SleepData - Sleep disorders clinical platform

Delayed sleep phase disorder

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Abstract

This dissertation presents the design and development of SleepData, a new information platform for managing clinical information on sleep disorders. The platform can integrate data from multiple sources produced by a diversity of monitoring devices and lab tests. SleepData provides tools for statistical analysis and diagnostic support tools specially designed to study patients with delayed sleep phase disorder (DSPD) and insomnia. The platform is designed to comply with the FAIR data principles for scientific data management, adopting FHIR, a standard for healthcare information exchange, and SNOMED CT and LOINC, two medical nomenclatures. Information is secured in compliance with the Portuguese Data Protection Authority recommendations. An initial study of patients with DSPD, based on data integrated into SleepData from a state of the art clinic, shows that this population presents a delay in phase of 1-4 hours, several comorbidities and common stress factors. The results point to the causes for DSPD in this set of patients being behavioural rather than physiological, as the delay is reduced when the surroundings have reduced stimuli. Additionally, the results of dim-light melatonin onset, a know marker for DSPD, are not consistent with the disorder.

Key words: Clinical sleep database, Clinical information systems, Delayed sleep phase disorder

1 Introduction

The diagnosis and analysis of patients with sleep disorders depend on a vast ensemble of documents and exams, which are very heterogeneous not only in terms of sources, but also in used file formats. Furthermore, besides the reports provided by those machines, all other reports and clinical notes are often non-standardised, making it even more difficult to study and analyse the existent data, not to mention the handicap it represents in terms of data mobility and reproduction. There is no software system to manage in an integrated way all the data used in sleep medicine. This causes the process of diagnosis and study of sleep disorders to be often slow and puts the burden of diagnosis on the doctor alone. Therefore, there is a clear need for a platform composed of:

1. A database capable of integrating diagnostic files from every source;
2. Software for the automatic processing of these data, in order to implement statistical analysis and diagnostic supporting tools.

To understand the requirements and ensure that the platform created is useful for clinical practice and to verify the usability of the tools created, the *Centro de Eletroencefalografia e Neurofisiologia Clínica* (CENC), a state of the art clinic focused on sleep medicine with more than 5000 patients with sleep disorders was used a case study. The lack of an integrated information system to support the handling and analysis of CENC's data highly limits the possibility for joint analysis of patients' clinical records.

As a proof of concept, a sleep disorder was studied in higher detail. Delayed Sleep Phase Disorder (DSPD) is a type of circadian rhythm disorder with a prevalence of about 16% in teenagers, with a reduction to 0.15% in the adult population, as indicated by Sheldon et al. (2014). DSPD is often often misdiagnosed as other comorbidities, especially psychiatric disorders, according to Stores (2007). As mentioned by the American Academy of Sleep Medicine (2014), one of the most useful methods of diagnostic for circadian rhythm disorders is the measurement of dim-light melatonin onset (DLMO). Recent studies raise doubt as to the importance of DLMO as a marker.

The worked presented on this paper has the following

main objectives:

- Conceptualisation and development of a new information platform for managing sleep disorders, called SleepData, which is able to integrate clinical information of patients with sleep disorders. SleepData enables the automatic update and processing of the data, to implement statistical analysis and tools specially designed with diagnostic purposes, as they give the physicians an overview of the patients' clinical records, as well as an overview of the set of population in study. This platform is scalable and adaptable for any clinic focused on sleep medicine. SleepData also aims to become a universal sleep data repository, being able to integrate the data of several clinics;

- Characterisation of CENC patients previously diagnosed with Delayed Sleep Phase Disorder (DSPD) using the SleepData platform. In particular, we intend to conclude whether dim-light melatonin onset measure is a reliable and effective marker, thus diagnostic method, for DSPD patients or not, taking in account this set of patients.

This work is described in higher detail in Pinho (2017), which focuses on DSPD, and Castanheira (2017), which focuses on insomnia.

