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Machine Learning algorithms for assessing REM Sleep Without Atonia in patients with Parkinson's Disease and Narcolepsy

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Abstract

REM Sleep Behavior Disorder (RBD) is a sleep disorder characterized by harmful motor behaviors occurring in conjunction with vivid dream experiences. Recent research has increasingly recognized RBD as an early manifestation of neurodegenerative conditions such as Parkinson's Disease, Multiple System Atrophy, and Dementia with Lewy bodies. Diagnosis traditionally relies on clinical history, polysomnography, and manual-visual scoring methods, which are time-consuming and require specialized expertise. This thesis explores the application of automated algorithms, particularly the REM Sleep Atonia Index (RAI), and Dissociation Index (DI) to identify and evaluate RBD.

RBD is characterized by a loss of muscle atonia during REM sleep, known as REM Sleep Without Atonia (RSWA). The development of a continuous DI has introduced a quantitative measure of RBD severity, offering potential benefits in monitoring and treatment. This study aims to assess the effectiveness of the DI, particularly in the context of RSWA observed in Parkinson's Disease and narcoleptic patients.

The link between RBD and Parkinson's Disease is strong, with RBD often preceding the clinical onset of neurodegeneration. Early identification of RSWA could serve as an invaluable marker for early intervention and treatment. Lifestyle modifications and emerging neuroprotective drugs have demonstrated potential in slowing disease progression, highlighting the need for early markers of neurodegeneration.

Furthermore, this research addresses the relationship between RBD and Narcolepsy Type 1 (NT1), specifically examining the phenomenon of Narcoleptic REM Sleep Behavior Disorder (N-RBD) in individuals with narcolepsy. Recent studies indicate that RBD may affect a significant proportion of NT1 patients, emphasizing the importance of efficient and practical diagnostic

methods.
While automated RSWA assessment methods are promising, they require high-quality polysomnography recordings and further validation, especially in large patient groups. Machine learning techniques have been instrumental in classifying RBD patients from healthy controls, and this study assesses a method for the blind identification of RSWA by analyzing spectral patterns of electromyogram (EMG) data during REM sleep.
The Dissociation Index, measuring the degree of dissociation between mind and body during RSWA episodes, holds potential as a tool for enhancing the evaluation and long-term monitoring of RBD. However, its robustness and reliability need comprehensive validation. This research seeks to advance our understanding of RBD and its association with neurodegenerative diseases and narcolepsy, ultimately contributing to the development of more effective diagnostic and monitoring tools for these conditions.

Résumé

Le Trouble du Comportement en Sommeil Paradoxal (TCSP) est un trouble du sommeil caractérisé par des comportements moteurs nuisibles survenant en conjonction avec des expériences de rêve vives. Des recherches récentes ont de plus en plus reconnu le TCSP comme une manifestation précoce de conditions neurodégénératives telles que la maladie de Parkinson, l'atrophie multisystémique et la démence à corps de Lewy. Le diagnostic repose traditionnellement sur l'historique clinique, la polysomnographie et les méthodes de notation manuelle-visuelle, qui sont chronophages et nécessitent une expertise spécialisée. Cette thèse explore l'application d'algorithmes automatisés, en particulier l'indice d'atonie du sommeil paradoxal (RAI) et l'indice de dissociation (DI), pour identifier et évaluer le TCSP.
Le TCSP se caractérise par la perte d'atonie en sommeil paradoxal (RSWA). Le développement d'un indice de dissociation continu a introduit une mesure quantitative de la gravité du TCSP, offrant des avantages potentiels en matière de suivi et de traitement. Cette étude vise à évaluer l'efficacité du DI, en particulier dans le contexte de la RSWA observée chez les patients atteints de la maladie de Parkinson et de la narcolepsie.
Le lien entre le TCSP et la maladie de Parkinson est fort, le TCSP précédant souvent le début clinique de la neurodégénérescence. L'identification précoce de la RSWA pourrait servir de marqueur inestimable pour une intervention et un traitement précoces. Les modifications du mode de vie et les médicaments neuroprotecteurs émergents ont démontré leur potentiel pour ralentir la progression de la maladie, soulignant la nécessité de marqueurs précoces de la neurodégénérescence.
De plus, cette recherche aborde la relation entre le TCSP et la Narcolepsie de Type 1 (NT1), examinant spécifiquement le phénomène du Trouble du Comportement en Sommeil REM Narcoleptique (N-RBD) chez les individus

atteints de narcolepsie. Des études récentes indiquent que le TCSP peut affecter une proportion significative des patients atteints de NT1, mettant en évidence l'importance de méthodes de diagnostic efficaces et pratiques. Bien que les méthodes d'évaluation automatisée de la RSWA montrent des promesses, elles nécessitent des enregistrements de polysomnographie de haute qualité et une validation supplémentaire, en particulier auprès de groupes de patients plus importants. Les techniques d'apprentissage automatique ont été essentielles pour classer les patients atteints de TCSP par rapport aux sujets sains, et cette étude évalue une méthode pour l'identification aveugle de la RSWA en analysant les modèles spectraux des données d'électromyogramme (EMG) pendant le sommeil paradoxal. L'indice de dissociation, mesurant le degré de dissociation entre l'esprit et le corps pendant les épisodes de RSWA, offre un potentiel en tant qu'outil pour améliorer l'évaluation et le suivi à long terme du TCSP. Cependant, sa robustesse et sa fiabilité doivent faire l'objet d'une validation complète. Cette recherche vise à faire progresser notre compréhension du TCSP et de son association avec les maladies neurodégénératives et la narcolepsie, contribuant ainsi au développement d'outils de diagnostic et de suivi plus efficaces pour ces conditions.

A Mamma,
a Papà
e a Enrico

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Acronyms

AI

Artificial Intelligence

ARI

Arousal Index

ASL

Average Segment Length

CDF

Cumulative Distribution Function

CI

Continuous Indicator

DI

Dissociation Index

DL

Deep Learning

EEG

Electroencephalogram

EMG

Electromyogram

EOG

Electrooculogram

IRBD

Idiopatic REM sleep Behavior Disorder

FN

False Negative

FDS

Flexor Digitorum Superficialis

FP

False Positive

HY

Hoehn & Yahr scale

HPI

High Potential for Incidence

iRBD

idiopathic REM sleep Behavior Disorder

IQR

Interquartile Range

LED

Levodopa Equivalent Dose

LOSOCV

Leave-One-Subject-Out Cross-Validation

MDF

Median Frequency of REM mini-epochs

ML

Machine Learning

MNF

Mean Frequency of REM mini-epochs

MREM

Minutes of REM Sleep

MSLT

Multiple Sleep Latency Tests

NT1

Narcolepsy Type 1

N-RBD

Narcoleptic REM Sleep Behavior Disorder

NFI

NREM Fragmentation Index

NREM

Non Rapid Eye Movement

OSA

Obstructive Sleep Apnea

PD

Parkinson's Disease

PD-RBD

PD-associated REM sleep Behavior Disorder

PPV

Positive Predictive Value

PSD

Power Spectral Density

PSG

Polysomnography

RAI

REM Atonia Index

REM

Rapid Eye Movement

RFI

REM Fragmentation Index

RLS

Restless Legs Syndrome

RBD

REM sleep Behavior Disorder

RSWA

REM Sleep Without Atonia

SE

Sleep Efficiency

SEF

Spectral Edge Frequencies

SINBAR

Sleep Innsbruck Barcelona

SOL

Sleep Onset Latency

SSP

Sleep Stage Proportion

STI

Sleep Transitions Index

SVM

Support Vector Machine

TIB

Time In Bed

TN

True Negative

TP

True Positive

TST

Total Sleep Time

UNS

Ullanlinna Narcolepsy Scale

UPDRS

Unified Parkinson's Disease Rating Scale

v-PSG

video-Polysomnography

WASO

Wake After Sleep Onset

WP

Wake Proportion

Part I

Introduction

Chapter 1

Context and motivation

1.1 REM Sleep Behavior Disorder

REM Sleep Behavior Disorder is a sleep disorder featured by harmful motor behaviors coupled with dream mental activity for the patient. Several studies of the last two decades dealt with RBD as more than a mere case of parasomnia: it reflects an early appearance of neurodegenerative disorders, such as Parkinson's Disease, Multiple System Atrophy and Dementia with Lewy bodies.[1, 2, 3, 4, 5, 6]
Under healthy conditions *EEG desynchronization* [1] and *muscle atonia* [2] occur during the REM phase. In patients with RBD, both phasic and tonic activity of REM sleep change: the main feature is the loss of tonic chin EMG atonia. Hence REM Sleep Without Atonia is a topic that triggers the Sleep Medicine Research.
Diagnosis of RBD is typically based on clinical history, polysomnography, and video monitoring. However, manual-visual methods for scoring, such

[1] Increase of power in higher frequencies and a decrease of power in lower frequencies [7]

[2] State of muscle relaxation, reduced muscle tone

as SINBAR [3] and Montreal [4], are time-consuming, expensive, and require specialized expertise: an automatic algorithm for scoring, known as the REM sleep Atonia Index (RAI), has been developed in order to face these limits [8, 9]. The RAI method, likely other visual scoring approach [10] based on further continuous measures, is more suitable for evaluating physiological function like RSWA. Furthermore, recent progress in machine learning classification have demonstrated potential in automating the identification of RBD. Notably, the utilization of electroencephalogram (EEG) patterns and machine learning protocols has shown an aptitude for classifying RBD patients from healthy controls.
The development of a continuous Dissociation Index has provided a quantitative measure of the severity of RBD [11], which could aid in the monitoring and treatment of the disorder.

1.1.1 RBD & Parkinson's Disease

There is a strong relationship between RBD and Parkinson's Disease (PD): RBD may be an early marker of neurodegeneration and may provide valuable insights into the pathophysiology of PD.
The estimated risk of evident neurodegeneration is around 97% at a 14-year follow-up, while the conversion rate to PD is about 90% [12].
Despite the absence of a curative treatment, making changes to patients lifestyle can significantly decelerate the advancement of the disease [13, 14]. In addition, new neuro-protective drugs are currently being investigated [15], with their possible efficacy relying on their administration during the preclinical and initial phases of the disease [16].
This emphasizes the requirement for early markers of neurodegeneration. Recent studies have shown that the automatic identification of RSWA is strongly correlated with manual-visual methods in PD patients. The assessment of RBD using machine learning classification and the DI may aid in the early diagnosis and treatment of PD.

[3]The Sleep Innsbruck Barcelona (SINBAR) is an approach for evaluating the electromyographic activity during REM sleep in patients with RBD.

[4]The Montréal method is a visual scoring method that has been used to assess muscle atonia in patients with RBD.

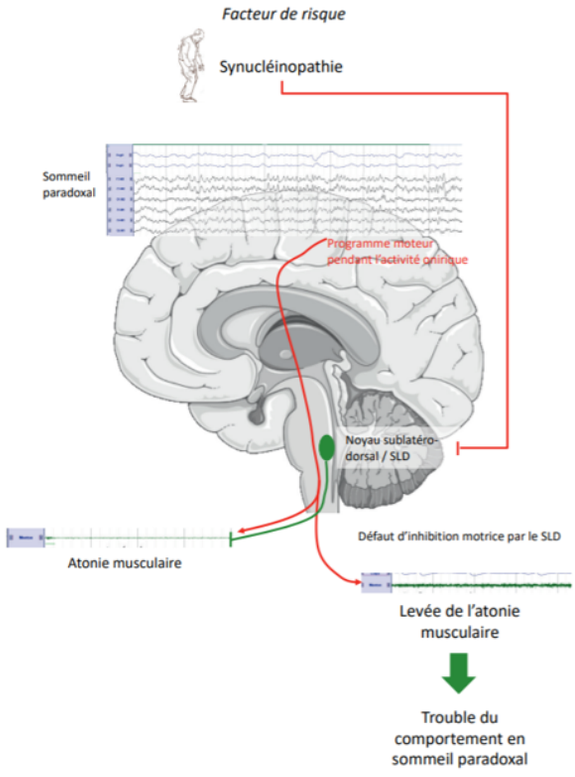

Figure 1.1: RBD is often considered an early sign of a synucleinopathy. It is characterized by sudden motor movements (loss of atonia) and limb jerks.

1.1.2 RBD & Narcolepsy

Narcolepsy is a sleep disorder characterized by the alteration of the normal sleep-wake cycle. The main symptoms are excessive daytime sleepiness and *cataplexy* [5][17].
There are two types of narcolepsy: in this study, the research addresses the relationship between RBD and Narcolepsy Type 1 (known as narcolepsy with cataplexy), which is related to a deficiency of the neurotransmitter hypocretin.
Recent papers cited that RBD affects about 30-60% of individuals with NT1: the term 'N-RBD' stands for Narcoleptic REM Sleep Behavior Disorder and refers to RBD occurring in individuals with narcolepsy.[18]

[5]Sudden loss of muscle tone often triggered by emotions

1.2 Problem Statement & Motivation

The traditional approach of manual-visual scoring for RSWA has a few limitations: it is time-consuming and requires expertises, which makes it less practical in clinical settings. In addition, these methods have only been validated in small groups of PD patients.
The automated method for assessing RSWA in PD patients with RBD has some drawbacks, including the requirement for high-quality polysomnography (PSG) recordings, the need for a trained technician to conduct the PSG recordings, and the necessity for further validation in larger groups of PD patients. Nonetheless, utilizing automated techniques to evaluate RSWA in PD patients with RBD has the potential to enhance the precision and efficiency of diagnosing and treating RBD in this patient population.
Consequently, there is growing interest for RBD in sleep medicine and movement disorder research.
With this work, we aim to analyze and validate a recently proposed method for automatic identification of RSWA in polysomnographic records.

1.3 Use case and proposed solution

Current achievements in automatic sleep analysis have experienced significant advantages from the application of Machine Learning (ML) techniques. In a previous study [19], researchers attempted to automatically identify sleep disorders, including RBD, using a combination of polysomnographic data, EMG and EOG (electrooculogram) data [20]. However, the classification algorithm proposed in that study was quite intricate, involving multiple types of data signals and a substantial number of features.
A key question in this area is to propose a method for blind identification of RSWA in PSG records, by analyzing the spectral patterns of EMG data specifically during REM sleep. ML techniques have been applied to classify individuals as either affected or unaffected by RSWA. Furthermore, in the study [11] a continuous measure called the *Dissociation Index* has been introducted: it quantifies the level of impairment experienced by individuals during RSWA episodes. This measure is calculated using Euclidean distance in appropriate vector spaces.

RSWA involves a state of dissociation between the mind and body. During REM sleep, while the EEG indicates that the individual is in the REM stage, the motor neurons remain active and excitable [18]. Describing the degree of dissociation is of great clinical interest and can facilitate long-term assessments.
The DI holds promise as a preliminary step towards a more refined evaluation and monitoring of RSWA but it requires comprehensive validation. The main purpose of this work is to assess the effectiveness of the Dissociation Score in the context of REM Sleep Without Atonia by applying it to a broader sample comprising Parkinson's Disease patients and narcoleptic patients. While the DI shows potential as an initial approach to enhance the evaluation and monitoring of RSWA, its robustness and reliability need to be thoroughly examined.

Part II

Background

Chapter 2

State of the art

2.1 Visual scoring of RSWA

Several manual-visual methods have been implemented to score RSWA: the first one was developed in 1992 by Lapierre and Montplaisir, for quantifying both tonic and phasic chin EMG activities [21]. This method has been employed to assess idiopathic RBD [1] and RBD associated with neurodegenerative diseases, such as PD and narcolepsy [23, 24, 25, 26, 27].
Notably, the SINBAR method and the Montréal method have gained prominence due to their efficacy in assessing REM sleep muscle activity. In the subsequent two subsections, we will delve into these methods, detailing their respective contributions to the field and their application in the evaluation of RBD in different patient groups.

2.1.1 SINBAR

The SINBAR method, short for Sleep Innsbruck Barcelona, is a specialized technique employed in sleep medicine. It involves the meticulous monitoring

[1]Patients with IRBD have no known neurological diseases or motor or cognitive complaints [22].

and analysis of EMG activity in specific muscles during sleep. Developed to enhance the precision of diagnosing rapid eye movement sleep behavior disorder, SINBAR utilizes a montage of electrodes placed strategically on muscles like the mentalis, flexor digitorum superficialis (FDS), and extensor digitorum brevis. This method plays a pivotal role in our investigation as we aim to establish normative values and comprehensively evaluate its effectiveness in the diagnosis of RBD within clinical practice.[28]
Recent studies [29] aimed to examine the overall sleep structure and specifically assess RSWA using the SINBAR EMG montage, which includes monitoring the mentalis and upper extremity muscles. This analysis was conducted in individuals with both early and advanced stages of PD. Early-stage PD patients exhibited significantly shorter REM sleep latency compared to those in the advanced stage of the disease. The study revealed that advanced-stage PD patients had notably higher SINBAR EMG index values. Furthermore, the SINBAR EMG index, tonic and any EMG activity in the mentalis muscle, and phasic EMG activity in the flexor digitorum superficialis muscles were significantly associated with disease duration. This aligns with the discovery that RBD tends to occur more frequently in individuals with advanced Parkinson's disease rather than those in the early stages of the condition.
When examining the whole REM sleep, as according to the international guidelines [30], the SINBAR group established validated thresholds for indices related to RSWA. These indices were calculated based on 30-second REM sleep epochs and involved the automatic assessment of phasic, "any," and tonic activity in the mentalis muscle, as well as phasic activity in the FDS muscles [31].
In this work the focus is around "any chin activity", the specific RSWA index that was computed is: 30-second "any" mentalis EMG activity, which represents the percentage of 30-second REM sleep epochs that exhibited at least five 3-second mini-epochs with "any" mentalis EMG activity.
There are a few drawbacks of the SINBAR approach, like the requirement for manual artifact correction and the utilization of 30-second epochs. In the recent paper [31] a novel technique is proposed: it involves automatic scoring and shorter epoch durations, so it might serve as a quicker and more reliable screening approach for RSWA.

2.1.2 Montréal

The Montréal Method is another approach used for RBD diagnosis and assessment during polysomnography studies. Lapierre and Montplaisir introduced this scoring method [21, 32] and its responsiveness to treatment with clonazepam [2] is demonstrated.
In accordance with the method explained in the previous cited works and adapted for 30-second epochs, each epoch was assessed as:

- *tonic* in case of sustained EMG activity present in more than 50% of the 30-second epoch duration, with an amplitude at least twice that of the background EMG muscle tone;
- *phasic* chin EMG density represented the proportion of 2-seconds mini-epochs that included EMG events lasting between 0.1 and 10 seconds, with an amplitude over four times the background activity.

As outlined in earlier studies, RSWA was characterized by the presence of tonic chin EMG activity in $\geq 30\%$ of 30-second REM sleep epochs and/or phasic chin activity in $\geq 15\%$ of 2-second REM sleep mini-epochs [33].

2.2 Automatic scoring of RSWA

Visual assessment of RSWA is a time-intensive process, can pose challenges, even for expert scorers and is often not readily accessible in clinical settings. Moreover, a drawback shared by both the Montréal and SINBAR visual methods is their dependence on binary measurements.
In contrast, automated analysis is rapid, can be consistently replicated and employ more continuous measures. As a result, there have been numerous efforts to develop computerized methods for quantifying and detecting RSWA [34, 35].
In this field, various automatic algorithms have been developed, addressing the following purposes:

[2] Clonazepam is effective in reducing the intensified muscle activity during REM sleep.

- assess the algorithms' ability to distinguish between RBD, Somnambulism, Restless Legs Syndrome (RLS) and Obstructive Sleep Apnea (OSA);
- determine cut-off values for short and long muscle activity;
- compare RSWA and recorded movements between automatic and visual videometry analysis [36].

Other existing automated methods discussed in the research paper [37] have initially demonstrated reasonable sensitivity and specificity. However, in comparative assessments, their performance has displayed variability, making it difficult to definitively identify the best approach [38], although the RAI, described in the following paragraph, has stood out as the most dependable for RBD identification.
To determine the most dependable algorithm for incorporation into everyday clinical scoring guidelines, more extensive comparative investigations with larger datasets are required. Nevertheless, as depicted in Figure 2.1, automated methods seem to perform just as accurately as visual methods.
Conversely, automatic analysis does come with its drawbacks, like its potential to miss significant artifacts and its absence from many standard sleep analysis software packages. Nevertheless, it is justifiable to suggest that in clinical practice, the initial assessment of RSWA should involve automatic analysis. Visual analysis can then be brought in when automatic analysis isn't feasible due to technical constraints or in cases where there is uncertainty, alongside the visual review of video-recorded behaviors.

2.2.1 RAI

RAI in Parkinson's Disease

One widely recognized method is the REM Atonia Index, introduced by Ferri et al. in 2008 [9, 8, 39]. This method assesses the amplitude of the rectified submentalis EMG signal in 1-second mini-epochs. The RAI ranges theoretically from 0 (complete loss of atonia) to 1 (complete atonia), with a

Study	Method	Marker Type	RBD Sample Size	Accuracy
Visual methods				
McCarter et al., 2014 [53] McCarter et al., 2017 [54]	AASM [41]	Diagnostic Diagnostic	35	0.750–0.978
McCarter et al., 2014 [53] McCarter et al., 2015 [45] McCarter et al., 2017 [54]	Mayo Clinic [53]	Diagnostic Diagnostic Diagnostic	65	0.817–1.000
McCarter et al., 2019 [56]		Prognostic	60	0.563–0.925
Ferri et al., 2014 [49] Figorilli et al., 2017 [55] Figorilli et al., 2020 [57]	Montreal Group [48]	Diagnostic Diagnostic Diagnostic	270	0.597–1.000
Figorilli et al., 2017 [55] Figorilli et al., 2020 [57] Nepozitek et al., 2019 [58]	SINBAR [51]	Diagnostic Diagnostic Diagnostic	203	0.548–0.952
Automatic methods				
Ferri et al., 2013 [59] Ferri et al., 2014 [49] Figorilli et al., 2017 [55] McCarter et al., 2014 [53] McCarter et al., 2015 [45] McCarter et al., 2017 [54]	RAI [60,61]	Diagnostic Diagnostic Diagnostic Diagnostic Diagnostic Diagnostic	214	0.633–1.000
Yoshino et al., 2015 [62]	AASM [62]	Diagnostic	24	0.854
Frauscher et al., 2014 [63]	SINBAR [63]	Diagnostic	20	0.563–0.925
Cesari et al., 2019 [64]	Danish Center [64]	Diagnostic	31	0.842

AASM = American Academy of Sleep Medicine; SINBAR = Sleep Innsbruck Barcelona Group; RAI = REM Sleep Atonia Index; Danish Center = Danish Center for Sleep Medicine.

Figure 2.1: Comparison of accuracy among different visual and automatic methods for diagnosing RBD based on RSWA measurement [37].

definitive RSWA threshold set below 0.8 [8].
This method has demonstrated relatively low night-to-night variability [40], good sensitivity and specificity and a strong correlation with visual methods [33]. It has been validated for patients with idiopathic RBD (iRBD), PD-associated RBD (PD-RBD) [41, 42], RBD with OSA [43] and the detection of RSWA in narcolepsy [44, 45], including pediatric cases [46].

RAI in Narcolepsy

The first study to use computerized quantitative analysis of EMG signals in narcolepsy is dealt in [44], with the goal to examine signs of RBD through polysomnography. The REM Sleep Atonia Index was lower in both groups of patients, with those with narcolepsy and RBD having the lowest values. Interestingly, unlike in the control group, this index did not show a correlation with age in the patient groups.

Interestingly, RBD in narcolepsy is not a nightly occurrence and is often identified through questionnaires or clinical interviews rather than video-polysomnography (v-PSG). This distinguishes narcolepsy from neurodegenerative diseases like multiple system atrophy, where RBD is readily detected through PSG. Detecting subclinical signs of RBD in narcolepsy patients using polysomnographic tracings could be valuable for research and clinical decision-making.
The main finding is that narcolepsy/cataplexy patients show significant motor dyscontrol in chin EMG during REM sleep, even those without clear clinical RBD complaints.
Comparing these findings to i-RBD patients, narcolepsy-associated RBD appears less severe and different in pattern.

Part III

Proposed solution

Chapter 3

Material and Method

3.1 Subjects and Data

The study first dataset comprised a total of forty-nine non-demented Parkinson's Disease patients, mean aged 62.80±7.35 years [Table 3.1], who meet the clinical diagnosis based on the criteria established by the United Kingdom Brain Bank [47]. They were selected for inclusion in the study during their routine evaluations at two prominent Movement Disorder Centers, which I personally visited to conduct my research:

- **Centre Hospitalier Universitaire (CHU) de Clermont-Ferrand, France**: it contributed data for 41 of the PD patients;
- **"Le Molinette" University Hospital in Turin, Italy**: an additional 8 PD patients were included from this center.

Patients were excluded from the study if they exhibited: clinically defined dementia; psychosis, as diagnosed according to DSM-V criteria [48]; the use of device-aided therapy for the treatment of their condition.
Demographic and clinical information, including details such as gender, age, the duration and the severity of PD, assessed through both the Hoehn & Yahr scale (HY) [49] and the Unified Parkinson's Disease Rating Scale (UPDRS) were systematically gathered for all patients. To quantify the medication

dosage, the total levodopa equivalent dose (LED) was calculated using the methodology outlined by Tomlinson et al.[50].

