healthy and PD segments as training set, an under-sampling window of 30 and a SB band of **3%** for $k \in [1, 3, 5, 11]$

Number of neighbors k	1		3		5		11	
Results	H	PD	H	PD	H	PD	H	PD
Precision	0.61	0.57	0.71	0.66	0.58	0.56	0.7	0.62
Recall	0.57	0.6	0.61	0.71	0.51	0.61	0.51	0.76
F1 score	0.56	0.57	0.64	0.67	0.53	0.58	0.56	0.68
Accuracy	0.59		0.66		0.56		0.63	

Table 5.2 – Results of the DTW-KNN-LBK algorithm with **77:77** healthy and PD segments as training set, an under-sampling window of 30 and a SB band of **5%** for $k \in [1, 3, 5, 11]$

Number of neighbors k	1		3		5		11	
Results	H	PD	H	PD	H	PD	H	PD
Precision	0.68	0.65	0.63	0.65	0.56	0.61	0.71	0.63
Recall	0.59	0.7	0.63	0.66	0.52	0.65	0.56	0.71
F1 score	0.61	0.65	0.62	0.64	0.52	0.61	0.6	0.65
Accuracy	0.65		0.65		0.58		0.64	

Table 5.3 – Results of the DTW-KNN-LBK algorithm with **77:77** healthy and PD segments as training set, an under-sampling window of 30 and a SB band of **10%** for $k \in [1, 3, 5, 11]$

Number of neighbors k	1		3		5		11	
Results	H	PD	H	PD	H	PD	H	PD
Precision	0.67	0.67	0.69	0.68	0.66	0.65	0.7	0.6
Recall	0.66	0.65	0.62	0.71	0.62	0.64	0.56	0.72
F1 score	0.65	0.65	0.63	0.67	0.62	0.62	0.6	0.65
Accuracy	0.66		0.67		0.63		0.64	

Table 5.4 – Results of the DTW-KNN-LBK algorithm with **77:77** healthy and PD segments as training set, an under-sampling window of 30 and a SB band of **20%** for $k \in [1, 3, 5, 11]$

Number of neighbors k	1		3		5		11	
Results	H	PD	H	PD	H	PD	H	PD
Precision	0.64	0.64	0.71	0.73	0.64	0.64	0.73	0.7
Recall	0.68	0.58	0.71	0.68	0.61	0.65	0.61	0.78
F1 score	0.65	0.6	0.7	0.69	0.61	0.63	0.64	0.72
Accuracy	0.63		0.7		0.63		0.7	

Table 5.5 – Results of the DTW-KNN-LBK algorithm with **77:77** healthy and PD segments as training set, an under-sampling window of 30 and a SB band of **50%** for $k \in [1, 3, 5, 11]$

Number of neighbors k	1		3		5		11	
Results	H	PD	H	PD	H	PD	H	PD
Precision	0.59	0.64	0.57	0.64	0.63	0.79	0.61	0.67
Recall	0.69	0.52	0.73	0.45	0.81	0.53	0.74	0.49
F1 score	0.64	0.56	0.64	0.51	0.7	0.61	0.65	0.54
Accuracy	0.61		0.59		0.67		0.62	

Table 5.6 – Results of the DTW-KNN-LBK algorithm with **150:77** healthy and PD segments as training set, an under-sampling window of 30 and a SB band of **3%** for $k \in [1, 3, 5, 11]$

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Number of neighbors k	1		3		5		11	
Results	H	PD	H	PD	H	PD	H	PD
Precision	0.56	0.61	0.56	0.65	0.61	0.75	0.61	0.73
Recall	0.7	0.44	0.75	0.4	0.88	0.4	0.83	0.43
F1 score	0.62	0.49	0.63	0.47	0.72	0.49	0.69	0.53
Accuracy	0.57		0.58		0.64		0.63	

Table 5.7 – Results of the DTW-KNN-LBK algorithm with **150:77** healthy and PD segments as training set, an under-sampling window of 30 and a SB band of **5%** for $k \in [1, 3, 5, 11]$

Number of neighbors k	1		3		5		11	
Results	H	PD	H	PD	H	PD	H	PD
Precision	0.71	0.8	0.63	0.71	0.66	0.84	0.58	0.64
Recall	0.81	0.66	0.87	0.43	0.86	0.53	0.83	0.36
F1 score	0.75	0.72	0.72	0.52	0.74	0.62	0.67	0.43
Accuracy	0.74		0.65		0.7		0.6	

Table 5.8 – Results of the DTW-KNN-LBK algorithm with **150:77** healthy and PD segments as training set, an under-sampling window of 30 and a SB band of **10%** for $k \in [1, 3, 5, 11]$

Number of neighbors k	1		3		5		11	
Results	H	PD	H	PD	H	PD	H	PD
Precision	0.61	0.62	0.62	0.76	0.52	0.64	0.58	0.69
Recall	0.81	0.43	0.85	0.42	0.79	0.36	0.86	0.35
F1 score	0.69	0.49	0.71	0.51	0.64	0.43	0.68	0.43
Accuracy	0.62		0.64		0.58		0.6	

Table 5.9 – Results of the DTW-KNN-LBK algorithm with **150:77** healthy and PD segments as training set, an under-sampling window of 30 and a SB band of **20%** for $k \in [1, 3, 5, 11]$

Number of neighbors k	1		3		5		11	
Results	H	PD	H	PD	H	PD	H	PD
Precision	0.65	0.76	0.64	0.81	0.62	0.68	0.55	0.57
Recall	0.79	0.58	0.83	0.52	0.82	0.46	0.82	0.3
F1 score	0.71	0.64	0.72	0.6	0.7	0.53	0.65	0.38
Accuracy	0.69		0.67		0.64		0.56	

Table 5.10 – Results of the DTW-KNN-LBK algorithm with **150:77** healthy and PD segments as training set, an under-sampling window of 30 and a SB band of **50%** for $k \in [1, 3, 5, 11]$

The results shows are widely different from an experiment from another. In red in the table, we highlighted the best candidates providing us with a high precision for the healthy class and a high recall for the PD class and an overall good accuracy of the model. Overall, the ratio of training samples 77 : 77 was performing better than the one with ratio 150 : 77. The best numbers of neighbors maximizing the recall and precision are 3 and 11. The best Sakoe-Chiba band is 50% with great results for 3 and 11 neighbors. This is very much contradicting the common references of one neighbors and a Sakoe-Chiba band of 10%. Both models achieve

an accuracy of 70% and achieve high precision on the healthy segments and high recall on the PD segments. It is though important to keep a 1 : 1 ratio of healthy and PD segments to reduce as much as possible the noise in the signal space.

The last step was to test the numerosity reduction on the night segments and ensure our segment under-sampling window is not having an unwanted impact on the performance of our algorithm. We tested on segments of five hours (length of 9000) with windows of 10, 20 and 30, taking the maximum value of the segment in those windows. To test the window size, we took the best k for number of neighbors, best Sakoe-Chiba bands and best number of healthy seniors segments and tested the different window sizes. The following tables show the results for the three different windows:

Number of neighbors k	3		11	
Results	H	PD	H	PD
Precision	0.75	0.73	0.79	0.73
Recall	0.69	0.71	0.78	0.82
F1 score	0.72	0.72	0.78	0.77
Accuracy	0.73		0.77	
Cohen's Kappa	0.71		0.73	
ROC AUC	0.75		0.79	

Table 5.11 – Results of the DTW-KNN-LBK algorithm with 77:77 healthy and PD segments as training set, an under-sampling window of **10** and a SB band of 50% for $k \in [3, 11]$

Number of neighbors k	3		11	
Results	H	PD	H	PD
Precision	0.72	0.69	0.72	0.72
Recall	0.67	0.76	0.65	0.78
F1 score	0.69	0.72	0.68	0.75
Accuracy	0.7		0.69	
Cohen's Kappa	0.68		0.74	
ROC AUC	0.74		0.78	

Table 5.12 – Results of the DTW-KNN-LBK algorithm with 77:77 healthy and PD segments as training set, an under-sampling window of **20** and a SB band of 50% for $k \in [3, 11]$

Number of neighbors k	3		11	
Results	H	PD	H	PD
Precision	0.71	0.73	0.73	0.7
Recall	0.71	0.68	0.61	0.78
F1 score	0.69	0.61	0.64	0.72
Accuracy	0.7		0.7	
Cohen's Kappa	0.68		0.72	
ROC AUC	0.74		0.76	

Table 5.13 – Results of the DTW-KNN-LBK algorithm with 77:77 healthy and PD segments as training set, an under-sampling window of 30 and a SB band of 50% for $k \in [3, 11]$

The results show a slight improvement when reducing the window of numerosity reduction from 30 to 20 and 10. Although, the difference is minimal but increases the ROC AUC and Cohen's Kappa scores, good balanced indicators for binary classification problems.

Those results prove indeed that differences do exist in the course of the night between the PD and healthy populations regarding their body movement, though this classifier can not be considered as fully reliable if we were to test it on new data. For the algorithm to better perform, we should increase the pool of PD night segments to achieve better performances. The next classifier based on the key data of the nights is an other solution explored in the recognition of Parkinson's sleep-related symptoms markers.

Performance of the Holistic classification algorithm

We saw that the DTW-KNN classifier is not optimal with such imbalanced data set. To tackle this we built classifiers taking into account all seven features selected in chapter 4. The algorithms selected were tuned with grid-search using 10-fold cross-validation and then assessed with also 10-fold cross-validation over 80% of the data set as training data. Finally, we validated the algorithms with the remaining 20% data unseen by the fitted model. We present below the results obtained by learning the best parameters to tune our algorithms, the assessment by cross-validation of those and their performance on the remaining 20% testing data.

The grid-search evaluated for each classifier the optimal parameters. The first tested is the Logistic Regression algorithm. The grid search was separated in two for two types of penalty (L1 and L2 norms loss functions) which optimizers do not handle the same way. The L1 penalty was tested with two optimization methods provided by sklearn: "liblinear" and "saga" and the L2 penalty was tested with "liblinear", "newton-cg", "lbfgs" and "sag". The regularization term was tested on the following range: [0.001, 0.01, 0.1, 1, 10, 100, 1000]. The grid search returns the parameters which maximizes the accuracy of the classifier. The final result was the selection of 'L2' penalty with the "liblinear" optimizer and the regularization threshold 0.001. On the training data set, it lead to a mean accuracy of 0.785.

We then tested the CART decision tree algorithm, we tested the maximum depth of the tree as well as the minimum number of samples to split the nodes or the minimum number of samples in leaf nodes: "maximum depth of the tree" $\in [3; 20, None]$, "minimum samples to split" $\in [2, 30]$ and "minimum samples in leaves" $\in [1, 30]$. The best result was obtained for the default configuration with the maximum depth set to "None" which stops the tree growing when all leaves contain less than the minimum number of leaves by default. The minimum number of samples to split is 2 and the minimum number of samples in the leaves is 1. Overall, the decision tree reaches an accuracy of 0.939 on the training data set and the with the averaged score from the 10-fold cross-validation.

Then the Random Forest was tuned by testing the optimal number of trees in the forest and the maximal depth of the trees. Parameters ranges are: "number of decision trees" $\in [1, 10, 50, 100, 200, 500, 700]$, "maximum depth of the trees" $\in [3; 20, None]$. The optimal parameter values obtained were a number of 500 decision trees and a depth of 16 for an optimal mean accuracy of 0.978.

The tests of the SVM focused on the penalty parameter for the loss function, the different kernels (linear, polynomial of degree 3, RBF and sigmoid) and their γ parameters. The tested range of the loss function C parameter is $C \in [0.001, 0.01, 0.1, 1, 10]$ and the tested range of the gamma parameter is $\gamma \in [0.001, 0.01, 0.1, 1]$. The optimal parameters were for a kernel RBF with a penalty parameter of 1 and a gamma parameter of 1. The mean accuracy based on the training data of the SVM algorithm with such parameters is of 0.561.

For the tuning of KNN we tested the number of neighbors taken into account and the distance metrics: "number of neighbors" $\in [1; 13]$ and "distance metric" $\in ['euclidean', 'minkowski']$. We obtained best results for a number of 1 neighbor and the Minkowski distance for a mean accuracy of 985.

Finally, we tested the multilayer perceptron parameters by tuning the number of hidden layers ($L \in [(100,), (200,), (300,), (400,), (500,), (100, 100, 1), (200, 200, 1)]$) which represent both one layers with from 100 to 500 perceptrons and two layers with (fir, the type of activation functions (hyperbolic , rectifier ($\max(0, x)$) and tanh), the penalty L2 regularization term $\in [1, 1e^{-1}, 1e^{-2}, 1e^{-3}, 1e^{-4}, 1e^{-5}]$, the learning rate step $\in [0.001, 0.01, 0.1]$ and the number of epochs $\in [100, 500]$. We obtain the best mean accuracy for a number one layer with 200 perceptrons, the Rectifier activation function, a penalty of $1e^{-5}$, a learning rate step of 0.01 and a number of iterations of 100 which gave us a mean accuracy over the training data of 0.643.

Following the tuning of our parameters, we performed 10-fold cross-validation on the training data set with the tuned parameters of each classifier in order to estimate how well our classifiers will perform on unseen testing data. Each metric is the mean of the 10-fold metric results. The following table 5.14 presents the metrics obtained with respect of the metrics presented at the start of section 5.3.1:

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10-fold cross-validation scores on training data set							
Classifier	Parameters	Accuracy score	Precision score	Recall score	F1 score	ROC AUC score	Cohen's Kappa score
Logistic Regression	L2 penalty type, 'liblinear' optimizer, regularization threshold 0.001	0.748	0.719	0.889	0.782	0.807	0.483
Decision Tree CART	Min number of samples in split of 2, Min number of samples in leaves of 1, No stopping to growing depth of tree	0.935	0.931	0.953	0.939	0.934	0.870
Random Forest	500 decision trees, maximal depth of 16	0.979	0.979	0.984	0.980	0.998	0.959
Support Vector Machine	RBF kernel, loss function penalty of 1, gamma of 1	0.555	0.550	1	0.710	0.550	0.029
K-Nearest-Neighbor	1 neighbor, Minkowski distance	0.985	0.978	0.994	0.988	0.984	0.969
Multilayer Perceptron	200 perceptrons on one hidden layer, Rectifier activation function, learning rate step of 0.01, 100 iterations, L2 penalty of 1e-5	0.631	0.613	0.757	0.504	0.666	0.247

Table 5.14 – 10-fold cross-validation of the six tuned models and run on 80% of the data set

The 10-fold cross-validation shows clearly a separation between the classifiers. Both KNN and Random Forest stand out from the other classifiers and seem to perform extremely well on the training data set. The 10-fold cross-validation shows that KNN and Random Forest are stable applied on random subsets of the training data and are promising for their performance on new unseen data.

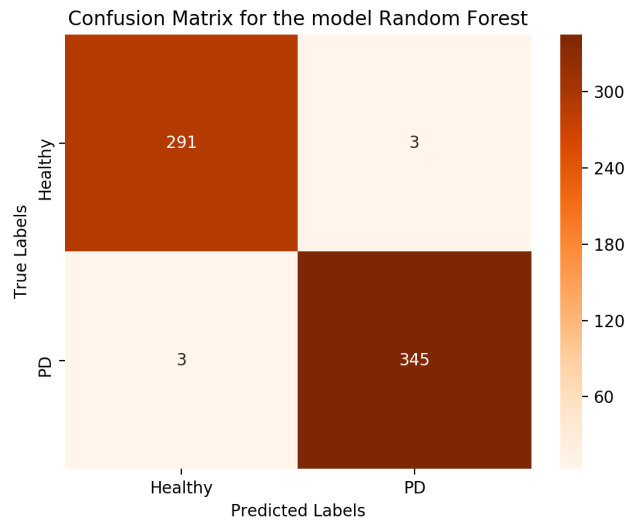
Finally we tested the classifiers over testing data, unseen by the fitted models by running each model with its best parameters and recorded their performance metrics to compare them. The following table 5.15 presents the results obtained with regards to the metrics presented at the beginning of 5.3.1:

5.3. Results

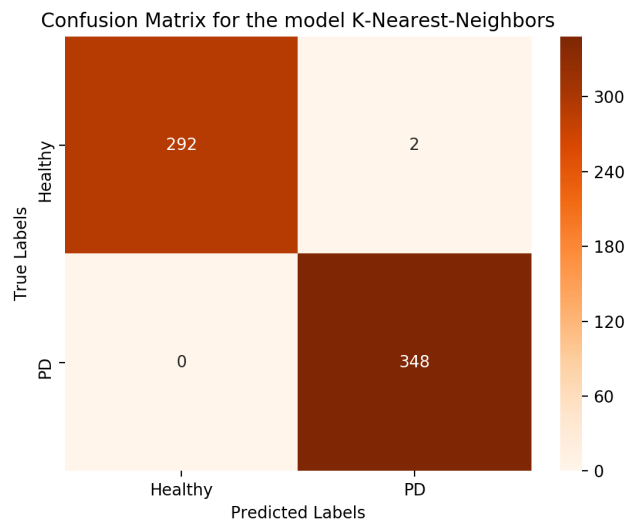
Validation on testing data set							
Classifier	Parameters	Accuracy score	Precision score	Recall score	F1 score	ROC AUC score	Cohen's Kappa score
Logistic Regression	L2 penalty type, 'liblinear' optimizer, regularizazion threshold 0.001	0.740	0.720	0.872	0.789	0.723	0.459
Decision Tree CART	Min number of samples in split of 2, Min number of samples in leaves of 1, No stopping to growing depth of tree	0.945	0.932	0.971	0.951	0.941	0.888
Random Forest	500 decision trees, maximal depth of 16	0.987	0.986	0.991	0.989	0.986	0.974
Support Vector Machine	RBF kernel, loss function penalty of 1, gamma of 1	0.566	0.561	1	0.719	0.510	0.023
K-Nearest-Neighbor	1 neighbor, Minkowski distance	0.987	0.986	0.991	0.988	0.986	0.974
Multilayer Perceptron	200 perceptrons on one hidden layer, Rectifier activation function, learning rate step of 0.01, 100 iterations, L2 penalty of 1e-5	0.618	0.593	1	0.744	0.569	0.151

Table 5.15 – Validation of the six tuned models with the remaining 20% testing data

The results of Table 5.15 shows outstanding results for the Random Forest and KNN algorithms tuned also with 10-fold cross-validation. For these classifiers, we observe that all their metrics are scoring above 0.970. The interpretation of the inter-agreement Cohen's Kappa score show very substantial results, almost perfect with these two algorithm with scores above 0.8 (considered as a substantial score). The ROC AUC score shows also substantial results which show that their is a good ratio of false positive rate (low) and true positive rate (high). To depict their efficiency, we present below in Figure 5.7 their confusion matrix which shows how each sample was categorized:



(a) Confusion matrix of the KNN algorithm



(b) Confusion matrix of the Random Forest algorithm

Figure 5.7 – Confusion matrices for the KNN model 5.7(a) and the Random Forest model 5.7(b) with tuned parameters and applied on unseen testing data

We can see that very few samples are misclassified by both algorithms. We can conclude that both classifiers are extremely efficient on recognizing symptoms from the PD population against the healthy population.

5.3.2 Discussion

To wrap up Section 5.3, we can highlight that the first built classifier DTW-KNN-LB_Keogh is not performing as well as it was planned and is suffering from the high imbalanced data set. We believe though that improvements could be made with a pool of more homogeneous sized samples which would imply much more data recording which was unfortunately impossible in the project.

On the other hand, we tested six classifiers over our 7 selected diagnosis features which concluded in very high performances from the KNN and Random Forest classifiers. These results were eventually highly improved thanks to the SMOTEEN procedure which transforms an imbalanced set to a balanced one based on KNN-based algorithms.

Finally, we would recommend the reader to go for one of the two successfully performing algorithm as long as all of these 7 measurements can be recorded.

6 Conclusion

The goal of this thesis was to perform a data analysis of sleep-related Parkinson's Disease (PD) symptoms thanks to a system of ambient sensors. This system captures motion inside the monitored person's apartment as well as the asleep person's micro-movements thanks to an advanced Ballistocardiography-based sensor. In order to perform this analysis and explore the possibilities of this system, we designed a clinical study and developed algorithms capable to distinguish someone with Parkinson's from someone healthy thanks to the sleep-related measurements made by the sensor.

At first, we provided the reader with necessary knowledge on the Parkinson's disease, its well-known motor symptoms such as the cardinal symptoms (Bradykinesia, rest tremor, rigidity, and postural and gait impairments) but more importantly the non-motor symptoms which are severely impacting the Quality of Life (QoL) of the patients. Non-motor symptoms impact Parkinson's patient even more during the night when they experience "wearing-off" of the medicine which provokes a wide range of discomfort from body stiffness to insomnia.

During the project, a study has been designed in order to collect the data needed to analyze the sleep-related symptoms. Unfortunately, the collected data was not as consequent as we expected but was compensated by the successful collection of bed sensor data for more than two thousands nights from healthy seniors and almost a hundred of nights from PD patients with the bed sensor.

From the obtained data set and the knowledge of sleep-related symptoms of PD, we derived a list of possible symptoms that could be matched to our available data. Four main symptoms were identified as being potentially reflected on the PD's bed sensor data: Sleep initiation disturbance, alterations to the total sleep time in bed, insomnia and body stiffness.

Therefore, from this list of symptoms, we linked nine of the bed sensor's biomarkers (Figure 3.1, page 21) which could be informative about the symptoms. In order to confirm this hypothesis, we performed a statistical analysis on these key biomarkers which showed non-parametric distributions. We established that indeed both data sets were presenting significant

Chapter 6. Conclusion

differences. PD patients present more fragmented nights with higher numbers of awakenings and bed exits, less movement in bed with a lower average activity and number of "toss and turns" as well as longer nights.

Although, it was necessary to confirm these assumptions by statistically testing that these numbers were not just lucky guesses. For that purpose, we used the Mann-Whitney U test which is robust against non-parametric data and gives us confirmation that the data set present sufficient significant differences with up to 95% of confidence. The results showed that from the nine selected biomarkers, seven were significantly different from a population to another: the numbers of bed exits, awakenings, toss and turns, the durations of sleep onset, total time spent in bed and asleep, and the average activity score per night.

With this first important conclusion, we experimented with different techniques of machine learning to explore the possibilities of using them to recognize a PD patient from a healthy person. At first, we experimented with a technique known as being highly effective on the classification of time-series called Dynamic Time Warping (DTW) and K-Nearest-Neighbors (KNN). As activity at night showed the most significant difference between populations, we implemented our algorithm to learn from segments recording the activity sampled every two seconds for every single night. The classifier, after pre-processing the data such as cropping the first five hours of the night, showed up to 77% accuracy with a tuned model.

Claiming that these results could be beaten by a more holistic approach including all seven selected biomarkers. We faced the difficulty of having a quite imbalanced data set with a 21:1 ratio of the negative (healthy seniors) class. To overcome it, we used the SMOTE and Edited Nearest Neighbors (SMOTEENN) technique which is a combination of oversampling and undersampling techniques to re-balance a data set and drastically improve the performances of classification algorithms. After this pre-processing, we tested six well-known classifiers and tuned them in order to get from the best results. We used grid search to test different parameters and 10-fold cross-validation to assess the fitted models. Both KNN and Random Forest algorithms showed promising results and, once tested on unseen data, achieved scores over 98% on all performance measures.

Outlook

The ongoing project behind this master thesis is continuing with the recruitment of new Parkinson's patients in the study designed to further populate the current data set, with the different ambient measures we evoked in Chapter 3. The addition of new measures from the motion sensors, door sensors, and meta-data collected through medical questionnaires and diaries will enable new correlations to be made between the different measures.

We expect the different developed algorithms to get more robust with an increased PD dataset. From this new classification methods, it is hoped to follow up on the long-term, the evolution of the population's sleep-related behavior and detect potential biomarkers of the disease. On the other hand, these results can be used to fine-tune the medication of PD patients with issues of medicine wearing-off during the night.

As the project was focused on exploratory analysis more than validation of existing algorithms, a control group was not included. However, in a second phase, a validation study will test for a period of six months the efficiency of the developed algorithms.



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Appendix A: SMOTE

The following algorithm is taken from Chawla et al. "SMOTE: Synthetic Minority Over-sampling Technique", 2002 [100] publication and reflects the used implementation in Python package imbalanced-learn.

```
Algorithm SMOTE( $T$ ,  $N$ ,  $k$ )
Input: Number of minority class samples  $T$ ; Amount of SMOTE  $N\%$ ; Number of nearest
neighbors  $k$ 
Output:  $(N/100) * T$  synthetic minority class samples
1. (* If  $N$  is less than 100%, randomize the minority class samples as only a random
percent of them will be SMOTEd. *)
2. if  $N < 100$ 
3.   then Randomize the  $T$  minority class samples
4.      $T = (N/100) * T$ 
5.      $N = 100$ 
6. endif
7.  $N = (int)(N/100)$  (* The amount of SMOTE is assumed to be in integral multiples of
100. *)
8.  $k$  = Number of nearest neighbors
9.  $numattrs$  = Number of attributes
10.  $Sample[ ][ ]$ : array for original minority class samples
11.  $newindex$ : keeps a count of number of synthetic samples generated, initialized to 0
12.  $Synthetic[ ][ ]$ : array for synthetic samples
    (* Compute  $k$  nearest neighbors for each minority class sample only. *)
13. for  $i \leftarrow 1$  to  $T$ 
14.   Compute  $k$  nearest neighbors for  $i$ , and save the indices in the  $nnarray$ 
15.    $Populate(N, i, nnarray)$ 
16. endfor

     $Populate(N, i, nnarray)$  (* Function to generate the synthetic samples. *)
17. while  $N \neq 0$ 
18.   Choose a random number between 1 and  $k$ , call it  $nn$ . This step chooses one of
the  $k$  nearest neighbors of  $i$ .
19.   for  $attr \leftarrow 1$  to  $numattrs$ 
20.     Compute:  $dif = Sample[nnarray[nn]][attr] - Sample[i][attr]$ 
21.     Compute:  $gap =$  random number between 0 and 1
22.      $Synthetic[newindex][attr] = Sample[i][attr] + gap * dif$ 
23.   endfor
24.    $newindex++$ 
25.    $N = N - 1$ 
26. endwhile
27. return (* End of  $Populate$ . *)
End of Pseudo-Code.
```