The main product of this work was SleepData, a platform for sleep medicine which is capable of integrating clinical information from several sources. SleepData provides tools for statistical analysis and diagnostic tools specially designed to study patients with DSPD or insomnia. Additionally, the set of patients with DSPD was characterised as having a sleep phase delay of one to four hours, several comorbidities and common stress factors. These patients show an ability to fall asleep earlier and have better sleep efficiency when certain stimuli, like bright light and screen time, are reduced near bed time hour. Concerning DLMO is was shown that it is not a good marker for DSPD for this set of patients.

SleepData meets the following requirements for clinical applications:

1. The data are FAIR due to the implementation of appropriate standards and nomenclatures;

2. Confidentiality, privacy, data security and encryption;

3. Scalable platform, capable of handling multiple users and simultaneous request.

2 Sleep disorders

Sleep has different states, NREM and REM, distinguishable by different neural activity. NREM sleep has minimal mental activity and is composed of three stages (N1, N2 and N3), distinguishable in the EEG. REM sleep has high neural activity, muscle atony and rapid eye movement. The process of "falling asleep" is not a discrete event, it is rather a continuous and progressive entry into a less vigilant state (Carskadon and Dement, 2011). There is consensus as to that the transition to sleep happens during N1 stage, followed by N2 and N3 stages. REM sleep occurs next, usually after 80 to 100 minutes of sleep. A normal sleep pattern is composed of about four cycles of NREM/REM sleep, with REM corresponding to about 25% of total sleep time. Variations in different age groups are expected (Billiard, 2008).

Sleep is one of the most important functions of the body, having a major role in six parameters:

1. Preservation of energy and promotion of anabolic processes;

2. Thermoregulation mechanisms;

3. Brain "detoxification";

4. Promotion of immunologic responses;

5. Brain development and maturation;

6. Memory consolidation and brain plasticity.

Sleep deprivation is a stressful event with severe consequences to the organism, such as fatigue, reduced psichomotor performance, lack of attention, reduced reaction time and ability to form new memories, bad mood and irritability.

The sleep-wake cycle can be explained by the interaction of the circadian rhythm with a homeostatic process (Geraldes and Paiva, 2014). The circadian rhythm is generated endogenously, having the suprachiasmatic nucleus as main responsible structure. The most powerful *zeitgeber* is light, being the main circadian synchroniser, with the ability to delay or advance the circadian phase. The homeostatic process related with the sleep-wake cycle works as regulator of the sleep *debt*, correspondent to the feeling of need of sleep (Koyama et al., 2014). A consolidated sleep can only be obtained if the circadian and homeostatic processes are in phase, according to this hypothesis.

One's preference of sleep schedules can be distinguished in chronotype: morning, intermediate and evening chronotypes. If these preferences are too extreme, the person may suffer from circadian rhythm sleep-wake disorders, as they may not be aligned with the social or professional demands. This misalignment between the two has consequences like increased fatigue, stress, decrease of sleep quality and impairments in social, occupational and educational performance.

2.1 Diagnostic methods for sleep disorders

The most used diagnostic tools for sleep disorders are anamnesis (or medical history), actigraphy and sleep logs,

polysomnography, dim-light melatonin onset measurement and sleep related questionnaires. Anamnesis and questionnaires give an overview of the outlines of a patient's complaints. Sleep logs are filled in by the patient to document their sleep habits and schedules. The actigraphy, conducted for several days or weeks, is able to distinguish sleep and awake periods, measure the activity/inactivity levels, total sleep time, sleep latency, sleep percentage, total awake time, awake percentage, number of awakenings. Paiva and Penzel (2011) highlight the usefulness of the actigraphy, as it allows the determination of a robust circadian pattern. Polysomnography (PSG) consists on the simultaneous and continuous recording of several electrograms and other variables through the course of one night. (Pandi-Perumal et al., 2007) state that the dim light melatonin onset (DLMO) is the most accurate marker for assessing the circadian phase and has been often used to evaluate problems related with the onset and offset of sleep. As mentioned by Fahey and Zee (2008), DLMO typically occurs around two to three hours before habitual bedtime. Quian et al. (2017) and Burgess et al. (2017) point out that the reference values for DLMO do not account individual differences and that patients that suffer from circadian disorders tend to present higher variations. These tools present a high variability of format and parameters depending on the patient, the studied disorder and the brand or model of the equipment. The files generated by diagnostic equipment can take up to 1 gigabyte of memory. The combined use of these tools provides a more complete and a better understanding of the possible diagnosis.

2.2 Delayed sleep phase disorder

Delayed sleep phase disorder is a type of circadian rhythm sleep-wake disorder, characterised by a significant delay in the sleep-wake cycle. These patients present normal sleep parameters when they are allowed to sleep in their preferred schedule (a delayed one, compared to the socially acceptable standard). The common causes to all age groups are environmental factors, such as, increased exposure to bright light during the evening or decreased exposure to light during the morning, inadequate adjustment to changes in work or social schedules, stimulants abuse, psychological, medical or environmental stressors (American Academy of Sleep Medicine, 2014). DSPD is often often misdiagnosed as other comorbidities, especially psychiatric disorders, leading to the inappropriate prescription of psychoactive drugs (Stores, 2007). The most common treatments for this disorder include phototherapy, melatonin and behavioural adaptation, preferably with combined use (Fahey and Zee, 2008).

3 Supporting technologies and tools

3.1 Data requirements for clinical applications

Clinical data follow the FAIR principles in order to facilitate the discovery, access, integration and analysis of scientific information, as well as to ensure proper data retrieval, annotation, archival and long-term care of the data. To ensure data has higher degree of "FAIRness", the use of standards is necessary (Wilkinson et al., 2016). HL7 has a complete standard protocol for information exchange, called FHIR[1], presenting a large set of modular components. Each component presents a data structure, including the type and description of each element. The use of FHIR ensure the data is more accessible and re-usable. Standards for medical nomenclatures are also important to make that FAIR, contributing to the interoperability and findability of the clinical data. SNOMED CT[2] and LOINC[3] are two of the most used nomenclatures, the first with focus on all types of clinical terms, the other with focus on laboratory medicine and result reporting. Both nomenclatures provide unique codes to each different term, ensuring data is unambiguously and clearly recorded. LOINC is incorporated in SNOMED CT, facilitating the combined used of the two.

Ensuring the confidentiality, privacy and data security aspects of the data is a moral obligation of the developers of any clinical platform. Protecting a patient's right to privacy and confidentiality brings benefits both for the individual and the society, by enabling better care for the patient and better public health for the society. The main guidelines regarding the use and treatment of personal data for Clinical Investigations, provided by CNPD to ensure data security include:

1. Ensuring logical separation between health and personal data;
2. Restricting access to different levels of data privileges;
3. Requiring passwords for authentication;
4. Transmission of data should be encrypted;
5. Physical and logical access to the servers should be restricted;
6. Regular backups should be made;
7. Measures to ensure safe circulation of data should be taken.

[1]HL7 FHIR Release 3 (Consulted: 29/08/2017) - `https://www.hl7.org/fhir/index.html`

[2]SNOMED International: SNOMED CT (Consulted: 30/08/2017) - `http://www.snomed.org/snomed-ct/what-is-snomed-ct`

[3]LOINC: Get Started (Consulted: 31/08/2017) - `https://loinc.org/get-started/`

3.2 Software requirements for the SleepData platform

SleepData will process large amounts of data, with varying data formats depending not only on the patients' cases but also the doctors' assessments. SleepData aims to be scalable and the platform will not require complex transactions. Additionally, SleepData will store both unstructured (like clinical notes manual reports) and structured data (like automatically generated reports and laboratory results). Hence, a document-based DBMS is the type that best suits the requirements. MongoDB, an open source document-based DBMS, came to our attention not only as the most popular open source document-based DBMS, but also as a system that fits the requirements of SleepData. MongoDB has the following properties:

1. Appropriate to store both structured and unstructured data;
2. