4

Assessment of Motor Symptoms

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4.1 Introduction

This chapter describes the methodology developed and used to obtain the elements of the REMPARK system devoted to monitor the related PD motor symptoms, according to the specifications discussed in the previous chapter. The monitoring part basically consists in the waist-worn device and its embedded algorithms for the analysis of the PD patients' movement and gait.

The development of such a device to assess motor symptoms has been divided into several steps that are summarised below:

- First, different questionnaires were administered to professionals and cargiveers to identify some system requirements and the most important symptoms to be monitored. This step has been already partially presented and used for the purpose of Chapter 3. The present chapter describes the details of these questionnaires and the obtained results.
- A methodology was developed to detect these symptoms, which is based on inertial sensors and machine learning techniques. This methodology is presented in Section 4.3.
- A database of signals was collected in order to develop automatic detection methods based on the mentioned methodology. The design of the experiment to collect such data and a summary of the data obtained are also detailed in Section 4.3.

- The algorithmic approach to exploit the database of signals based on machine learning techniques is presented in Section 4.4. Each symptom and parameter detected by an algorithm is described in a different subsection.
- Finally, some conclusions are drawn.

4.2 Decision on the Most Relevant Symptoms to Be Detected and Assessed

During REMPARK project, specific tasks were devoted both to the collection of clinical information and to understand aspects that may be relevant for the REMPARK system. These tasks were carried out during the first months of the project through the administration of two questionnaires addressed to patients and related professionals [1]. Their results were included in the system design to set the technical specification of the system (partially discussed in Chapter 3).

The most relevant issues addressed in the questionnaires administered to professionals are summarised below:

- First, on the salient clinical features of PD in the different stages of the disease. Here, for instance, professionals were requested to indicate the symptoms with higher priority for treatment, to report which monitored symptoms may have a greater impact on daily living, and which are the most frequent symptoms according to a mild, moderate or severe PD.
- Second, information was collected on how the professional expects to be helped by REMPARK system in the therapeutic management of the individuals with PD. "*At which PD stages do you think REMPARK may be useful?*", "*For the improvement of which symptoms do you think REMPARK may be useful?*", are examples of the related questions made to the professionals to acquire valuable information at this level of analysis.
- The third issue addressed consisted on how data had to be organised for an optimal use and updating of the PD treatment in the disease course. At this level professionals were required to express their opinion on the usability of REMPARK in PD patients as a function of symptoms severity.

Furthermore, the interviews helped the consortium to understand the perspective, the expectations and the general attitude of the care service (i.e., clinical professional) against the REMPARK approach. At this regard, emphasis was paid in capturing different perspectives. For this reason, the questionnaires were administered to different kind of professionals belonging to the medical (i.e., neurologists, geriatricians) and technical rehabilitative (i.e., physiotherapist, occupational therapist) areas.

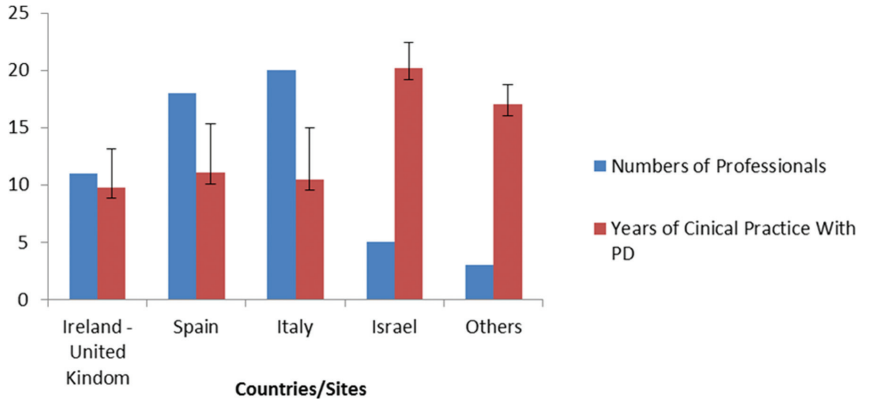

Figure 4.1 Illustration of the number of professional who filled the questionnaire divided according to their country of origin. Years of clinical practice in PD area are also reported in the average, also in this case individually for each country. Vertical bars represent the standard deviation.

4.2.1 Subjects

Some characteristics of the 57 professionals recruited for the administration of the questionnaires are reported in Figure 4.1. The average number of years of clinical expertise with PD patients was 13.7 (SD=4.6). Most of the clinicians were employed in Public Health Service (n=36) while 18 of them were employed in private or "intermediate" health care system.

Across the different countries/sites, it must be noted that the three kinds of professional who took part in the study were neurologists, geriatricians and physiotherapists. The majority of participating professionals were neurologists (n=23), followed by physiotherapists (n=22) and, then, by geriatricians (n=10).

4.2.2 Questionnaire

The characteristics of the questionnaire including the formulation of the items and methodology for answering questions were developed through a continuous consultation between the four medical partners participating in REMPARK: Centro Medico Teknon (Spain), Fondazione Santa Lucia (Italy), Maccabi Healthcare Services (Israel) and the National University of Ireland at Galway (Ireland).

The questionnaire is composed of three main sections.

- An initial social-demographic section in which the participant is required to provide personal information regarding, for instance, own specialty, the country of origin and the years of clinical experience with PD patients.

- A second central section that addresses clinical issues related to PD. This is the section in which participants indicate the clinical relevance of PD symptoms according to the three disease stages (i.e., mild, moderate and advanced). Questions such as the following ones were posed:
  - *What do you consider are the three most characteristic motor symptoms of this phase?*
  - *What do you consider are the 3 motor symptoms that interfere the most, with the quality of life of people with Parkinson's at this stage of the disease?*
  - *What do you consider are the three priorities to treat symptoms at this stage of the disease?*

The professional was asked to answer by ticking a square box in a mixed multiple alternative forced choice paradigm. In fact, for most questions, if the professional feels that the right answer does not fit with the proposed alternatives he can tick the square box corresponding to "other" and, then, is allowed to better specify his response.

- The third and final section of the questionnaire aimed at investigating the potential utility of REMPARK system for the clinical management of PD, as it is perceived by professionals. Questions like the following ones were proposed here:
  - *Do you consider that a system such as REMPARK would be useful to improve motor problems of your people with Parkinson's?*
  - *In your clinical practice, do you consider that a system such as REMPARK would be a useful system for monitoring motor problems of your people with Parkinson's?*

In the case of the professional expressing a positive judgment about REMPARK utility by ticking the "yes" box, he is required to indicate both the PD stage for which REMPARK could be better applicable (i.e., mild, moderate or advanced stages) and which PD symptoms would benefit from REMPARK utilisation. Also for these questions the professional has to respond by ticking a square box in a mixed multiple alternative forced choice paradigm.

4.2.3 Results

4.2.3.1 Analysis of the correlation between responses on clinical questions

A first item analysis was performed to investigate the coherence of the professionals' response relating the clinical answers. More specifically, the

participant is required to evaluate the clinical relevance of a PD symptom by indicating:

- The three most characteristic motor symptoms of PD.
- The three motor symptoms that interfere more with the quality of life of people with PD.
- The three symptoms that have priority for treatment.

All three questions were individually addressed for mild, moderate and advanced PD stage. The three questions are apparently related since it can be reasonably posited that the most characteristic symptoms of PD have a great probability to be those symptoms that interfere with quality of life and, furthermore, those for which a treatment is imperative. Therefore, from the statistical point of view, the existence of a significant correlation between the responses on these items could be a parameter to verify the reliability of responses themselves.

In order to examine the correlation between the professionals' responses on the above three items/questions, Pearson' r statistic was performed. For the purpose of these analyses, in order to quantify the relative weight of each symptom, the responses were classified according to a Likert-type scale ranging from 0 to 3, resulting in most of the correlations analysed being significant. In these cases, the r value ranged from 0.27 to 0.72 being $>$ 0.40 in about 67% of all cases. The significance of the correlation was only approached in one case relating to the analysis that involved the "Difficulty in Turning" symptom (i.e., the correlation between the score attributed to "most characteristic symptoms" and to the "priority for treatment items").

Therefore, the correlation analyses, by confirming the existence of a significant relationship between the professionals' response, indicate a global coherence of the responses themselves.

4.2.3.2 Investigation of the clinical relevance of the motor symptoms in the three PD phases (i.e., mild, moderate and advanced)

The clinical relevance of the PD symptoms as reported by professionals was investigated by means of descriptive analyses firstly without taking into consideration the particular country/site where the data were collected and, then, in a second step, individually for each country/site. This was made in order to have both a general view on data and to evidence possible differences as a function of the country/site the professional belongs to.

For the purpose of these analyses, a unique score was computed by collapsing the score attributed to each individual item in the three clinical questions mentioned in the previous sub-section:

An index of clinical relevance for each symptom was, thus, computed by averaging the score attributed by professionals to that symptom in the three questions. For instance, the index of clinical relevance for "small steps" was represented by averaging the scores attributed to it in questions *1*), *2*) and *3)*. Also in this case, for the purpose of these analyses, in order to quantify the relative weight of each symptom a score of 3 was attributed to the symptoms the professional indicated as first, a score of 2 was attributed to a symptom indicated as second, a score of 1 was given to the symptom indicated as third and, finally, a score of 0 was attributed to the symptoms not included in the first three symptoms list.

As showed in Figure 4.2, independently from the countries/sites where data were collected, the analysis of the index of clinical relevance computed for PD motor symptoms evidence some differences according to the PD stage considered.

In fact, in the mild stage (represented by blue columns in the figure), "reduced walking speed", "small steps", "difficulty in turning" and "shuffle" were the four symptoms with the higher index of clinical relevance with and index value of 1.74, 1.24, 0.68 and 0.66, respectively.

In the moderate stage (represented by red columns in the figure), the most clinically relevant symptoms were "freezing of gait", "difficulty in turning",

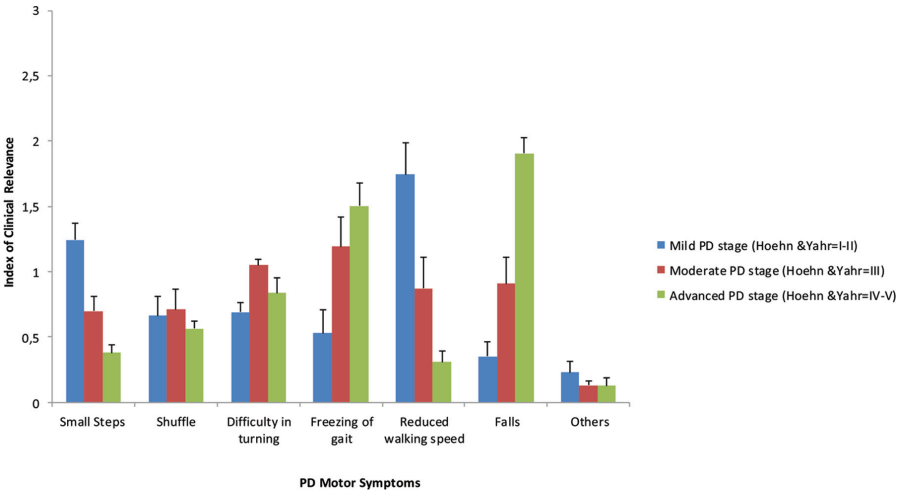

Figure 4.2 Indices of clinical relevance for each PD motor symptoms examined referred to the mild (blue columns), moderate (red columns) and advanced (green columns) PD stages. Vertical bars represent standard errors.

"falls" and "reduced walking speed" with an index value of 1.19, 1.05, 0.91 and 0.87, respectively.

Finally, as for the advanced stage (represented by green columns in the figure), the symptoms with a higher index of clinical relevance were "falls", "freezing of gait", "difficulty in turning" and "shuffle" with an index value of 1.91, 1.50, 0.84 and 0.56, respectively.

According to the majority of professionals, patients with PD adopt some specific strategies to improve gait difficulties particularly in the moderate-advanced stages of the disease. More specifically, more than 80% (n=48) and about 91% (n=52) of professionals indicates that PD patients use strategies to improve gait in the moderate and advanced phases, respectively, compared to the 33% who report this behaviour in the mild stages of the disease. *The strategies more frequently adopted by patients in the moderate-advance disease stages would be stick use, verbal cueing, attention focus on walking and steps counting*. These strategies have been indicated by about 79% (n=38) of professionals for the moderate stage and by the 80% (n=42) of them for the advanced stage.

However, according to professionals, the most useful strategies to be adopted in the moderate-advanced PD would be the use of verbal cueing for about 32% (n=18), steps counting for about 16% (n=9) and stick use for about 14% (n=8) of them. As for the advanced stage, also in this case the majority of professionals indicated verbal cueing as the most useful strategy to be adopted (about 26% of responses; n=15) followed by stick (about 23% of responses; n=13) and metronome (about 12% of responses; n=7) use.

4.2.3.3 Analysis of REMPARK utility for PD patients

A large majority of professionals considered REMPARK potentially useful for PD management. More specifically, about 96% of professionals (n=55) judged REMPARK a useful system for symptoms improvement and 93% (n=53) considered REMPARK potentially useful for symptoms monitoring. The REMPARK utility for both symptoms improvement and monitoring, was perceived by professionals for the intervention in the moderate stages (49% and 40% of responses, respectively) and at a lesser extent in the mild (about 21% and 23% of responses, respectively) and advanced (about 9% and 19% of responses) stages. However, the presence of missing data (n=13) related to the lack of responses on the specification of the PD phase for which the application of REMPARK system would be more useful, reduces the reliability of these findings.

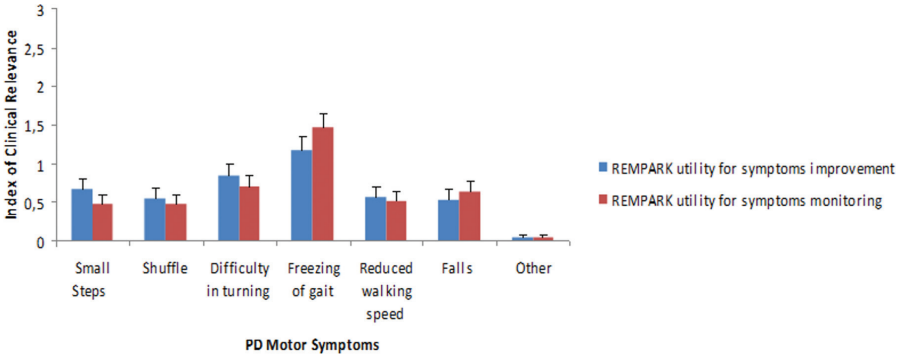

Figure 4.3 Subjective judgment expressed by professionals about the utility of REMPARK system for both improvement and monitoring of motor symptoms. Vertical bars represent standard errors.

In order to quantify the professionals' judgements about which symptoms REMPARK system would be more useful, in terms of both improvement and monitoring, the professionals' responses were classified on a Likert-type scale ranging from 0 to 3, where 0 represents the minimum value assigned to the effect of REMPARK system on a specified symptom and, conversely, 3 indicates the highest value.

As Figure 4.3 illustrates, a substantial coherence is noted about the symptoms that would better benefit from the application of the REMPARK system in terms of symptoms improvement and monitoring. Indeed, according to professionals' opinions, the symptoms on which the REMPARK system would have a greater positive impact would be "freezing of gait" and "reduced walking speed".

4.2.4 Discussion and Conclusive Remarks

A first critical issue the questionnaires are focussed on is the understanding of the salient clinical features of PD in the different stages of the disease. The answers should also give valuable information about clinicians' expectations on the REMPARK utility and usability in the clinical management of PD.

A first preliminary comment has to be devoted to the reliability of the professional's answers. Regarding this aspect, some indicators such as the absence of missing data on content questions as well as a substantial coherence of responses on clinical questions suggests that the questionnaires have been filled correctly and congruently.

The descriptive and inferential statistics applied to data allowed us to evidence some main points of interest.

- First, as expected, different symptoms achieve a clinical relevance and require a therapeutic intervention as a function of different PD phase considered and, thus, in particular in the mild stage of PD "**reduced walking speed**" and "**small steps**", were the most clinically relevant symptoms whereas in the moderate stages "**freezing of gait**" and "**difficulty in turning**" appear to be more important clinical signs. Moreover, in the advanced stages, "**falls**" arises as a new main clinical occurrence. As mentioned above, this finding is expected on the basis of the neurological characteristics of PD [2]. Indeed, PD is a neurodegenerative disease that progressively affects different motor and non-motor brain circuitries with a related modification of both the qualitative and quantitative (i.e., severity) clinical features of the disease [3–5]. An interesting aspect to be remarked is that according to professionals, PD patients use strategies to improve symptoms mainly in the moderate-advanced stages, rather than in the mild ones. This finding is obviously expected on the basis of the greater impact that symptoms severity progressively exerts on daily living. However, according to professionals, ***the strategies that PD patients seem to adopt for improving their gait difficulties do not appear to be the most useful***. In particular, professionals judge to be useful strategies to be adopted in both the moderate and advanced stages the verbal cueing whereas it seems that PD patients tend to use stick more frequently.

Furthermore, the analysis of questionnaires outlines a substantial convergence of the professionals' clinical judgements between the different countries/sites for mild and advanced stages of the disease. However, it should be noted that the same judgements appear to be more heterogeneous when applied to moderate PD stages. A possible interpretation of this heterogeneity is related to the objective difficulty to clinically define the moderate stages in respect to mild and advanced ones.

- A second main point evidenced by the analysis is that ***REMPARK system is perceived by professionals as a potentially useful instrument for the management and treatment of PD***. This is particularly observed in the moderate stages of the disease. As a matter of fact, the majority of professionals indicated the moderate phases of the disease as the best target phase for REMPARK. In this regard, it should be noted here that, as previously discussed, the moderate stage of the disease is the stage

for which the judgment on the clinical relevance of symptoms is more heterogeneous. This provides a clear indication for REMPARK. Indeed, the multifaceted clinical expression of PD during this phase should be taken into account carefully to develop a functional system.

- Finally, as for the advanced stage, the symptoms with a higher index of clinical relevance were "falls", "freezing of gait", "difficulty in turning" and "shuffle" with an index value of 1.91, 1.50, 0.84 and 0.56, respectively.

In conclusion, from the analysis and considerations done, the ***REMPARK system appears to be perceived particularly useful to be applied for both monitoring and improving PD symptoms in the moderate-advanced stages of the disease***.

REMPARK system might be a useful and well accepted instrument for the therapeutic management of PD. Additionally, there exists evidence that PD patients spontaneously adopt strategies to improve gait disorders by using external aids.

4.3 Methodology and Database to Monitor Motor Symptoms

This section presents the implemented methodology in REMPARK system for the detection of the main motor symptoms discussed above. As this methodology will be based on an artificial intelligence approach, it is necessary the construction of a specific database for the required knowledge extraction.

4.3.1 An Artificial Intelligence Approach and the Need of Relevant Data

The main objective of the REMPARK project is to obtain a system capable of assessing PD motor and non-motor symptoms. This is a clinical goal that is intended to be solved through technological solutions.

Firstly, REMPARK system involves inertial sensors to monitor PD motor symptoms given their nature. Since motor symptoms affect movement, inertial sensors capable of measuring such movement are used to automatically detect these symptoms. Secondly, the techniques used to determine their presence come from the Artificial Intelligence (AI) field; more concretely, machine learning techniques are well-known to provide high accuracies in these tasks. In this case, REMPARK work was focused on supervised learning methods.

Supervised learning techniques for classification tasks are mathematical and statistical methods that are capable of recognising patterns to associate them with specific classes. These methods require sets of labelled data in which patterns and their corresponding class labels are given. In the case of REMPARK, inertial signals labelled with the presence of symptoms are needed. In consequence, a specific data capture is required to gather such **labelled datasets**.

Machine learning techniques require the maximum amount of data and the most variability in them in order to properly generalise an automatic detection from them. In addition, labels must be as accurate as possible. Through these data, highly accurate models capable of automatically classifying the patterns can be obtained. In consequence, REMPARK envisaged the construction of a database of labelled inertial signals from 90 PD patients from 4 different countries.

It must be taken into account that the usage of supervised learning techniques creates some restrictions into the algorithmic development, which will be carried out after the database collection. Data collection must follow a strict protocol designed according to clinical restrictions in order to capture the required variety of PD symptoms in different severities. The statistical representability of the data will enable supervised learning techniques to extract the embedded knowledge and, thus, precisely detect the presence of symptoms into the signals provided by inertial sensors.

4.3.2 Protocol for the Database Construction

The data for the database were collected in the most homogeneous possible way, and under the best conditions to ensure good enough generalization capabilities. It is a very relevant task since the validity of the REMPARK system for assessing a patient's motor status relies on the quality of the data in the database.

A specific clinical study was designed and carried out in order to collect the database. It was a multicentre international study that was conducted in four European settings: Centro Médico Teknon (Spain), National University of Ireland, Galway (Ireland), Fondazione Santa Lucia (Italy) and Maccabi (Israel).

The primary objectives of the study that collected the data were:

- To obtain a database of properly identified inertial signals, which will allow the training of processing **algorithms for motor phase** detection (ON/OFF) in PD patients.

- To obtain a database of properly identified inertial signals, which will allow to train processing **algorithms for motor symptoms** detection in PD patients.
    - To obtain identified inertial signals of hand tremor.
    - To obtain identified inertial signals of freezing of gait.
    - To obtain identified inertial signals of bradykinesia of the lower and upper limbs.
    - To obtain identified inertial signals of dyskinesia of the trunk and limbs.
- To obtain a database of properly identified inertial signals corresponding to movements and activities that can be mistaken for PD **motor symptoms** (potential **false positives**).
- To obtain a database of properly identified inertial signals corresponding to **gait parameters**.
    - To obtain identified inertial signals of gait speed.
    - To obtain identified inertial signals of step/stride length.
- To obtain a database of properly identified inertial signals corresponding to movements and activities that can be mistaken for **falls** (potential **false positives**).

The reference population was that formed by Parkinson's patients with moderate to severe disease and motor symptoms (Hoehn and Yahr greater or equal to 2.5 including ON/OFF phases, FOG or dyskinesia). The total number of recruited patients was 92, distributed among the clinical centres (26 in Spain, 16 in Ireland, 24 in Italy and 26 in Israel). A convenience sampling stratified by symptoms was conducted, keeping desired minimum proportions of patients with different motor symptoms. At least 50% of the sample were set to have ON/OFF motor fluctuations, with the OFF state characterized by bradykinesia. Furthermore, at least 25% of the sample had to present FOG episodes and, finally, at least 25% of the sample was set to present dyskinesia (at least 15% will present trunk dyskinesia).

The inclusion criteria for these patients were:

- to have a clinical diagnosis of Idiopathic Parkinson's Disease according to the UK Parkinson's Disease Society Brain Bank [6]
- disease in moderate-severe phase (Hoehn and Yahr greater or equal to 2.5) with motor fluctuations with bradykinesia, FOG and/or dyskinesia
- aged between 50 and 75 years and willing to participate in the study and wanting to co-operate in all its parts

- accepting the performance regulations and procedures provided by the researchers.

Patients fulfilling the following criteria were excluded from the study:

- other health problems that hamper physical activity
- rheumatologic, neuromuscular, respiratory, cardiologic problems or significant pain
- carriers of implanted electronic devices: cardiac pacemaker, implantable automatic defibrillator ...
- patients receiving continuous therapy using intestinal duodopa or apomorphine
- patients who have received deep cerebral stimulation therapy (neurosurgical procedure)
- chronic consumption of psychotropic drugs and/or alcohol
- known mental disease, such as dementia, according to clinical criteria -DSM-IV-TR and MMSE score ≤ 24 or neuropsychiatric disorders
- patients who are participating in another clinical trial
- patients unable to fully understand the potential risks and benefits of the study and give informed consent
- subjects who are unable or unwilling to cooperate with study procedures.

The data capture was conducted in two visits. The first visit comprised both the inclusion and basal visit, where the inclusion criteria were confirmed, and initial clinical and socio-demographic data of the patient were gathered. The second visit was devoted to the experimental procedures, where the maximum number of physical signs related to the disease were recorded using the inertial sensors and standard methods. This visit had two types of experiments that will happen in interleaved manner (according to the symptoms that the patient may present in each moment).

- The first type of experiments consists in short controlled tests, where the patient was asked to perform certain activities, with the aim of capturing specific motor symptoms (bradykinesia, dyskinesia, freezing of gait, etc.). These tests were closely controlled, using video recording as a gold standard.
- The second kind of experiments that took place in this visit involved monitoring of the free activity of the patient, and recording the natural symptoms that he/she spontaneously may present. This monitoring lasted hours, and the activity and symptoms were electronically recorded by trained observers (using a tabled and specific software).

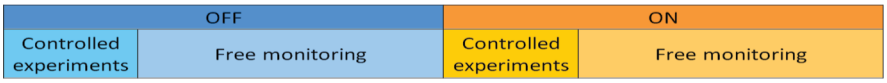

Figure 4.4 Design of the experimental visit.

The two types of experiments took place alternatively, according to the motor state and the symptoms that the patient presented. That is to say that when the patient was in an OFF phase, the specific controlled tests for the OFF symptoms were conducted (e.g., FOG) and the remaining OFF state time was used for monitoring their free-natural activity. Similarly, when the patient entered the ON phase, some specific short tests for capturing ON symptoms (e.g., dyskinesia) were performed, with the rest of the time devoted to monitoring the free natural activity of the patient in this state. Figure 4.4 summarizes the experiment done.

All participants were trained to follow the specific study procedures, according to a common protocol that was the same for all the study sites. Patients also received specific training for recognizing their own OFF state. For this purpose, specific videos showing other patients in ON and OFF states were displayed, and detailed explanations on symptoms defining the OFF state were provided.

The investigators received a 3-day training session, comprising theoretical sessions including guidelines and instructions of all the instruments and questions of the Case Report Form (CRF), and practical sessions with pretended patients who behaved according a number of pre-established situations which served an example of the most relevant cases. The entire experimental test was performed at least twice by all the researchers, and every researcher conducted an example free monitoring session of at least 60 minutes.

During this training session, investigators were also trained into the usage of the designed labelling tools:

- Labelling for the controlled experiments was done once the data capturing with the patients had finished. Researchers were trained into the usage of the tool, that allowed, first, the synchronisation of the inertial signals with the videos, and, second, the labelling of the different symptoms that were listed in the objective of the study.
- Labelling of the free-monitoring experiment was done in-situ by the investigators. A tablet with a specific application were used by them. This application enabled the annotation of the different symptoms at the same time that the inertial signals were captured.

Finally, the Principal Investigator, or his designee, in accordance with institutional policy, obtained an Informed Consent that was reviewed and accepted by the Ethics Committee. A written consent form bearing the full name, date and signature of the patient and the local investigator were obtained from each patient. The signed Informed Consent constitutes a confidential document and therefore was archived in the study binder. A copy of the consent was also given to the patient.

The inertial signals captured during this data collection phase were obtained through two sensors: a waist sensor and a wrist sensor. The waist sensor was worn inside a pocket within a neoprene belt. The wrist sensor was worn through a strap. Figures 4.5 and 4.6 present both devices.

Figure 4.5 Waist sensor.

Figure 4.6 Wrist sensor.

4.3.3 Gathered Database Description

The following data were included in the database for each patient:

1. Socio-demographic data: Age, Sex, Educational level and Marital status
2. Parkinson's Disease related information:
    - Parkinson's severity, as measured by Hoehn and Yahr scale
    - Date of symptoms' onset
    - Date of PD diagnosis
    - Motor section of UPDRS in OFF phase
    - Motor section of UPDRS in ON phase
    - Information on OFF periods characteristics and duration (UPDRS motor complications section – motor fluctuations)
    - Information on FOG presence, characteristics and duration (FOG questionnaire)
    - Information on dyskinesia presence, characteristics and duration (UPDRS motor complications section – dyskinesia)
    - List of treatments
3. Co-morbidity related information. Cognitive status: Mini-Mental State Examination, Test of Attentional Performance and List of conditions.
4. Inertial signals labelled according to the following motor symptoms:
    - Motor phases. Signals were labelled among the three following options: ON, OFF and Intermediate state.
    - Dyskinesia severity and location. Dyskinesia is a side effect of medication, not a PD symptom, and signals were labelled according to the following modalities: Weak Trunk dyskinesia, Weak Foot/Leg dyskinesia, Weak Hand/Arm dyskinesia, Weak Head dyskinesia, Strong Trunk dyskinesia, Strong Foot/Leg dyskinesia, Strong Hand/Arm dyskinesia, Strong Head dyskinesia.
    - Bradykinetic gait (presence/absence). This symptom describes a difficulty to walk and slow gait, including small steps, shuffling and difficulty to turn.
    - FOG type. Episodes were labelled according to their type: Start Hesitation FOG, Straight Line FOG, Turning FOG, Tight FOG, Destination FOG.
    - Tremor location and severity: Modalities labelled were: Right Hand/Arm tremor, Right Foot/Leg tremor, Trunk tremor, Left Hand/Arm tremor, Left Foot/Leg tremor.
5. Inertial signals labelled according to body postures and activities: sitting, standing, walking, going upstairs, going downstairs, elevator (down),

elevator (up), walk with FOG, carrying delicate object, carrying heavy object, lying, jumping, running

6. Other information from inertial signals:
   - Falls
   - Walking aids: scooter, walking stick, walker, crutch, crutches, lean on furniture, tripod walking stick

Organization of the complete set of data from each patient is summarised in Figure 4.7.

Database contains clinical data from 92 participants with idiopathic Parkinson's Disease. Regarding the sociodemographic data, as Table 4.1 shows, fifty-six of them are male (60.9%) and 36 (39.1%) are female. The average age of the participants is 68 (SD 7.9). Seventy-four patients are married or live with a couple (80.5%), 10 (10.8%) single or divorced, and 8 (8.7%) widow.

All the participants in the database construction are patients with moderate disease, having a Hoehn and Yahr scale of 2 or more. Average Hoehn and Yahr score is 3 (IQR 0.5). The average time from diagnosis of the disease was 10.5 years (SD 12.2). Eighty-nine patients (96.7%) of the database have OFF periods, according to the "motor complications" section of the UPDRS. Sixty-eight (73.9%) had predictable off periods, 54 (58.7%) had unpredictable

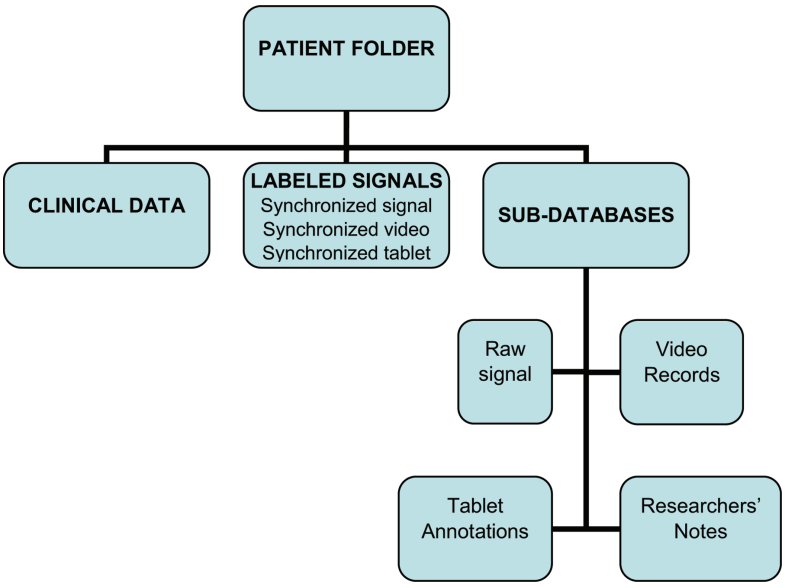

Figure 4.7 Data structure collected from each patient.

Table 4.1 Sociodemographic data

Age (Mean ± SD)	68 (7.9)
Gender	
Female	36 (39.1%)
Male	56 (60.9%)
Marital Status	
Single	5 (5.4%)
Married/partner	74 (80.5%)
Widowed	8 (8.7%)
Separated/divorced	5 (5.4%)

off periods and 33 (35.9%) had sudden off periods. Most of them spend less than a quarter of the day in OFF. 34.7% of the total declared to spend more than 50% of the daytime in off.

Sixty-four patients (69.6%) present some degree of dyskinesia, being non-disabling dyskinesia in 54.3% and non-painful in 78.3%. Twenty-five patients have dystonia (27.2%). Only 5 patients have a 0 score in the FOG-Q, meaning that the rest of them present some gait problems.

The database contains inertial signals properly identified and labelled according to Parkinson's motor symptoms and body postures and activities. In total, the database contains 406 hours of inertial signals. Information on the motor status of the participant is available for 346 hours of inertial signals of the database (see Table 4.2).

A total of 175 hours of motor symptoms are recorded and identified in the database (including bradykinesia, dyskinesia, FOG and tremor). Thirty-two of them correspond to inertial signals labelled against a video record gold standard, and the rest correspond to inertial signals which have been labelled using the real-time notations of an observer (tablet-PC annotations). Table 4.3 summarizes the time (hours) of symptoms recorded and labelled in the database.

Table 4.4 shows the amount of motor symptoms (bradykinesia, dyskinesia, FOG and tremor) recorded in each motor phase (ON, OFF or "Intermediate"), according to the gold standard used (video records vs tablet-PC annotations).

Table 4.2 Recorded time of the different motor periods

Motor Phase	Time Recorded (hours)
ON	163
OFF	111
Intermediate	72

Table 4.3 Video recording duration per symptom in the database

	Dyskinesia	Bradykinesia	FOG	Tremor	TOTAL
Video	8,10 h	15,78 h	2,45 h	5,60 h	31,92 h
Tablet-PC	62,82 h	31,82 h	2,96 h	45,82 h	143,43 h
Total	70,93 h	47,60 h	5,41 h	51,42 h	175,36 h

Table 4.4 Summary of motor symptoms per motor phase

	On (minutes)		Off (minutes)		Intermediate (minutes)		Motor Phase Not Available		TOTAL (minutes)	
	Video	Tablet	Video	Tablet	Video	Tablet	Video	Tablet	Video	Tablet
Dyskinesia	355	2500	28	431	18	712	85	126	486	3769
Bradykinesia	50	122	790	1394	25	308	81	85	947	1909
FOG	21	33	113	76	7	36	6	34	147	178
Tremor	94	789	224	1200	15	680	2	80	336	2749
Total	520	3444	1155	3100	65	1737	174	325		

4.4 Algorithmic Approach and Results

Once presented the complete scenario of the objective motor symptoms to be studied from a clinical perspective, it is necessary to propose an algorithmic methodological approach to bring all this knowledge closer to the achievement of machine-learning classifiers (algorithms) for the motor states monitoring tasks.

The methodological proposal to estimate the motor state (ON or OFF periods) of a PD patient wearing an inertial device is based on the use of a hierarchical system. In a first level, the system permits to put in context the patient's activity and a second level is in charge of the detection of the symptomatology of interest. The hierarchical system uses the output of the detection algorithms in this second level for the assessment of the patient's motor status. Some details are presented in Figure 4.8.

The contextualization of the patient's activity and posture is very important because the evaluation of the different PD symptoms is related to the activity developed by the patient. Thus, evaluation of bradykinesia will only be performed when the patient is walking, since it is during self-executing activities when this symptom is clearly manifested. In this way, the inertial signals from the primary accelerometer sensor are analysed using temporary windowing with a set of algorithms that determines if the patient is walking and, if so, signals are analysed to determine the presence of Bradykinesia. This strategy is applied in a similar way for Dyskinesia, where the detection is performed only in the case that the contextualization algorithms determine that

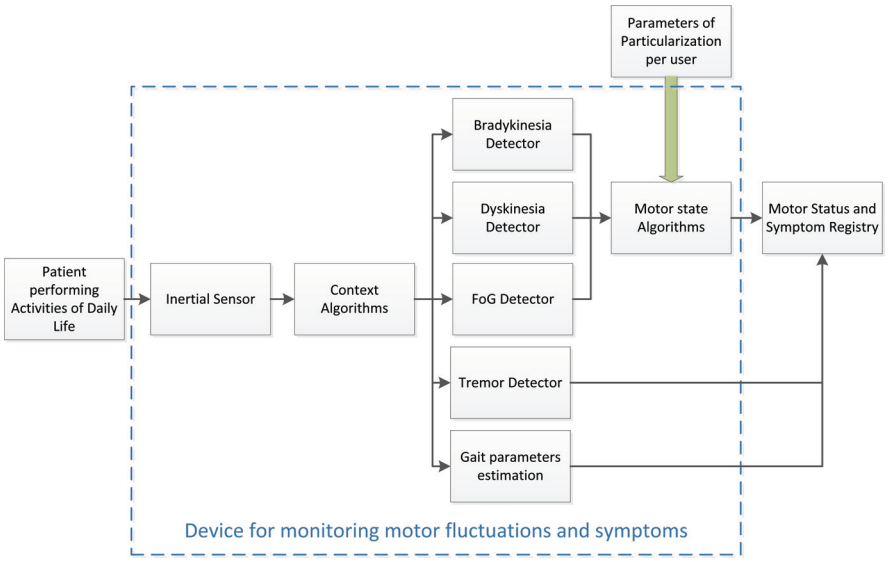

Figure 4.8 Outline of the structure defined for the algorithms for detecting symptoms of PD.

the patient is not walking during the windowed analysis, since it is considered that the gait hides dyskinetic movements.

The information obtained from the detectors of bradykinesia and dyskinesia, together with the FOG detector results will be analysed through a set of additional algorithms, which will determine the final motor state of the PD patient (ON/OFF states). At this stage, as it is indicated in Figure 4.8, it is necessary to use some personal parameters of the patient (basically obtained from previous medical history information).

The development of the different detection algorithms, corresponding to each considered symptom was done independently, taking as a starting point some relevant papers published so far, analysing them, exploiting the acquired signals contained in the REMPARK database and trying to improve, when possible, the previous published results. As it has been already mentioned, the methodology used is based on a machine-learning approach, mainly using supervised learning techniques. The available database described in the above Section 4.3 was used for this purpose.

In the machine-learning area, it is a common practice to divide the Database into different sub-sets. One sub-set is strictly used for algorithmic training purposes and other sub-set is only used for testing. Related works performed in REMPARK project used this approach and the results of the different

techniques were evaluated with the patients' data not used in the training process of the supervised learning algorithms.

The signals labelled according to the symptoms listed in Table 4.4 were used to train the different supervised learning models. It must be considered that all the included algorithms process accelerometer measurements sampled at 40 Hz. In addition to the symptoms listed in Table 4.4 (dyskinesia, bradykinesia, FOG, and tremor), there is another subsection devoted to describe the estimation of gait parameters. A description of the algorithmic work done is presented in the following subsections.

4.4.1 Dyskinesia Detection Algorithm

A processing method based on a frequency analysis of the signal was implemented and used for Dyskinesia detection. The method considers the power spectrum of the concrete band between 1 and 4 Hz for the detection of Dyskinesia, provided that information corresponding to higher frequency band (from 8 to 20 Hz) could correspond to false positives such as walking or climbing stairs. Additionally, a number of conditions are added in order to allow a better contextualization of the patient's movement and consequently, to improve the specificity of the algorithm. The algorithm has been subdivided into two steps (detailed below), one at window level and one at the minute level.

- In the first step (at window level), the evaluation of the presence of Dyskinesia is done through the analysis of three separate frequency bands:
  - **Dyskinesia Band**: A high spectral power density in this band is a clear indication that the patient is suffering Dyskinesia, although it may also mean that the patient is walking or climbing stairs. This band is covering from 0.68 Hz to 4 Hz.
  - **Non-dyskinetic band**: It is considered that this band covers from 8 to 20 Hz. This frequency band allows to discriminate if an increase of spectral power in the band of Dyskinesia is due to the appearance of a Dyskinesia or because the patient is walking (or doing similar activities).
  - **Postural transition band**: This is the band from 0 to 0.68 Hz. The posture transition is a very common action and involves very low frequencies that can generate harmonics in the Dyskinesia band, which may provoke false positives.
- The detection of Dyskinesia, based on frequency band analysis allows us to know, in a given time window, whether or not the patient has

Table 4.5 Dyskinesia algorithm results

Type of Choreic Dyskinesia		Num. of Patients with This Type of	Equal Weight per Minute		
Severity	Body Part	Choreic Dyskinesia	Specificity (%)	Sensitivity (%)	Total Minutes
Weak	Trunk	16	95	78	953
Strong	Trunk	4	95	100	895
Weak	No-trunk	32	95	39	1110
Strong	No-trunk	7	95	90	917

Dyskinesia. However, Dyskinesia is a symptom that is repeated over time for many minutes, this fact can be used to minimize, using an aggregation process, the presence of false positives. This method of aggregation allows us to examine the appearance of Dyskinesia in several consecutive windows over time by performing an aggregation of the output of each window providing a unique output in a given time slot (it has been considered a period of 1 minute in the implemented algorithms).

This signal processing method was applied to the database of signals by using a leave-one-patient-out scheme on the minute-basis output of the algorithm.

The main reference for this work is [7] and a summary of the results obtained is provided in Table 4.5. The results were obtained with REMPARK's database of video-labelled signals from 92 PD patients.

Specificities and sensitivities are provided for each different type of dyskinesia. With regards to the most important in the clinical sense, i.e. the strong trunk dyskinesia, the algorithm achieves a specificity of 95% and a sensitivity of 100%.

4.4.2 Bradykinesia Detection Algorithm

Bradykinesia appears when plasma's dopamine level is low, seriously complicating the general mobility of the patient and, in particular, causing changes and compromising the way of walking.

The analysis done has been based on the gait cycles characterization. The detector algorithm identifies, on the one hand, the strides that the patient is currently carrying out and, on the other hand, characterizes these gait cycles, allowing the analysis of Bradykinesia through specific characteristics that correlate with the presence of a pathological alteration.

In the analysis of the database, it was concluded that the most important feature that helps to diagnose the occurrence of Bradykinesia is the *fluidity of movement* when walking. Fluidity is a **highly subjective variable** that is not currently objectively measurable. When a patient presents a very low

movement fluidity, the probability of manifesting Bradykinesia is very high. This principle allows to generate an algorithmic approach that objectively measures characteristics associated with the fluidity of the movement and, furthermore, enables the detection of the symptom based on comparative thresholds, which determines when the symptom is present.

The bradykinesia detection algorithm is structured using a three-stage scheme (see Figure 4.9). In the first one, the contextualization of the movement is realized, detecting if the patient is walking or not. In the second block, a process of recognition and identification of strides/steps is performed, and the last block performs the analysis of the characteristics of strides/steps that may be representative of the occurrence of Bradykinesia.

The walking detection done at the first stage is performed through a process of pattern recognition from the obtained accelerometer signals. A binary-classification procedure has been approached to detect gait through the use of Support Vector Machines (SVM). The input of the SVM consists of a group of features, which are extracted from a temporary window of signal obtained from the accelerometer. The training set for the SVM was generated through the windows obtained from the signals corresponding to a group of 10 patients, which were acquired from a previously obtained database and its associated gold standard. It should be noted that these patients were not used, later, in the validation group of the final implemented algorithm. The most relevant considered characteristics for the detection of the gait are the power spectra in the three spatial axes, for the bands from 0.1 to 3 Hz and from 0.1 to 10 Hz.

The step detection process is launched when the SVM walking detection has been positive on a given window. This step detection is carried out by recognizing the biomechanical characteristics of walking in the acceleration measurements taken from the sensor (located in the waist).

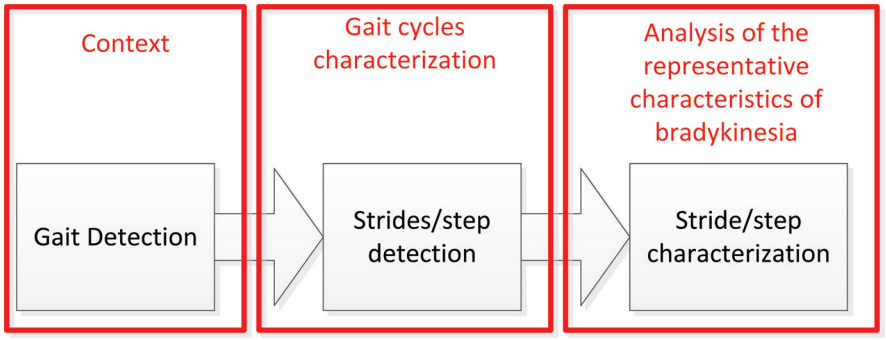

Figure 4.9 Scheme of the bradykinesia detection algorithm.

Table 4.6 Bradykinesia algorithm results

Specificity	Sensitivity	PPV	NPV
81%	88%	89%	84%

The interest of the analysis focuses on the strides (two consecutive steps of each feet) and their characterization, in order to represent the fluidity of the patient's movement. Several statistical markers have been studied and evaluated for this purpose, bearing in mind that the best marker is the one maximizing the separation between the presence and absence of Bradykinesia.

Additionally, it must be considered that the states (Bradykinesia presence or not) are very dependent on the user and, therefore, the threshold that correctly separates the states of a particular patient may have a value different from the threshold of another patient. The main reference of this work is [8] and a summary of results is provided in Table 4.6. These results were obtained by analysing the data from the 92 PD patients who participated in the database construction.

4.4.3 Tremor Detection Algorithm

Tremor was evaluated by analysing the signals provided by the wrist sensor included in the REMPARK system. A frequency analysis of the signals was performed, permitting the extraction of several characteristic features in order to determine the presence of the symptom. The process is based on a SVM model.

The signal processing approach is divided into two different phases: the window level in which tremor is recognized based on short duration signals and the meta-analysis level that aggregates several window detections.

1. At the window level, frequency related features of the signals are used, because this is one of the most common methods. We observed that frequencies in the band from 4 to 6 Hz appear when Parkinsonian tremor is present, and these frequencies are not observed when this type of tremor is absent (which is in agreement with current literature).

   Given the main frequency behaviour of this sort of tremor, it could be theoretically detected only using frequency characteristics. However, a list of other features has been used in the literature for this purpose (for instance, Fast Fourier Transform (FFT), Peak frequency and its amplitude, Entropy of signal, Sum of first, second and third harmonic . . .). In order to measure the impact of non-frequency features in the accurate detection of tremor, two approaches were defined. On the one hand, a first method only used frequency features while, on the other hand, the second

approach also included non-frequency features that were previously used in the literature (see reference [9] for additional details).

Both approaches are composed of two phases in order to determine if tremor is present in a certain time window:

- Feature extraction phase. Features are defined depending on the used approach: frequency features alone or combined with those mentioned above. Frequency features from three axes were obtained, and their amplitudes were summed up without taking into account the amplitude of the zero-frequency harmonic. Thus, dependence on the sensor's orientation is avoided. From this, the previously described features were acquired.
- Learning phase. An SVM classifier is trained to distinguish tremor and non-tremor windows based on the chosen feature set.

2. At the meta-analysis level, since it is very important to minimize the resources needed for tremor detection, time windows must be as short as possible (i.e. about few seconds). However, short windows are likely to produce false positives (e.g. a single segment with tremor surrounded by non-tremor segments) since short movement may be confused with tremor (e.g. teeth brushing). Thus, a meta-analysis is added in order to enhance the reliability of the proposed approaches.

   The employed meta-analysis method considers the algorithm's outputs in a set of several consecutive windows covering a period of several seconds. These outputs are aggregated into a value representing the probability of having tremor in the corresponding period. This period is considered as tremor if the probability is greater than a certain threshold.

Following the common procedure in the field, the database was split into three non-overlapping sub-datasets: training, holdout and test. A SVM classifier was trained to distinguish tremor and non-tremor windows, using the training sub-dataset. The final evaluation was done on the test dataset and indicates the performance of the developed algorithms.

In total two feature sets (i.e. only frequency features vs. commonly employed features) and two SVM kernels (i.e. linear vs. Radial Basis Function (RBF)) were evaluated.

The main reference for the tremor algorithmic approach is [9] and a summary of results is provided in Table 4.7, where each column represents a different learning model: "RBF+ Freq." corresponds to a SVM with RBF kernel and frequency features, "Lin+Freq." corresponds to a SVM with linear kernel and frequency features, "RBF+All" corresponds to a SVM with

Table 4.7 Tremor algorithm results as presented in [9]

	RBF+Freq.	Lin.+Freq.	RBF+All	Lin.+All
Sensitivity (holdout)	100,00%	100,00%	100,00%	90,00%
Specificity (holdout)	98,50%	99,50%	99,30%	97,20%
Data Usage (holdout)	57,70%	41,10%	42,00%	82,10%
Sensitivity (test)	97,30%	91,00%	98,10%	92,10%
Specificity (test)	96,90%	99,00%	98,60%	97,50%
Data Usage (test)	55,50%	40,80%	42,00%	79,90%
Geometric Mean (test)	97,10%	94,90%	98,40%	94,80%
Accuracy (test)	96,90%	98,60%	98,60%	97,30%

RBF kernel and both frequency and temporal features, and, finally, "Lin+All" corresponds to a SVM with linear kernel and both temporal and frequency features. These results were obtained by training the method with data from 18 patients and validating it with data from 74 patients.

4.4.4 Freezing of Gait (FOG) Detection Algorithm

Freezing of Gait (FOG) is a widely studied and evaluated symptom from the point of view of automatic detection methodology, since it is one of the most disabling symptoms for the patients and one of the most difficult to be evaluated by clinicians.

As it is clear from the current literature, detection techniques for the laboratory setting are highly developed at the moment, and they have had relatively high success rates. However, many problems arise when we tried to apply these methods to the daily living activities, because many false positive appeared due to the new situations and movements appearing under non-controlled scenarios.

In the literature, it has been identified a frequency band on the acceleration signals from the lower limbs of PD patients associated with FOG episodes and ranged between 3 and 8 Hz. In consulted work, a freezing index is defined based on the ratio of the square of the spectral power of these frequencies associated with the freezing band to the square of the spectral power of the frequency band corresponding to the act of walking, (between 0.5 and 3 Hz).

Since FOG mainly occurs when starting, during or at the end of the gait, it is essential to contextualize the patient's activity through a gait detection algorithm. We can take advantage of the gait detector based on the SVM presented in the Subsection 4.4.2 (for Bradykinesia detection). Some points must be considered:

- Contextualization was implemented in the sense that positive FOG detection is validated when the algorithm detected that the patient is walking or has been walking for the last 5 seconds.
- The onset of gait is a complex detection since, in the case of a *posteriori* detection, the condition that validates the detection may never occur because probably the patient would experiment a fall, or because the patient's FOG lasts longer than the imposed temporary condition.
- In addition to adding the validation condition of 5 seconds walking to the formulation, some significant detectable events were considered to know when a patient is rising from the sit position (transition from sitting to standing). This action is very important for the contextualization of FOG since a large number of episodes occurs some moments after the patient is performing this action and try to walk. With this objective, the postural transition band was used for the detection of these events.

In summary, this symptom is detected based on a set of both temporal and frequency features, similarly to the tremor detection algorithm, although the presented contextualisation is added. The main reference for the algorithmic approach is [10] and a summary of results is provided in Table 4.8, where each column represents a different learning model: "RBF freq." corresponds to a SVM with RBF kernel and frequency features, "Linear Freq." corresponds to a SVM with linear kernel and frequency features, "RBF All" corresponds to a SVM with RBF kernel and both frequency and temporal features, and, finally,

Table 4.8 Freezing of Gait algorithm results

Kernel	RBF	Linear	RBF	Linear
Features	Freq.	Freq.	All	All
Sensitivity (train)	100,00%	92,30%	100,00%	92,30%
Specificity (train)	100,00%	100,00%	100,00%	100,00%
Data Usage (train)	69,60%	89,10%	90,60%	98,60%
Geometric Mean (train)	100,00%	96,10%	100,00%	96,10%
Accuracy (train)	100,00%	98,70%	100,00%	98,50%
True Positives	9	8	9	12
False Positives	0	0	0	0
True Negatives	55	82	65	65
False Negatives	1	1	1	1
Sensitivity (test)	90,00%	88,90%	90,00%	92,30%
Specificity (test)	100,00%	100,00%	100,00%	100,00%
Data Usage (test)	82,30%	91,90%	94,90%	98,70%
Geometric Mean (test)	94,90%	94,30%	94,90%	96,10%
Accuracy (test)	98,50%	98,90%	98,70%	98,70%

"Linear All" corresponds to a SVM with linear kernel and both temporal and frequency features.

In this case, a subset of the whole REMPARK database was used. More specifically, these results were obtained by using signals from 15 patients as a training set and the resulting model being evaluated with signals from other 5 patients. Training was done with patients who had FOG episodes. Validation was done with both patients with FOG and patients without FOG.

4.4.5 Gait Parameters Estimation

Algorithms for the correct estimation of the gait parameters were included in the sensor embedded software. Some previous activity and the collection of a labelled database was performed in order to implement the most suitable approach.

As part of a series of controlled tests, patients performed a gait test in which their average step length and average step velocity was measured. These values were estimated through the waist-sensor signals and a novel inverted-pendulum model. The sensor location used in REMPARK provides a different kind and shape of signals than those previously obtained in the literature, that commonly are using the Anterior Superior Iliac Spine position for the reported experiments.

Figure 4.10(b) and 4.10(c) show the acceleration signal from lower back (around L4–L5) and left lateral side (near ASIS) of waist, obtained with the REMPARK sensor. It can be seen that the symmetry among left-right steps is lost in signals obtained from the lateral side. Signals from the left leg are more prominent than those from the right leg which impose new restriction on step detection and step length estimation.

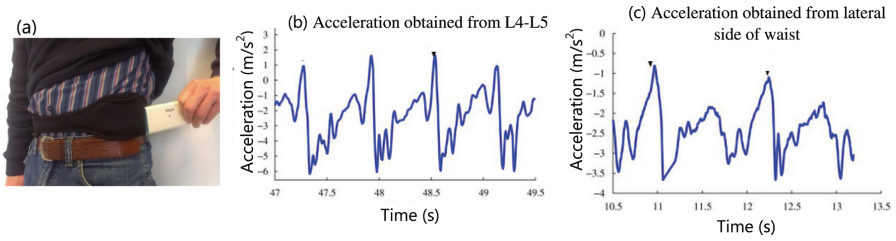

Figure 4.10 (a) The inertial system prototype (9 × 2, Version 6) positioned in a neoprene belt on left lateral side of waist. Acceleration signals obtained from (a) Lumbosecaral point of waist and (b) left lateral side of waist.

The signals from the lateral side differ from those from the lower back of waist. A newly developed step detection method called SWAT [11] was developed, combined with an adapted step length estimator based to accurately estimate the step lengths from this position. From the left lateral point of view, the proposed gait model considers vertical displacement of waist as an inverted pendulum (IP) model during right step and during single support phase of left step.

Step detection performs an average window that is calculated over the magnitude of the acceleration signals. Mean is removed from this average window signal, and, then, the resulting signal is used to identify left and right initial contacts (IC) and toe-offs (TO) events. When the foot's heal touches the ground, the event is called as IC, and when the foot leaves it is called as toe-off (TO).

The initial contact and toe-off events of left and right legs are noted here as LIC, LTO, RIC and RTO respectively. As the sensor was placed on the left lateral side, the local maximum lateral signal can be used to identify incidents of LICs immediately before or after it. For every local maximum in the SWAT signal, if there was no incident of LIC in the lateral signal immediate before or after it, then it is determined to be a RIC. If there is an incident of LIC, the mid-point from the local maximum to zero is considered to be a LIC. For each detected RIC, the next zero crossing point is considered as a LTO. For each LIC, the mid-point of next zero to the local minimum are searched and considered as a RTO.

The main reference for this work is [11], where it is shown that the results obtained by the proposed method in 28 patients from the REMPARK database show that gait parameters can be estimated with an average RMSE error below 0,04 meters.

4.4.6 Fall Detection Algorithm

The set of algorithms developed and implemented in the REMPARK project is complemented by a fall detection algorithm that was previously developed by one of the partners (UPC). This algorithm enables the detection of falls based on specific computations through accelerometer measurements sampled at 40 Hz. This algorithm is included in the set of algorithms implemented in order to provide more information through the REMPARK system and include the possibility of raising alarms.

The fall detection algorithm has been successfully validated in the "Fall Detection for the Elderly" (FATE) project (CIP-ICT-PSP-2011-5-297178) [12]. It has shown a sensitivity and specificity above 95% along a pilot in which more than 200 users from three countries (Spain, Italy and Ireland) participated.

4.4.7 ON/OFF Motor State Estimation

The algorithmic part for determining the motor state (ON/OFF state) of a person with Parkinson is very complex, because the high degree of subjectivity included in the construction process of a correct model to be used. A main problem is due to the fact that patients, sometimes, are not able to correctly identify their own symptoms and, in some cases, may confuse them with non-motor symptoms. Additionally, when non-motor symptoms are present, it is even more difficult for these persons a correct identification.

This could be a very compromising situation when a machine learning approach is intended to be used, since the most common gold-standard, in these cases, is the patient-diary where the patient should annotate the experimented symptoms every hour, along the day.

In order to be able to implement an objective algorithmic approach to the problem, the related medical literature was reviewed and useful discussions were organized with professionals for determining as much as possible the set of objective conditions characterizing the ON/OFF states. The most widespread definition of the OFF state is to refer to those periods in which low dopaminergic levels occur, in which Bradykinesia is the most correlated symptom. In addition, one can also use the fact that the appearance of Chorea Dyskinesia is commonly produced by high levels of dopamine.

This approach makes possible, based on the algorithms of motor symptoms that have been discussed along this section, to approximate the motor states of the patient with the help of a decision tree technique:

- The algorithm determines that the patient is in ON state when either non-bradykinetic gait or Dyskinesia are detected.
- OFF state is assumed when bradykinetic gait is detected.

This algorithmic approach was tested in the final pilots of REMPARK and its output was compared to the diaries annotated by patients during 3 days. Results are presented in the Chapter 9 and the original public deliverable document (with the reference D9.2) is available at the REMPARK website. The specificity and sensitivity on detecting OFF and ON motor states in 33 PD patients was 89% and 98%, respectively.

4.5 Conclusions

This chapter has presented a huge effort made by REMPARK consortium in order to develop a system capable of monitoring PD motor symptoms in ambulatory conditions. A highly accurate database of labelled signals and clinical questionnaires were collected from 92 PD patients, with more than 340 hours of recorded signals. The labelled signals have been used to train different machine learning methods. The resulting approaches have shown that the selected PD motor symptoms can be accurately monitored through the corresponding sensors, with specificities and sensitivities about 90% in most cases.

Many different algorithms and their results have been presented. The algorithms covering Bradykinesia, Dyskinesia, Tremor, Freezing of Gait (FOG) and gait parameters, employing the collected REMPARK database have been commented and their results presented. However, the ON/OFF algorithm was only tested in the final pilots, since it had to be validated with ON/OFF diaries filled by the patients, used as gold-standard.

References

[1] REMPARK Deliverable D1.2 – Questionnaire addressed to doctors/ physiotherapists. Answers and statistical results. Publicly available.

[2] Agid, Y., Ruberg, M., Hirsch, E., Raisman-Vozari, R., Vyas, S., Faucheux, B., Michel, P., Kastner, A., Blanchard, V., Damier., P., Villares, J., & Zhang, P. (1993). Are dopaminergic neurons selectively vulnerable to Parkinson's disease? Advances in Neurology, 60, 148–164.

[3] Braak, H., Del Tredici, K., Rub, U. et al. (2003). Staging of brain pathology related to sporadic Parkinson's disease. Neurobiol Aging 24: 197–211.

[4] Chase, T. N., Juncos, J. L. Fabbrini, G., Mouradian, M. M. (1988). Motor response complication in advanced Parkinson's disease. Function Neurol 3(4): 429–436.

[5] Dauer, W., & Przedborski, S. (2003). Parkinson's disease: Mechanism and models. Neuron, 39, 889–909.

[6] Hughes, A. J., Daniel, S. E., Kilford, L., Lees, A. J. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. J Neurol Neurosurg Psychiatry 1992; 55: 181–184.

[7] Pérez-López, C., Samà, A., Rodríguez-Martín, D., Moreno-Aróstegui, J. M., Cabestany, J., Bayes, A., . . . & Sweeney, D. (2016). Dopaminergic-induced dyskinesia assessment based on a single belt-worn accelerometer. *Artificial intelligence in medicine*, *67*, 47–56.

[8] Samà, A., Perez-Lopez, C., Romagosa, J., Rodriguez-Martin, D., Catala, A., Cabestany, J., . . . & Rodriguez-Molinero, A. (2012, August). Dyskinesia and motor state detection in Parkinson's disease patients with a single movement sensor. In *2012 Annual International Conference of the IEEE Engineering in Medicine and Biology Society* (pp. 1194–1197). IEEE.

[9] Ahlrichs, C., & Samà, A. (2014, May). Is frequency distribution enough to detect tremor in PD patients using a wrist worn accelerometer? In *Proceedings of the 8th International Conference on Pervasive Computing Technologies for Healthcare* (pp. 65–71). ICST (Institute for Computer Sciences, Social-Informatics and Telecommunications Engineering).

[10] Ahlrichs, C., Samà, A., Lawo, M., Cabestany, J., Rodríguez-Martín, D., Pérez-López, C., . . . & Browne, P. (2016). Detecting freezing of gait with a tri-axial accelerometer in Parkinson's disease patients. *Medical & biological engineering & computing*, *54*(1), 223–233.

[11] Sayeed, T., Samà, A., Català, A., Rodríguez-Molinero, A., & Cabestany, J. (2015). Adapted step length estimators for patients with Parkinson's disease using a lateral belt worn accelerometer. *Technology and Health Care*, *23*(2), 179–194.

[12] FATE project website. www.project-fate.eu.