Dataset PD patients					
Males	Females	PD-RBD	PD-noRBD	Age	Deviation from Age
26	23	29	20	62.80	7.35

Table 3.1: Description of the dataset related to Parkinson's Disease patients.

The study second dataset comprised a total of fifty-three children with narcolepsy, aged between 5.7 and 16.8 years [Table 3.2]. The database was registered with the French national data protection agency (Commission Nationale de l'Informatique et des Libertés, CNIL registration n° 19-087).
I examined data obtained from the pediatric sleep unit at the **Hôpital Femme Mère Enfant in Lyon, France** (recognized as a national reference center for narcolepsy in the country), which I visited to collect data thanks to Dr. Aurore Guyon and Prof. Patricia Franco.
The patients underwent nocturnal PSG, which was accompanied by sessions of standard multiple sleep latency tests (MSLT), both described in the research paper [51]. Scoring of sleep stages, arousals, and respiratory events was conducted manually by the sleep specialist [52].

Dataset narcoleptic children			
Males	Females	Age	Deviation from Age
25	28	12.30	3.18

Table 3.2: Description of the dataset related to narcoleptic children.

3.2 Data acquisition

3.2.1 Polysomnographic recording

Each participant underwent a complete overnight v-PSG recording within a dedicated sleep laboratory, utilizing the digital polysomnography technology 'Micromed System Plus Evolution'. Importantly, during the entire recording

duration, the participants remained under constant observation, facilitated by synchronized infrared video recording, which ran concurrently with the PSG data collection.
The group were equipped with a comprehensive array of sensors and electrodes. The setup included electroencephalographic leads positioned at F3-A2, F4-A1, C3-A2, C4-A1, O1-A2, O2-A1, left and right EOG channels, bilateral surface EMG channels that covered the submentalis muscle [Figure 3.1], FDS on upper limbs, and tibialis anterior on lower limbs. Additionally, electrocardiography was employed to continuously monitor heart activity. Furthermore, respiratory analysis was conducted using a range of sensors, including nasal thermistors and nasal pressure sensors for assessing airflow, sensors to measure thoracic and abdominal respiratory effort, a pulse oximeter for monitoring blood oxygen levels and a microphone for audio recording [53]. The video footage needs to be aligned or matched precisely with the polysomnography data. The quality should be sufficiently high to enable zooming in during later analysis without any reduction in image detail [Figure 3.2] [54]. The camera should be installed on the wall in a way that captures the entire bed within its view, providing a wide-angle perspective. It is important that when a patient is lying on the bed, they are seen in the frame from their head to their feet in a symmetrical manner [55].

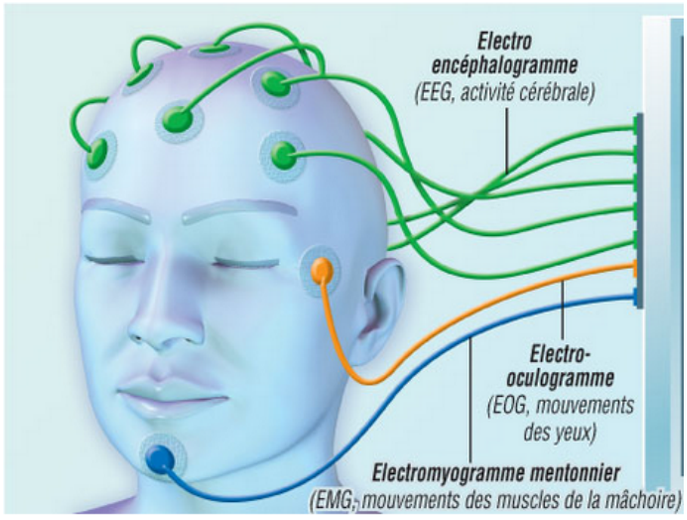

Figure 3.1: Electrodes setup: on the scalp to measure brain activity; near the eyes to measure eye movements; on the chin to measure jaw muscle movements.https://les-troubles-du-sommeil.webnode.fr/la-polysomnographie/

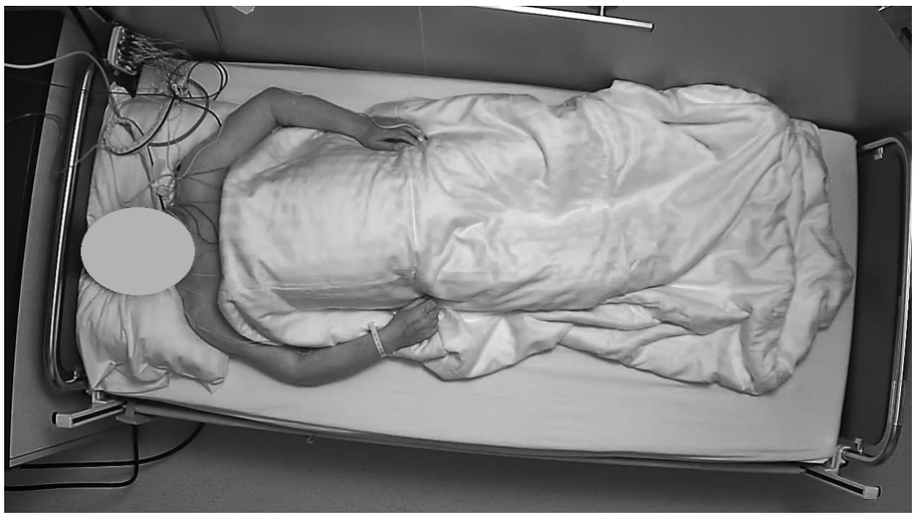

Figure 3.2: Image captured with a high-density camera. The resolution allows to zoom-in on the image without any loss of quality.

3.2.2 REM Atonia Index Computation

In this study, RAI was computed from sleep data in two distinct formats: the European Data Format, which contains the PSG traces, and the corresponding files containing the sleep hypnogram information denoting sleep stages for each epoch.
The RAI calculation was performed using two separate approaches. Firstly, the automatic software HypnoLab, developed by SWS Soft and overseen by Raffaele Ferri, was employed. This software utilizes an Automatic Chin Analysis method to extract RAI values from the EMG signal recorded from the chin channel, following prior filtering steps. Subsequently, a comparison was conducted by implementing an independent RAI calculation algorithm in MATLAB R2022b. This step was undertaken to assess the consistency and agreement between the results obtained from HypnoLab and MATLAB. Moreover, within the MATLAB environment, further adjustments were made to ensure harmonization with the software in which the Dissociation Index was also implemented, facilitating a more comprehensive analysis of sleep data.

3.3 Features of the study

To begin with, it was necessary to determine a suitable set of features that could be used as input for the classification algorithms. In this research, we incorporate widely used polysomnographic parameters [56], which are derived through computational analysis of the manually annotated hypnogram. These parameters encompass; Sleep Onset Latency (SOL), Wake After Sleep Onset (WASO), Total Sleep Time (TST), Time In Bed (TIB), Sleep Efficiency (SE), Arousal Index (ARI), Minutes of REM Sleep (MREM); comprehensive definitions are expressed in Table 3.3. Additionally, in accordance with the findings from [57], this analysis covers further polysomnographic characteristics, specifically: the mean duration and percentage of segments categorized under the same sleep stage, the Sleep Transition Index (STI), and the Fragmentation Indices for REM and non-REM (NREM) sleep (RFI and NFI). These indices serve as indicators of sleep fragmentation patterns often observed in individuals with disrupted sleep quality [38]. Once more, more explanations of these features can be found in Table 3.3.
The REM Sleep Atonia Index evaluates the degree of muscle atonia experienced during REM sleep. It is calculated using the submental EMG signal within 1-second mini-epochs, taking into consideration the percentage of mini-epochs with an amplitude less than 1 μV. This index falls within the range of [0, 1], with a value of 1 indicating normal sleep conditions. Recent research [58] has suggested that the RAI could potentially be used as an initial approach to detect RSWA.
In conclusion, the set of features we considered includes fresh insights derived from the spectral analysis of EMG signals during REM sleep. We opted for 1-second mini-epochs to align with RAI calculations and employed the Welch modified periodogram with a Hamming window to estimate the Power Spectral Density (PSD) [11]. From this analysis, we obtained three distinct features: the Mean Frequency, which provides an averaged representation of the PSD center; the Median Frequency (also known as Spectral Edge Frequency at 50%, SEF50), indicating the frequency below which 50% of the total power is concentrated; and the Spectral Edge Frequency at 95% (SEF95), signifying the frequency below which 95% of the total power is concentrated. A comprehensive list of the features along with concise descriptions, is presented in Table 3.3.

3.3.1 Spectral features

The following features 3.4 provide valuable insights into the spectral characteristics of sleep data, which can be useful for analyzing sleep patterns and identifying anomalies:

- *SEF50 Median:* represents the median value of Spectral Edge Frequency at 50% of the total spectral power. It indicates the central frequency below which half of the spectral power is distributed and it can be related to the dominant frequency during certain sleep stages.
- *SEF50 25th:* is the 25th percentile of Spectral Edge Frequency at 50%. It quantifies the lower boundary of the spectral distribution, indicating the frequency below which a quarter of the spectral power falls.
- *SEF50 75th:* is the 75th percentile of Spectral Edge Frequency at 50%. It quantifies the upper boundary of the spectral distribution, indicating the frequency below which three-quarters of the spectral power falls.
- *SEF50 Kurtosis:* measures the "tailedness" of the distribution of Spectral Edge Frequency at 50%. High kurtosis indicates heavy tails, while low kurtosis indicates light tails, providing insights into the shape of the distribution.
- *SEF50 Skewness:* quantifies the asymmetry of the distribution of Spectral Edge Frequency at 50%. Positive skewness indicates a right-skewed distribution (tail to the right), while negative skewness indicates a left-skewed distribution (tail to the left).
- *SEF50 Std:* is the standard deviation of Spectral Edge Frequency at 50%. It measures the spread or variability of data points around the mean value, providing information about the dispersion of frequencies.
- *SEF50 IQRPlus:* represents the upper bound of the Interquartile Range (IQR) of Spectral Edge Frequency at 50%. It indicates the frequency above which the top 25% of spectral power is distributed.
- *SEF50 IQRMinus:* represents the lower bound of the IQR of Spectral Edge Frequency at 50%. It indicates the frequency below which the bottom 25% of spectral power is distributed.

- *SEF95 Median:* represents the median value of Spectral Edge Frequency at 95% of the total spectral power. It indicates the central frequency below which half of the spectral power at 95% lies.
- *SEF95 25th:* is the 25th percentile of Spectral Edge Frequency at 95%. It quantifies the lower boundary of the spectral distribution, indicating the frequency below which a quarter of the spectral power at 95% falls.
- *SEF95 75th:* is the 75th percentile of Spectral Edge Frequency at 95%. It quantifies the upper boundary of the spectral distribution, indicating the frequency below which three-quarters of the spectral power at 95% falls.
- *SEF95 Kurtosis:* measures the "tailedness" of the distribution of Spectral Edge Frequency at 95%. It provides insights into the shape of the distribution of frequencies at 95%.
- *SEF95 Skewness:* quantifies the asymmetry of the distribution of Spectral Edge Frequency at 95%. Positive skewness indicates a right-skewed distribution, while negative skewness indicates a left-skewed distribution at 95%.
- *SEF95 Std:* is the standard deviation of Spectral Edge Frequency at 95%. It measures the spread or variability of data points around the mean value of the spectral power at 95%.
- *SEF95 IQRPlus:* represents the upper bound of the IQR of Spectral Edge Frequency at 95%. It indicates the frequency above which the top 25% of spectral power at 95% is distributed.
- *SEF95 IQRMinus:* represents the lower bound of the IQR of Spectral Edge Frequency at 95%. It indicates the frequency below which the bottom 25% of spectral power at 95% is distributed.
- *AvgPow Median:* is the median value of Average Power. It provides the central tendency of the average power values in the dataset.
- *AvgPow 25th:* is the 25th percentile of Average Power. It quantifies the lower boundary of the distribution of average power values.
- *AvgPow 75th:* is the 75th percentile of Average Power. It quantifies the upper boundary of the distribution of average power values.

- *AvgPow Kurtosis:* measures the "tailedness" of the distribution of Average Power. It provides insights into the shape of the distribution of average power values.
- *AvgPow Skewness:* quantifies the asymmetry of the distribution of Average Power. Positive skewness indicates a right-skewed distribution, while negative skewness indicates a left-skewed distribution.
- *AvgPow Std:* is the standard deviation of Average Power. It measures the spread or variability of data points around the mean value of average power.
- *AvgPow IQRPlus:* represents the upper bound of the IQR of Average Power. It indicates the upper boundary of the distribution of average power values.
- *AvgPow IQRMinus:* represents the lower bound of the IQR of Average Power. It indicates the lower boundary of the distribution of average power values.

Polysomnographic features	**Meaning**
Sleep Onset Latency (SOL)	The time duration required to fall asleep
Wake After Sleep Onset (WASO)	The time duration the patient is awake during the acquisition
Total Sleep Time (TST)	Total sleep time in hours
Sleep Efficiency (SE)	The ratio between TST and Time in Bed
Time in Bed (TIB)	Interval from lights-off to lights on in hours
Arousal Index (ARI)	The rate at which arousal happens
Minutes of REM Sleep (MREM)	Total REM Sleep in minutes
Sleep Stage Proportion (SSP)	Ratio of different sleep stages
NREM Fragmentation Index (NFI)	Metric quantifying the transitions between NREM sleep
REM Fragmentation Index (RFI)	Metric quantifying the transitions between REM sleep
Wake Proportion (WP)	Wakefulness during the night
Sleep Transitions Index (STI)	Metric quantifying the transitions between NREM and REM sleep
Average Segment Length (ASL)	Length of uninterrupted sleep single stage
EMG, time domain	**Meaning**
REM Sleep Atonia Index (RAI)	Metric assessing the amount of muscle atonia
EMG, frequency domain	**Meaning**
Cumulative Distribution Function (CDF) of PSD	Distribution of power across different frequency components
Mean Frequency of REM mini-epochs (MNF)	Mean Frequency of EMG signal during REM sleep
Median Frequency of REM mini-epochs (MDF)	Median Frequency of EMG signal during REM sleep
Spectral Edge Frequency at 95% of REM mini-epochs (SEF95)	Frequency at which 95% of the spectral power in the EMG signal in REM sleep is concentrated

Table 3.3: Features incorporates in the study, associated with their acronyms and a brief description of the meaning. These features fall into three distinct categories: polysomnographic data and EMG features in both the time and frequency domain.

Feature Name	Extended Name
SEF50 Median	Spectral Edge Frequency at 50%
SEF50 25th	25th Percentile of SEF at 50%
SEF50 75th	75th Percentile of SEF at 50%
SEF50 Kurtosis	Kurtosis of SEF at 50%
SEF50 Skewness	Skewness of SEF at 50%
SEF50 Std	Standard Deviation of SEF at 50%
SEF50 IQRPlus	Upper Bound of IQR of SEF at 50%
SEF50 IQRMinus	Lower Bound of IQR of SEF at 50%
SEF95 Median	Median Spectral Edge Frequency at 95%
SEF95 25th	25th Percentile of SEF at 95%
SEF95 75th	75th Percentile of SEF at 95%
SEF95 Kurtosis	Kurtosis of SEF at 95%
SEF95 Skewness	Skewness of SEF at 95%
SEF95 Std	Standard Deviation of SEF at 95%
SEF95 IQRPlus	Upper Bound of IQR of SEF at 95%
SEF95 IQRMinus	Lower Bound of IQR of SEF at 95%
AvgPow Median	Median Average Power
AvgPow 25th	25th Percentile of Average Power
AvgPow 75th	75th Percentile of Average Power
AvgPow Kurtosis	Kurtosis of Average Power
AvgPow Skewness	Skewness of Average Power
AvgPow Std	Standard Deviation of Average Power
AvgPow IQRPlus	Upper Bound of the Interquartile Range of Average Power
AvgPow IQRMinus	Lower Bound of the Interquartile Range of Average Power
RBD	Presence-absence of REM Sleep Behavior Disorder

Table 3.4: Summary of the spectral features with their extended names

3.3.2 Clinical features in PD adults

The following features play a critical role in understanding the clinical characteristics, progression, and treatment outcomes of Parkinson's Disease in patients, providing valuable insights for both research and clinical management.

- *RAI:* REM Atonia Index is a quantitative measure used to assess the presence or absence of RBD. In this analysis, a threshold of 0.7 has been applied to classify patients: RAI greater than 0.7 express the absence of pathology in PD patients; if RAI is below the threshold, the patient is categorized as RBD, suggesting abnormal REM sleep patterns. This threshold-based classification aids in identifying individuals with RBD based on their RAI values.

- *DI (Dissociation Index):* it is a continuous measure implemented to quantify the extent of impairment between mind and body experienced by the individual, using Euclidean distance measurements within a relevant vector space [11]. This index is particularly relevant because RSWA (REM Sleep Without Atonia) involves a state of dissociation between the mental and physical aspects of the subject: when EEG data indicates that the subject is in the REM sleep stage, their motor neurons remain excitable.
  In this research study it is used to assess the extent of dissociation between two values, specifically the reference value and a subject value (atonia index), relative to a reference population.The resulting scores are indicative of how far each subjVal deviates from the reference value, normalized within a range of 0 to 1.

- *Durée Diagnosis:* it refers to the duration of time that patients have been diagnosed with Parkinson's Disease. It quantifies how long individuals have been living with the condition since their official diagnosis. This feature is crucial in understanding the progression of the disease and its impact on patients over time.

- *HY (Hoehn and Yahr Scale):* it is a commonly used clinical tool to assess the progression of Parkinson's Disease. It categorizes patients into stages based on the severity of motor symptoms and functional impairment, ranging from stage 0 (no symptoms) to stage 5 (advanced disease with severe disability). HY provides valuable information about the disease stage and its impact on a patient daily life.

- *UPDRS II:* it is a section of the Unified Parkinson's Disease Rating Scale (UPDRS) focused on assessing the activities of daily living. It evaluates non-motor aspects of PD, such as mood, behavior, and activities related to daily life. UPDRS-II scores help clinicians and researchers understand the impact of PD on a patient ability to perform everyday tasks.

- *UPDRS III:* it is another section of the Unified Parkinson's Disease Rating Scale, primarily focused on motor symptoms. It assesses various motor functions, including tremors, rigidity, bradykinesia (slowness of movement), and postural stability. UPDRS-III scores provide an objective measure of the severity of motor symptoms in PD.

- *UPDRS IV:* it is a section of the Unified Parkinson's Disease Rating Scale that evaluates complications related to Parkinson's Disease treatment, including motor fluctuations and dyskinesias. It helps healthcare professionals assess the effectiveness of PD medications and their impact on a patient daily life.

- *UPDRS TOT:* it represents the total score obtained by summing the scores from all sections of the Unified Parkinson's Disease Rating Scale (Parts I to IV). It provides an overall assessment of a patient condition, considering both motor and non-motor symptoms, and is a comprehensive measure of disease severity.

- *LED (Levodopa Equivalent Dose):* it is a measure used to standardize and compare different medications used in the treatment of Parkinson's Disease. Since various drugs have different potencies, LED allows healthcare providers to calculate an equivalent dose of levodopa, a common PD medication, to assess the overall treatment regimen effectiveness and safety.

- *RBD:* it is a binary feature that takes the value of 1 if the subject has RBD and 0 if they do not. It is determined based on a threshold on the RAI of 0.7. RAI measures the loss of muscle atonia during REM sleep, and a value exceeding 0.7 suggests the absence of RBD.

- *Continuous Indicator:* it serves as a continuous measure that quantifies the degree of dissimilarity between the two classes (RBD and noRBD) for each data point. It essentially provides a numerical indication of how strongly a data point is associated with one class over the other. In this study, it ranges between -1 and +1, as 0 is the hyperplane. It is a valuable tool in assessing the continuous nature of class separability in the classification task.

Feature Name
RAI (Rem Atonia Index)
DI (Dissociation Index)
Durée Diagnosis
HY (Hoehn and Yahr Scale)
UPDRS II
UPDRS III
UPDRS IV
UPDRS TOT
LED (Levodopa Equivalent Dose)
Continuous Indicator

Table 3.5: Summary of clinical features in PD patients study

3.3.3 Clinical features in narcoleptic children

These features [Table 3.6] provide insights into the clinical presentation, severity, and impact of narcolepsy in pediatric patients. Understanding these aspects is essential for accurate diagnosis and tailored management strategies to improve the quality of life and overall well-being of affected children.

- *Ullanlinna Scale:* The Ullanlinna Narcolepsy Scale (UNS) is a method used to assess the symptoms of narcolepsy through the two primary features of narcolepsy: abnormal sleeping tendencies and cataplexy. The total score on the UNS can range from 0 to 44.
  The reliability of scale and accuracy have been validated through research. Data from a variety of non-institutionalized adults in Finland were used to establish its sensitivity and specificity. A cut-off score of 14 on the UNS had a sensitivity of 100% (accurately detecting narcolepsy) and a specificity of 98.8% (correctly ruling out narcolepsy) in the studied subjects.[59]

- *HPI (High-Probability Interval or High Potential for Incidence):* it refers to a period or situation in which individuals with narcolepsy are at a higher risk of experiencing narcoleptic symptoms, such as sudden daytime sleepiness or cataplexy. It is important to consider cognitive abilities of

the child and potential when diagnosing and managing narcolepsy, as narcolepsy can affect academic performance and cognitive functioning.

- *Cataplexy:* it is a hallmark symptom of narcolepsy characterized by sudden and temporary muscle weakness or loss of muscle control, often triggered by strong emotions such as laughter, surprise, or anger. Assessing the frequency and severity of cataplexy episodes is crucial for diagnosing and managing narcolepsy in pediatric patients.

- *Cauchemars (Nightmares):* they are vivid and disturbing dreams that can disrupt the child sleep in narcolepsy. Evaluating the presence and frequency of nightmares is important as they can contribute to sleep disturbances and daytime sleepiness in pediatric narcoleptic patients.

- *Paralysie du Sommeil (Sleep Paralysis):* it is a phenomenon where individuals temporarily experience an inability to move or speak while falling asleep or waking up. It is a common symptom of narcolepsy. Assessing the occurrence of sleep paralysis episodes helps in diagnosing and managing narcolepsy.

- *Hallucinations:* particularly hypnagogic and hypnopompic hallucinations, can occur in pediatric narcoleptic patients. These hallucinations involve vivid sensory experiences, such as seeing, hearing, or feeling things that are not real, during the transition between wakefulness and sleep. Evaluating the presence and nature of hallucinations is important for diagnosing narcolepsy and addressing related sleep disturbances.

Feature Name
Ullanlinna Scale
HPI (High Potential for Incidence)
Cataplexy
Cauchemars
Paralysie du Summeil
Hallucinations

Table 3.6: Summary of clinical features in narcoleptic children study

3.4 Machine Learning Classification

3.4.1 Measurement Selection and Rationale

In this study, certain parameters were subjected to a dual measurement process, with values recorded both before and after the administration of a pharmaceutical treatment. The decision to focus on the measurements taken before treatment initiation is a crucial aspect of the experimental design and warrants explanation.
The rationale behind utilizing the pre-treatment measurements is rooted in the desire to capture the baseline condition of the study participants, specifically targeting the initial severity or manifestation of the pathology under investigation. This approach allows for a comprehensive evaluation of the untreated pathological state, enabling a robust understanding of the disease natural course before intervention.
By selecting the pre-treatment measurements, we aimed to assess the worst phase of the pathology, as this initial state often represents the highest degree of impairment and clinical significance.

3.4.2 Data partitioning and model training

The subsequent step was to split the dataset into two distinct parts: the training set and the test set.

- *Training Set:* within this segment of the original dataset, the model is educated. It corresponds to the data the model encounters during the learning phase, aiding in the adjustment of the model internal settings.
- *Test Set:* is a completely separate portion of the original data used to evaluate how well the model performs. Once the model has undergone training using the training set, it is tested on the test set to determine its capability to apply what it has learned to new, unseen data. Importantly, the test set is not used in any way during the model training process.
- *Validation Set*: is an additional subset of the original dataset employed to fine-tune the model hyperparameters, which are responsible for managing

its complexity. The validation set plays a crucial role in selecting the optimal values for these hyperparameters, thereby enhancing the model capacity to make accurate predictions on fresh data.

In essence, the dataset was partitioned into these three components: training for learning, testing for evaluation, and validation for hyperparameter optimization. This approach ensures that the model is effectively prepared, assessed, and optimized for its predictive abilities.

Dataset	**Purpose**
Training Set	Model training and learning
Testing Set	Model evaluation and performance assessment
Validation Set	Hyperparameter optimization

Table 3.7: Data Partitioning for Model Training and Evaluation.

3.4.3 Classification Using Binary SVM

The classification model leverages a set of carefully selected input features: they encompass various aspects of sleep patterns and spectral analysis, such as spectral edge frequencies (SEF), statistical measures like kurtosis and skewness and characteristics of average power [Table 3.4].
A binary Support Vector Machine (SVM) classifier was employed as a powerful tool for classifying medical data, specifically in the context of distinguishing between two distinct groups: REM Behavior Disorder (*RBD*) and NO REM Behavior Disorder (*noRBD*) subjects.
As illustrated in Figure 3.4, the classification algorithm follows a structured process.
The choice of a linear kernel function was made to create a linear decision boundary, which separates the two classes optimally. The training process involved finding the hyperplane that maximized the margin between the two

classes while minimizing classification errors [Figure 3.3]. This hyperplane acts as the decision boundary used for classifying new, unseen data.

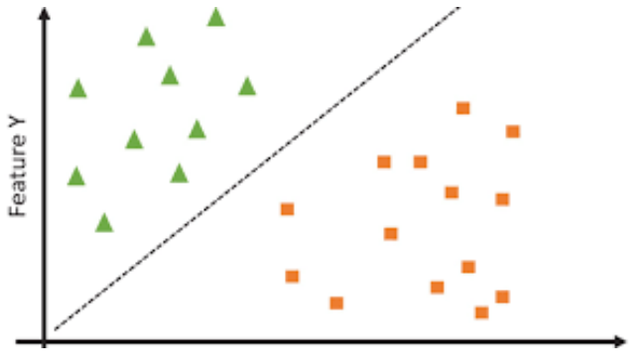

Figure 3.3: Core Mechanism of the Support Vector Machine Classifier [60]

The trained SVM model was then evaluated using a Leave-One-Subject-Out Cross-Validation approach. This method ensures that each subject data is left out as the test set while the model is trained on the remaining data, effectively simulating real-world scenarios. The model performance was assessed using metrics such as accuracy, precision, recall, and F1-score to gauge the SVM effectiveness in distinguishing between RBD and noRBD patients.

3.4.4 Leave-One-Subject-Out Cross-Validation

In the process of evaluating our model performance, we employed a specialized technique known as Leave-One-Subject-Out Cross-Validation (LOSOCV). This method is a variation of traditional k-fold cross-validation [61], where each 'fold' consists of data from a single individual.
The LOSOCV procedure entails systematically withholding data from one subject at a time, utilizing the remaining dataset for training, and then assessing the model performance on the omitted subject data. This process is repeated iteratively for each subject in our dataset, allowing each individual data to serve as the test set once while the model is trained on the data from the remaining subjects [62].
In order to assess LOSOCV technique, a confusion matrix is used. This matrix serves as a critical instrument in our evaluation, allowing to dissect the model outcomes into four essential categories:

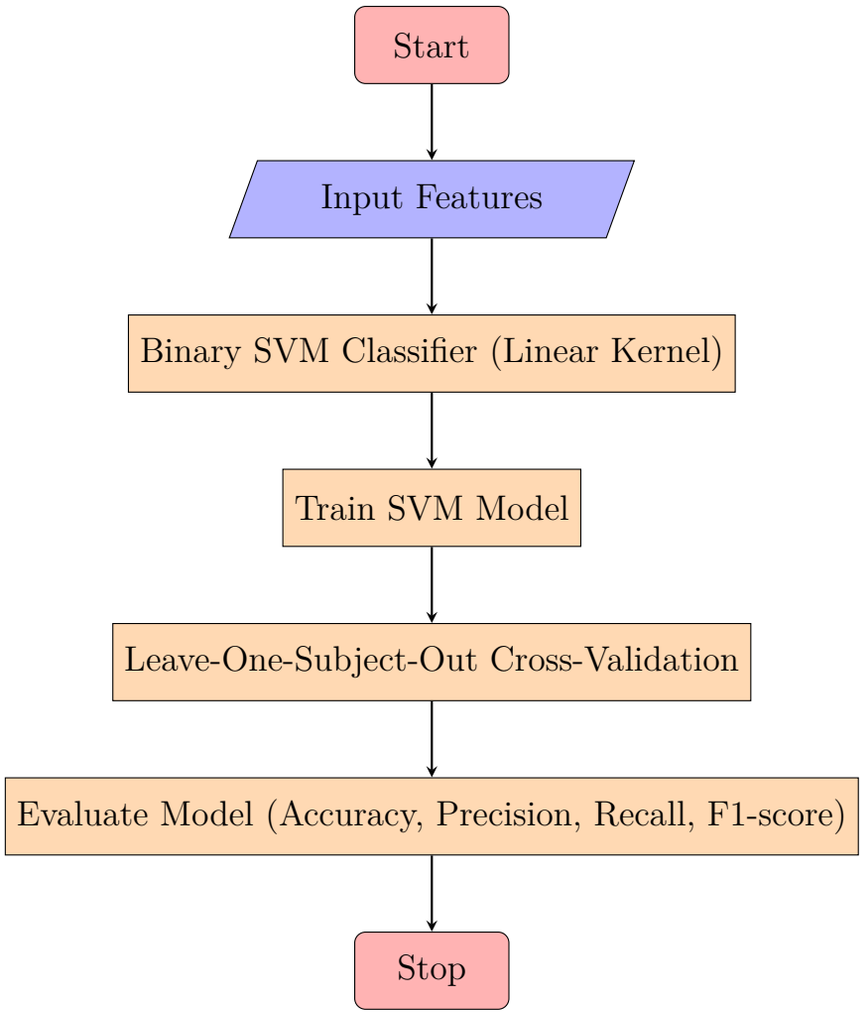

Figure 3.4: Flowchart depicting the steps of the classification algorithm.

- True Positive (TP) and True Negative (TN) represent the number of samples correctly identified as positive and negative, respectively;
- False Positive (FP) and False Negative (FN) represent the instances where the model incorrectly categorizes samples as positive or negative.

With the aim of gain a more comprehensive understanding of the model performance, we utilize the following metrics:

- Accuracy: essential metric that measures the proportion of correctly

classified samples,

$$\text{Accuracy} = \frac{TP + TN}{TP + TN + FP + FN}$$

- Precision: evaluates the model ability to correctly identify positive samples,

$$\text{Precision} = \frac{TP}{TP + FP}$$

- Recall: assesses its capability to capture all positive samples in the dataset.

$$\text{Recall} = \frac{TP}{TP + FN}$$

- F1-Score: a harmonic mean of precision and recall, provides a balanced measure that considers both false positives and false negatives in the assessment.

$$\text{F1-Score} = 2 \cdot \frac{\text{Precision} \cdot \text{Recall}}{\text{Precision} + \text{Recall}}$$

These metrics collectively offer a thorough evaluation of our model classification performance and help us gauge its effectiveness in distinguishing between different classes within the dataset.

3.5 Correlation analysis of clinical and diagnostic features

In this section, we explore the relationships between the REM Atonia Index and several clinical and diagnostic features associated with Parkinson's Disease. In this research, the dataset consists of patients' RAI values alongside variables such as (Table 3.5):

- Dissociation Index;
- Duration of Diagnosis;
- Hoehn and Yahr Scale (HY);

- Unified Parkinson's Disease Rating Scale II (UPDRS II), related to the activities of daily living;
- Unified Parkinson's Disease Rating Scale III (UPDRS III), associated to the motor examination;
- Unified Parkinson's Disease Rating Scale IV (UPDRS IV), connected to motor complications;
- Total Unified Parkinson's Disease Rating Scale (UPDRS TOT);
- Levodopa Equivalent Dose (LED);
- RBD: presence (1) or absence (0) of pathology;
- Continuous Indicator.

To quantify these relationships, we calculated correlation coefficients between RAI and each of the aforementioned variables.
Our findings show significant correlations, and these relationships can offer critical clinical implications.
On MATLAB, the Pearson correlation coefficient method was employed to assess the linear associations between these parameters.

3.5.1 Pearson correlation coefficient analysis

In the course of this research, one of the fundamental statistical methods employed for evaluating the relationships between different features of Parkinson's Disease patients is the Pearson correlation coefficient. The formula for calculating it between two variables X and Y with n data points is as follows [63]:

$$r = \frac{\sum_{i=1}^{n}(X_i - \bar{X})(Y_i - \bar{Y})}{\sqrt{\sum_{i=1}^{n}(X_i - \bar{X})^2 \sum_{i=1}^{n}(Y_i - \bar{Y})^2}}$$

Where: X_i and Y_i are the individual data points of X and Y, while $\bar{X}$ and $\bar{Y}$ are the means (averages) of X and Y.

The Pearson correlation coefficient (r) can also be expressed in terms of covariance. Here is the formula for calculating r using covariance:

$$r = \frac{\text{Cov}(X, Y)}{\sigma_X \sigma_Y}$$

Where: $\text{Cov}(X, Y)$ represents the covariance between variables X and Y, while σ_X denotes the standard deviation of X, and σ_Y denotes the standard deviation of Y.
Pearson correlation coefficient ranges from -1 to 1,specifically:

- **-1** indicates a perfect negative linear relationship;
- **0** indicates no linear relationship;
- **1** indicates a perfect positive linear relationship.

This method allows us to gain insights into the strength and direction of relationships between the features in Table 3.5, aiding in the understanding of potential correlations within the Parkinson's disease patient population.

3.6 Correlation Analysis in Narcoleptic Children

In the investigation of narcoleptic children, MATLAB has been employed to conduct a comprehensive correlation analysis among various clinical parameters, shedding light on potential relationships within this unique population. The dataset encompassed variables of clinical relevance, including the RAI, Ullanlinna Narcolepsy Scale, High-Probability Interval, Cataplexy, Cauchemars (Nightmares), Sleep Paralysis and Hallucinations.
To explore the associations between these variables, we calculated the Pearson correlation coefficients, which measure linear relationships between pairs of variables. The resulting correlation matrix was generated to provide a comprehensive overview of these relationships.
This correlation analysis not only advances our understanding of narcoleptic children clinical profiles but also highlights the utility of MATLAB as a

versatile tool for conducting statistical analyses in clinical research. These findings may contribute to the development of targeted interventions and personalized treatment strategies for this patient population.

Part IV

Results

Chapter 4

Results

In this chapter, we describe all the challenges and issues that have arisen during the exploration of this research work. It is essential to acknowledge and address these obstacles in order to ensure the validity and reliability of the results. This section will explore some of the potential issues that we encountered during the research experiment and discuss strategies for overcoming them. By anticipating and effectively managing these challenges, other researchers could work towards achieving the goals of their study and producing meaningful findings.

4.1 Correlations in Parkinson's Disease Patients

In this section, the results of a comprehensive correlation analysis among various clinical features in PD patients are presented. The dataset encompassed essential parameters shown in Table 3.5: the investigation revealed noteworthy relationships within this cohort. A comprehensive overview of the correlations among key features in PD patients is presented in Table 4.1. The RAI exhibited a strong negative correlation with the DI, indicating a significant inverse relationship. Similarly, RAI also demonstrated a strong negative correlation with RBD, suggesting that higher RAI values are associated with the absence of REM Behavior Disorder. Conversely, DI showed

a strong positive correlation with RBD, indicating that higher DI values correspond to the presence of REM Behavior Disorder. These findings are widely described in the following subsections.
Furthermore, the duration of diagnosis (Duree Diagn) displayed weak positive correlations with Hoehn and Yahr Scale, Unified Parkinson's Disease Rating Scale Part III, and Unified Parkinson's Disease Rating Scale Part IV, indicating that as the duration of diagnosis increases, so does the severity of motor symptoms and complications related to PD treatment.
The observed weak correlations between the parameters regarding the duration and the severity of PD, warrant a thoughtful consideration of the underlying dynamics. One plausible explanation for these modest associations is the heterogeneity, in terms of disease duration within the PD patient population, particularly with respect to the stage and progression of the disease. To address this limitation and enhance the comprehensiveness of our analysis, a prospective clinical study employing a longitudinal approach is proposed in the next chapter.

4.1.1 REM Atonia Index & RBD

The RBD diagnosis of individuals within the cohort relied on the establishment of a threshold at RAI = 0.7. It serves as a critical delineation point, effectively distinguishing between PD patients with RBD and those without. The rationale behind this threshold selection is rooted in the diagnosis of RBD within the dataset, as discussed in previous chapters and supported by empirical evidence.
The scatter plot 4.1 shows the comparison between RAI and RBD presence with a Pearson coefficient r = -0.895196. It is negative because when RAI values were below the threshold of 0.7, the patient exhibits symptoms of RBD (RBD presence = '1'), indicating disrupted REM sleep patterns and associated behaviors. Conversely, patients with RAI values exceeding 0.7 demonstrated a reduced likelihood of RBD, suggesting a closer adherence to normal REM sleep patterns.
These findings underscore the potential utility of RAI as a diagnostic marker for RBD in PD patients. The RAI threshold of 0.7 serves as an effective cutoff point, aiding in the identification of individuals with of RBD, thereby enabling early intervention and tailored treatment strategies.

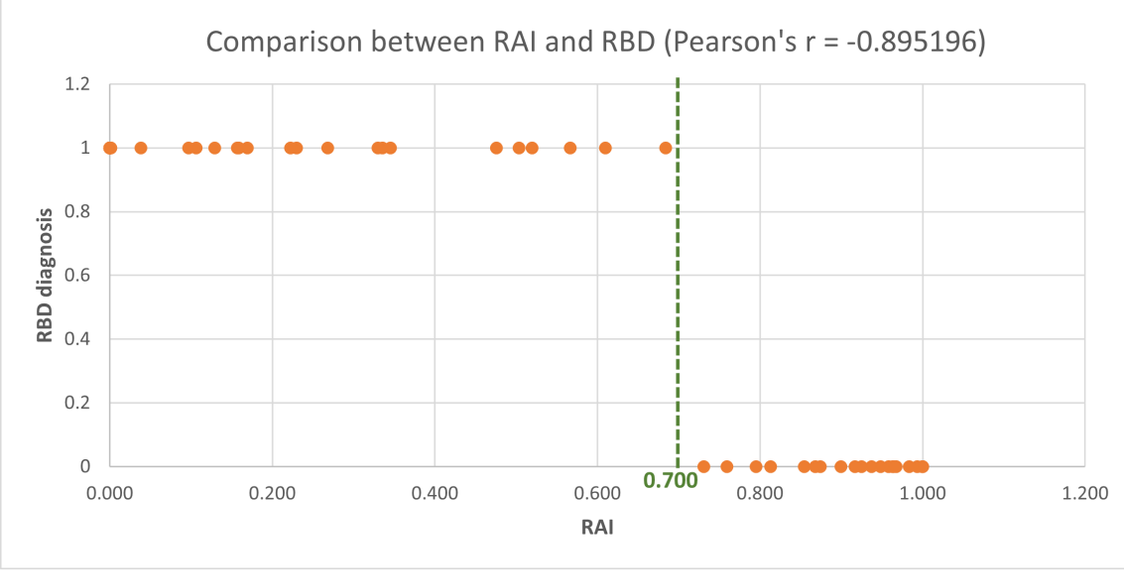

Figure 4.1: Comparison between REM Atonia Index and REM Behavior Disorder diagnosis in PD patients.

4.1.2 REM Atonia Index & Dissociation Index

The results gained in this study show a higher negative correlation between the RAI and the DI in Parkinson's disease patients: it implies an inverse relationship between these two variables.
Specifically, it is indicated that as the Dissociation Index approaches 0, the RAI tends to gravitate toward 1, and conversely, when the Dissociation Index is high, the RAI tends to decrease. This means that individuals with lower Dissociation Index exhibit a higher Atonia Index. Recalling the meaning of DI, it represents the extent to which a patient deviates from the physiological condition during the REM phase of sleep.
As shown in the scatter plot the findings of this study reveal a Pearson correlation coefficient of -0.999879: this results close to -1 underscores the robust association between RAI and DI. A lower DI value signifies a closer adherence to the normal physiological state, where muscular atonia during REM sleep is expected. In such cases, the RAI tends to be higher, indicating minimal disturbances in muscular atonia during sleep.

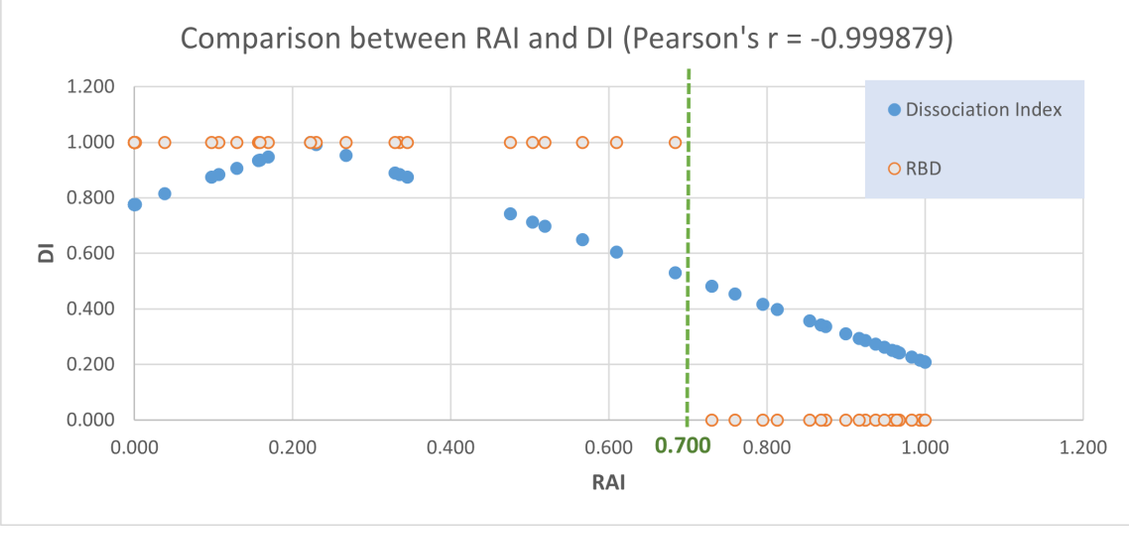

Figure 4.2: Comparison between REM Atonia Index and Dissociation Index, merging RBD (1) and noRBD (0) in PD patients.

4.1.3 Dissociation Index & RBD

This paragraph outlines the findings about the relationship between the Dissociation Index and the presence of REM Sleep Behavior Disorder in Parkinson's Disease patients.
The resulting DI scores provide insight into the degree of deviation of each subject atonia index from the reference value, normalized within the range 0-1. RBD, on the other hand, is a binary feature that takes on the value of 1 if a subject exhibits REM Sleep Behavior Disorder and 0 if they do not.
Notably, we found a strong positive correlation between DI and RBD, with a Pearson correlation coefficient of r = 0.929099. This results underscores the potential clinical significance of DI in assessing the presence or absence of RBD in PD patients, as demonstrated in the following scatter plot [Figure 4.3]. A highlighted band is prominently displayed, marking the threshold on the DI the range of transition from RBD = 0 (indicating the absence of REM Sleep Behavior Disorder) to RBD = 1 (indicating the presence of REM Sleep Behavior Disorder). This distinctive band on the plot acts as a visual indicator, clearly illustrating the boundary where the DI values cross over, thereby aiding in the classification of individuals.

4.2 Assessment of SVM Classification: RBD and non-RBD in PD patients

This section deals with the outcomes of a binary classification algorithm applied to Parkinson's Disease (PD) patients, specifically focusing on the classification between Rapid Eye Movement Behavior Disorder and non-RBD cases. The Support Vector Machine model has been employed: it incorporates a feature set comprising various spectral features listed on Table 3.4.
The classification results were evaluated using a confusion matrix to assess the model performance. Results indicated that the binary SVM classifier achieved high accuracy in distinguishing between RBD and noRBD subjects, making it a promising tool for automated diagnosis and classification in sleep medicine.
The confusion chart, shown in Figure 4.4 provides a comprehensive visualization of the classifier performance in the binary classification task between

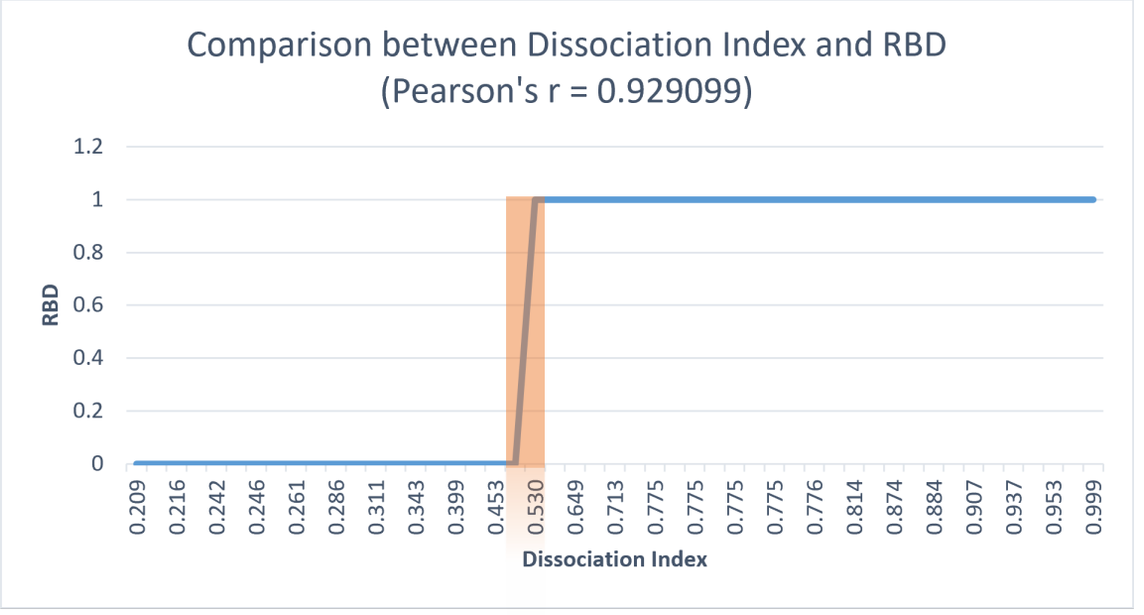

Figure 4.3: Comparison between Dissociation Index and RBD.

'RBD' and 'noRBD' PD patients. It consists of the following key components:

- Confusion Matrix: the central portion of the chart displays the raw counts of true positives, true negatives, false positives, and false negatives. Specifically, there are 28 instances correctly classified as 'RBD' (True Positives), 18 instances correctly classified as 'noRBD' (True Negatives), 1 instance incorrectly classified as 'noRBD' (False Negatives), and 2 instances incorrectly classified as 'RBD' (False Positives).
- Percentages on the right: on the right side of the confusion chart, two columns of percentages are presented. The percentages in the left column represent the precision (Positive Predictive Value) for each class.
- Percentages under the confusion matrix: below the confusion matrix, two rows of percentages are displayed. The percentages in the top row show the recall (True Positive Rate) for each true class.

The high percentages in precision and recall underscore the classifier strong

performance in distinguishing between the two classes.

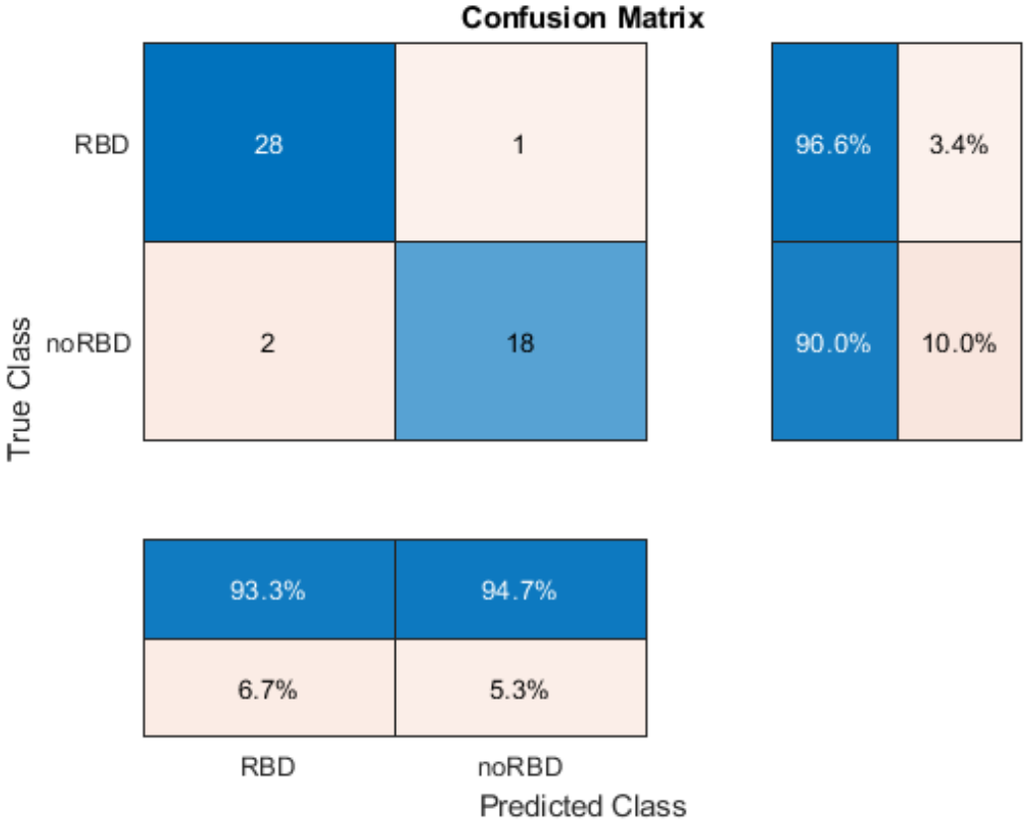

Figure 4.4: Confusion chart for the visualization of the classifier's performance.

To assess the classifier predictions, the Continuous Indicator (CI) has been calculated: it serves as a measure of the model confidence in its classifications. This parameter was derived from the SVM model decision function values, providing a numerical representation of the likelihood of a sample belonging to a specific class.
CI played a crucial role in our analysis, allowing us to make informed decisions based on the SVM classifier outputs and contributing to a more comprehensive evaluation of its performance.
The correlation matrix between the Continuous Indicator and the clinical features analyzed in this study, is shown in Figure 4.5.
In the following paragraphs the main results, regarding the key correlations with the Continuous Indicator, are in-depth detailed.

	Continuous Index
RAI	-0.676134
Dissociation Index	0.685527
Duree Diagn	-0.029176
HY	0.167414
UPDRS-II	0.209121
UPDRS-III	0.175686
UPDRS-IV	0.088039
UPDRS TOT	0.015535
LED	-0.026829
RBD	0.776753

Figure 4.5: Correlation matrix between CI and the clinical features analyzed in PD patients.

4.2.1 REM Atonia Index & Continuous Indicator

The correlation analysis between the RAI and the CI has been conducted: its result revealed a substantial correlation of nearly 70% (r = -0,676134) between these two variables, indicative of a strong and statistically significant relationship.
This is a key result of utmost significance in this study: it is observed that individuals with a positive Continuous Indicator (from 0 to 1) consistently exhibited RAI values below the threshold of 0.7, implying a higher likelihood of experiencing RBD symptoms. Conversely, among those with a negative Continuous Indicator (from 0 to -1) the majority displayed 'RAI' scores exceeding 0.7, describing a healthy condition (absence of RBD). It is worth noting that within the latter group [Figure 4.6] a few outliers were observed. These outliers may be attributed to noise and/or reduced REM duration during the PSG recording.
Beneath the horizontal line depicted on the plot, a distinct separation is evident: above this line, positive CI values are prominently associated with the RBD presence, while below the line, negative CI values are notably aligned with the RBD absence.
Based on these findings, it appears that the machine learning algorithm demonstrates enhanced classification capabilities between the two distinct

groups: PD patients with RBD and PD patients without RBD. This performance becomes particularly evident in this case where neurodegeneration has advanced significantly. The subsequent section provides a comparative analysis between these results and the study *Assessing REM Sleep Behaviour Disorder: From Machine Learning Classification to the Definition of a Continuous Dissociation Index*, where the same algorithm was applied to patients in the early stages of Parkinson's Disease neurodegenerative pathology.

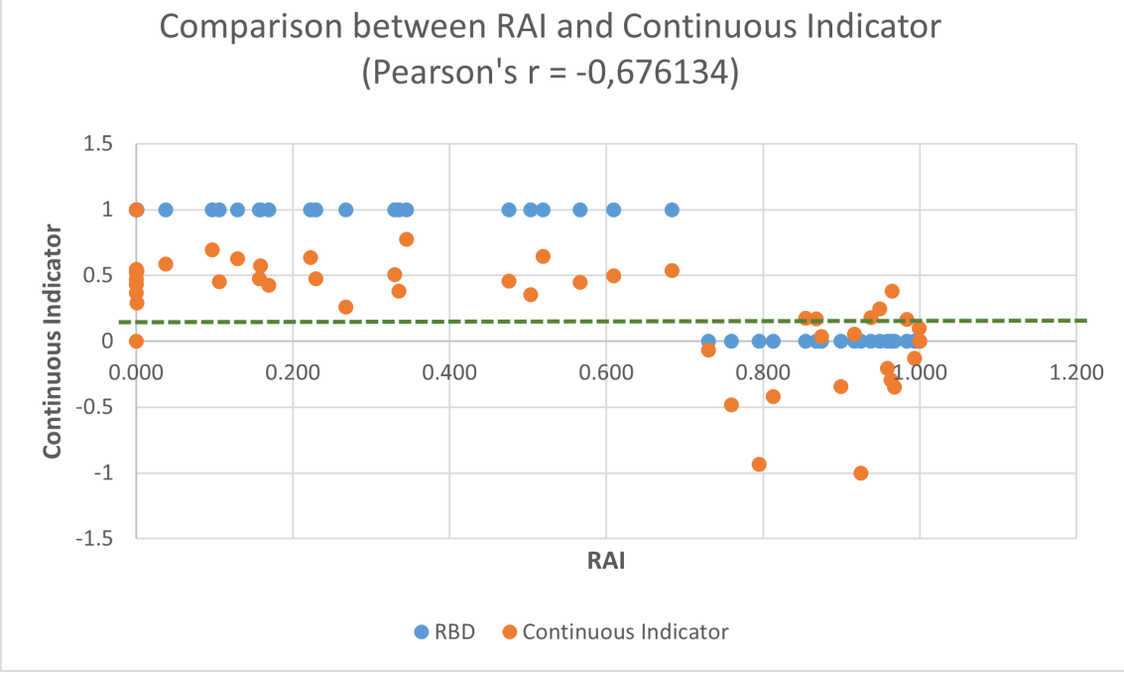

Figure 4.6: Comparison between REM Atonia Index and Continuous Indicator in PD patients

4.2.2 Dissociation Index & Continuous Indicator

At the heart of this research study lies the pivotal discovery: a robust correlation between DI and the Continuous Indicator expressed by the Pearson's coefficient r = 0,685527.
In comparison to the study conducted by Irene Rechichi et Al. [11], this research work represents a complementary approach. In the early cited work a SVM classification algorithm has been employed to differentiate between healthy subjects, in terms of individuals without Parkinson's Disease

and without REM Behavior Disorder, and subjects with primary RBD, some of whom subsequently developed PD. Therefore, that analysis focused on subjects in an early stage of the neurodegeneration, as these patients first developed RBD and eventually later Parkinson's. The results of that classification are shown in Figure 4.7 yielding good values such as accuracy at 82.61%, sensitivity at 86.67%, specificity at 75%, positive predictive value (PPV) at 86.67%. My research study examined all Parkinson's Disease

	Accuracy	**Sensitivity**	**Specificity**	**PPV**	**FDR**
K-NN	86.96%	93.33%	75%	87.50%	12.50%
SVM	82.61%	86.67%	75%	86.67%	13.33%

Figure 4.7: Cross–validation performance of the two classifiers applied in the study of comparison in [11]

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patients in a more advanced stage of the degeneration, including some with RBD and others without. This allowed for higher classification results using the same algorithm and features, both in-depth analysis in prior chapters. The classification accuracy was found to be 93.88%, also the other metrics shows higher values [Table 4.2].
Recall and *sensitivity* are similar as both evaluate a model ability to correctly identify positive instances within a dataset. They are used interchangeably in most contexts, as they share the same definition and mathematical formula. Similarly, *PPV* (Positive Predictive Value) and *precision* assess the accuracy of positive predictions made by a model. They are conceptually identical and can be used interchangeably.

	RAI	DI	Duree Diagn	HY	UPDRS-II	UPDRS-III	UPDRS-IV	UPDRS TOT	LED	RBD
RAI	1	-0.999879	-0.239813	-0.358490	-0.200824	-0.104055	-0.111819	-0.090207	-0.029175	-0.895196
DI	-0.999879	1	0.236436	0.360532	0.201145	0.108886	0.110809	0.093924	0.029006	0.894970
Duree Diagn	-0.239813	0.236436	1	0.438411	-0.030115	0.040124	0.174081	0.223705	0.384336	0.183977
HY	-0.358490	0.360532	0.438411	1	0.097491	0.479818	0.498616	0.564780	0.244335	0.346342
UPDRS-II	-0.200824	0.201145	-0.030115	0.097491	1	-0.117305	0.685588	-0.299105	-0.344205	0.191105
UPDRS-III	-0.104055	0.108886	0.040124	0.479818	-0.117305	1	0.193022	0.923937	0.208032	0.103208
UPDRS-IV	-0.111819	0.110809	0.174081	0.498616	0.685588	0.193022	1	0.142193	-0.030300	0.084304
UPDRS TOT	-0.090207	0.093924	0.223705	0.564780	-0.299105	0.923937	0.142193	1	0.384601	0.033426
LED	-0.029175	0.029006	0.384336	0.244335	-0.344205	0.208032	-0.030300	0.384601	1	-0.014524
RBD	-0.895196	0.894970	0.183977	0.346342	0.191105	0.103208	0.084304	0.033426	-0.014524	1

Table 4.1: Correlations among key features in Parkinson's Disease patients.

	Accuracy	Sensitivity	Specificity	PPV	F1-Score
SVM	93.88%	90.00%	96.55%	94.74%	92.31%

Table 4.2: SVM classification performance in distinguing between RBD and no RBD Parkinson's Disease individuals.

It is evident that neurodegeneration impacts classification: the algorithm yields better results in distinguishing between subjects with RBD and those without RBD when neurodegeneration (Parkinson's Disease) is in a more advanced stage. This suggests that, in this advanced clinical phase, the algorithm detects significant differences between Parkinson's patients with RBD and those without RBD.
The plot in Figure 4.8 illustrates the relationship between the Dissociation Index and a Continuous Indicator: it is observed that when the CI exhibited positive values (area above the reference line at 0), there is a clear dissociation from the physiological condition (DI $>$ 0.47), which is indicative of the presence of RBD. Conversely, when the Continuous Indicator displayed negative values (area below the 0 line), it was predominantly linked to patients with a DI below 0.47, characterizing individuals without RBD. Notably, there were a few outliers pointed out in the light red area of the plot, where the continuous indicator exhibited positive values (even if in proximity to the 0 reference line). These outliers were associated with subjects who did not have RBD but displayed some atypical characteristics in their CI values. It is crucial to underscore that these exceptions hold paramount importance for forthcoming clinical studies.
These results raise important questions for healthcare practitioners, as they suggest that classification is more successful in populations in advanced disease stages, where differences between Parkinson's patients with or without RBD are more pronounced.
It is crucial to consider that, from a clinical perspective, the motor and cognitive symptoms of Parkinson's patients with RBD and without RBD can be similar, underscoring the need for objective identification of these differences through machine learning techniques.
To give an overview, the results indicate that the classification algorithm, used both in my study and [11] exhibits excellent performance and high accuracy. However, the last one described ability to discriminate the presence of RBD in populations in advanced stages of neurodegeneration is more

challenging. This difference is significant, emphasizing the importance of thorough objective differentiation between patient groups and highlighting the crucial role of machine learning techniques in this clinical context.

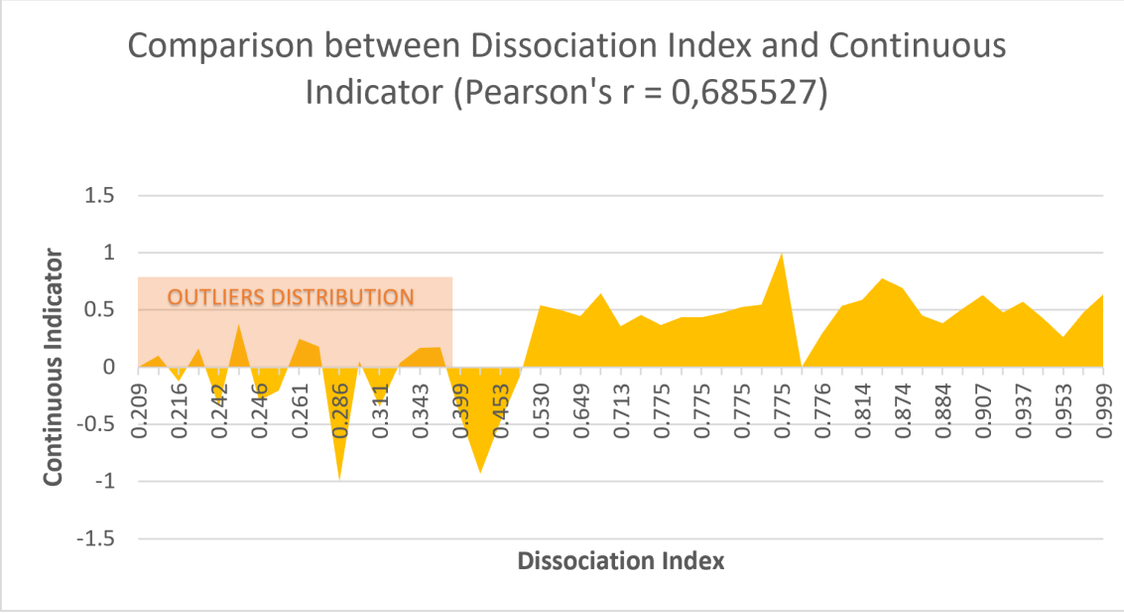

Figure 4.8: Relationship between Dissociation Index and Continuous Indicator, highlighting distinct areas in RBD analysis.

4.2.3 Continuous Indicator & RBD

In this study, the correlation between the variable Continuous Indicator and the presence of REM sleep Behavior Disorder in PD patients has been explored. The results revealed a strong and interpretable relationship between these two variables, as shown in the scatter plot in Figure 4.9.
The yellow-marked areas on the graph highlight that all patients with a positive Continuous Indicator were found to have RBD symptoms, indicating a consistent presence of RBD in this subgroup. Conversely, among the PD patients with negative CI values, a significant number exhibited healthy condition (referring to RBD pathology). This observation underscores the utility of the machine learning classification algorithm as a potential predictive technique for objectively distinguishing between PD patients with and without RBD in their diagnosis.

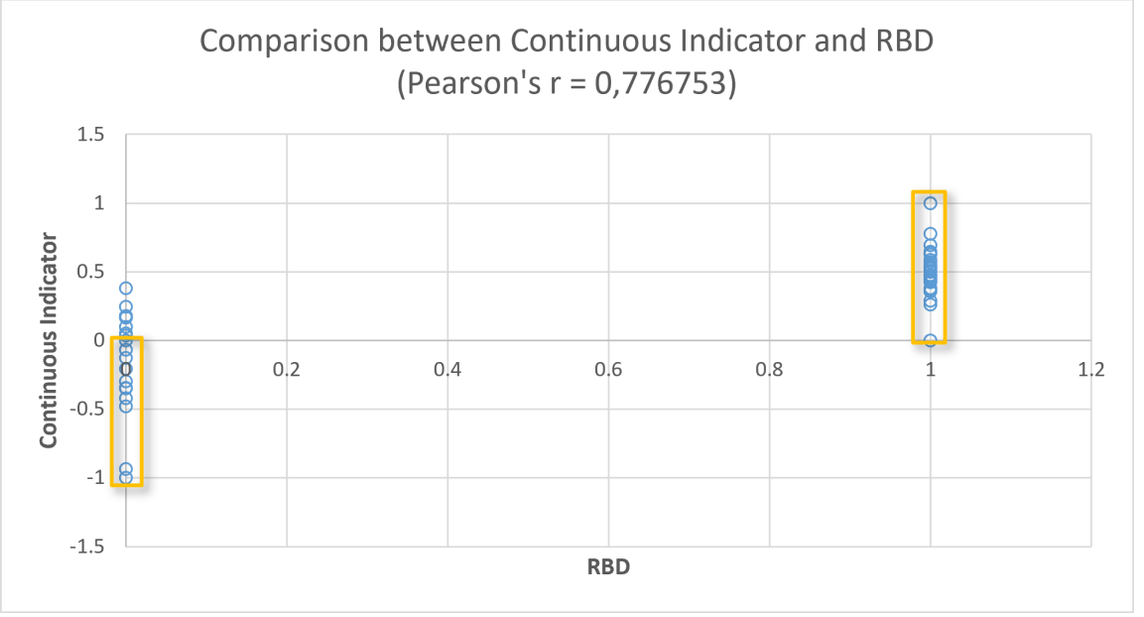

Figure 4.9: Relationship between Continuous Indicator and REM Behavior Disorder presence in PD patients.

4.3 Correlations in Narcoleptic Children

This section deals with the correlation analysis conducted among a set of clinical features in narcoleptic children, including the REM Atonia Index. The dataset encompassed essential parameters, including the Ullanlinna Scale, High Potential for Incidence, Cataplexy, Cauchemars (Nightmares), Paralysie du Sommeil (Sleep Paralysis) and Hallucinations.
The Pearson's correlation coefficients are shown in Table 4.3.
These correlations provide insights into the relationships between the REM Atonia Index and various clinical parameters related to narcolepsy in children. RAI and UNS have a positive but weak correlation of 0.1107: this suggests a weak association between the REM Atonia Index and the Ullanlinna Narcolepsy Scale scores, possibly indicating that as RAI increases (indicating less pathology), the UNS scores tend to increase as well.
RAI and HPI exhibit a positive but weak correlation of 0.0795. This suggests a slight connection between the REM Atonia Index and the High-Probability Interval, indicating that higher RAI values may correspond to slightly higher HPI values.

RAI and Cataplexy show a very weak negative correlation of -0.0561.
RAI and Cauchemars (nightmares) exhibit a weak negative correlation of -0.1769. This mild inverse association indicates that higher RAI values (less pathology) may be associated with a lower frequency or severity of nightmares.
RAI and Paralysies have a very weak positive correlation of 0.0303. This indicates a minimal connection, suggesting that RAI values do not correlate with the occurrence of sleep paralysis.
RAI and Hallucinations demonstrate a mild negative correlation of -0.3384. This suggests a noticeable inverse relationship, indicating that higher RAI values (indicating less pathology) may be associated with a lower occurrence or severity of hallucinations in narcoleptic children.

4.3.1 Dissociation Index in Narcolepsy

The Pearson's correlations between DI and the clinical parameters in narcoleptic children are detailed described, referring to the Figure 4.10.
DI and RAI show a very strong negative correlation of r = -0.9480 [Figure 4.11]. This correlation is notable, but it must be interpreted with caution. The Dissociation Index was created and calculated using a reference value based on healthy adult subjects, aged between 27 and 63 years.
Since the sleep architecture of children aged between 5.7 and 16.8 years is known to differ significantly from that of adults, the strong negative correlation between DI and RAI may not directly apply to narcoleptic children. It suggests that as RAI increases, DI tends to decrease significantly. However, the applicability of this correlation to the pediatric narcoleptic population may be limited due to age-related differences in sleep patterns.
DI and both UNS and HPI exhibit a very weak negative correlation.
DI and Cataplexy display a weak positive correlation of 0.1243. This suggests a mild positive association, indicating that higher DI values may be associated with a slightly higher frequency or severity of cataplexy.
DI and Cauchemars exhibit a weak positive correlation of 0.1200. There could be a mild positive association, indicating that higher DI values may be associated with a slightly higher frequency or severity of nightmares.
DI and Paralysies have a very weak positive correlation of r = 0.0138.
DI and Hallucinations show a moderate positive correlation of 0.3554. This suggests a noticeable positive association, indicating that higher DI values may be associated with a higher occurrence or severity of hallucinations in narcoleptic children.

	Dissociation Score
RAI	-0.948007
UNS	-0.067160
HPI	-0.065135
Cataplexie	0.124262
Cauchemars	0.119959
Paralysies	0.013792
Hallucinations	0.355435

Figure 4.10: Pearson's correlation coefficients between Dissociation Index and clinical parameters in narcoleptic children.

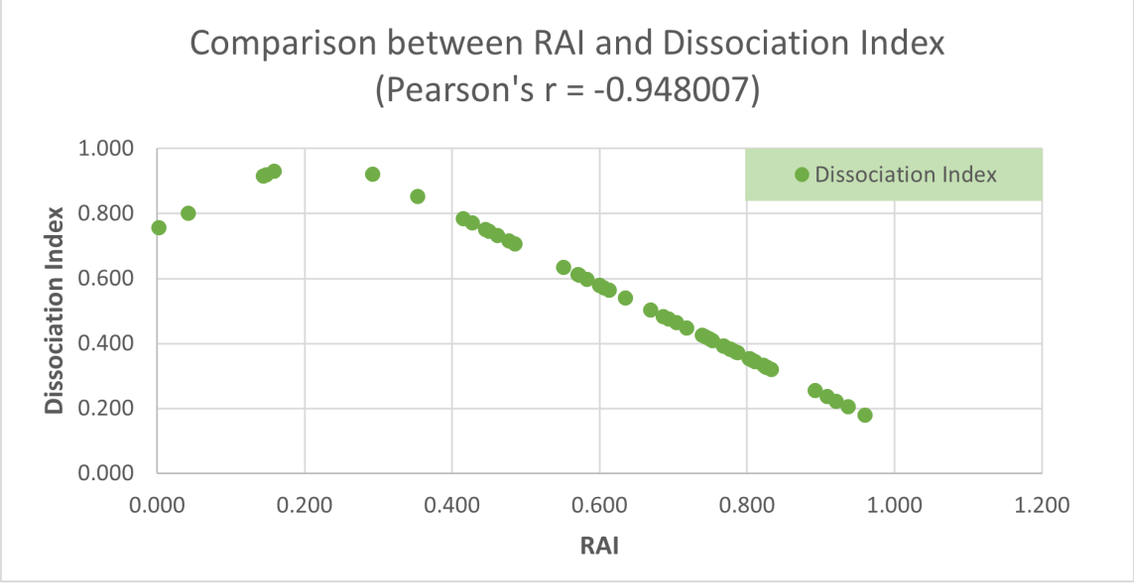

Figure 4.11: Comparison between RAI and DI in narcoleptic children.

	RAI	**UNS**	**HPI**	**Cataplexy**	**Cauchemars**	**Paralysies**	**Hallucinations**
RAI	1.000000	0.110718	0.079451	-0.056139	-0.176942	0.030277	-0.338408
UNS	0.110718	1.000000	-0.113023	0.265300	0.034561	0.003445	0.077484
HPI	0.079451	-0.113023	1.000000	0.041092	-0.086711	-0.141844	-0.316945
Cataplexy	-0.056139	0.265300	0.041092	1.000000	0.247457	0.179092	0.227648
Cauchemars	-0.176942	0.034561	-0.086711	0.247457	1.000000	0.298556	0.349315
Paralysies	0.030277	0.003445	-0.141844	0.179092	0.298556	1.000000	0.485768
Hallucinations	-0.338408	0.077484	-0.316945	0.227648	0.349315	0.485768	1.000000

Table 4.3: Pearson's coefficient expressing the correlations between the main clinical parameters of narcolepsy pathology

Part V

Conclusion

Chapter 5

Conclusion and Future Works

5.1 Conclusions - Parkinson's Disease study

This work serves to demonstrate the importance of Machine Learning techniques in objectively identifying differences between Parkinson's Disease patients with and without REM Behavior Disorder. Given the similarity in motor and cognitive symptoms between these two groups, the results underscore the need for accurate and objective differentiation.
This research embarked on the validation of the Dissociation Index for the diagnosis of RBD within PD individuals, also exploring correlations among relevant clinical parameters.
The objective of this research was successfully achieved by applying the Support Vector Machine classification algorithm. Leveraging a feature set comprising various spectral features, the SVM model achieved high accuracy, making it a promising tool for automated diagnosis and classification in sleep medicine.

5.1.1 Key findings and interpreting results

One of the most significant findings of our study was the robust correlation between the Dissociation Index and the Continuous Indicator: it underscores the potential of our methodology in objectively identifying patients with REM Behavior Disorder, a crucial aspect for healthcare practitioners. About this correlation, is essential to underscore the significance of exceptional data points displaying atypical patterns on the continuous indicator: their unique characteristics hold paramount importance for future clinical investigations. Despite these valuable insights, our study acknowledges the limitations posed by the heterogeneity within the PD patient population. Variability in disease progression and diagnosis duration could account for the observed modest associations between these parameters.

5.1.2 Future Directions

To enhance the comprehensiveness of this analysis, a prospective clinical study employing a longitudinal approach is proposed. It consists in categorizing PD patients into distinct groups based on the duration of their PD diagnosis. For instance, one group could encompass individuals diagnosed within the past 5 years, another could involve those diagnosed between 5 and 10 years ago and a third group might comprise patients with a diagnosis exceeding 10 years.In so doing, the study would inherently account for the temporal evolution of PD within each subgroup (RBD and non-RBD). This will allow researchers and engineers to explore these dynamics in greater depth and offer more accurate assessments.
Another advantage of such a longitudinal design lies in its potential to enable the identification of critical time points and thresholds at which certain clinical features become more pronounced.
To conclude, this study presents valuable insights into the correlations among clinical parameters in PD patients and offers a promising approach for the diagnosis of RBD within this population.
As further refinement of methodologies and the conduct of longitudinal studies take place, this work is expected to make a significant contribution to the field of Parkinson's Disease research and sleep medicine.

5.2 Conclusions - Narcolepsy study

In this study, also a comprehensive correlation analysis was conducted among a set of clinical features in narcoleptic children, with a particular focus on the REM Atonia Index.
It is important to note that while some of these correlations are weak, they provide valuable information about potential associations and trends in the data. However, it is essential to interpret cautiously the findings about the Dissociation Index, in the field of narcolepsy. The age-related differences in sleep patterns between children and adults must be taken into consideration. To enhance the understanding of narcolepsy in children, future research may focus on refining the DI and its applicability to the pediatric narcoleptic population. Additionally, deeper exploration of the correlations between DI and clinical parameters like Cataplexy, Cauchemars, Paralysies, and Hallucinations could provide valuable insights into the diagnostic and therapeutic aspects of narcolepsy in children.

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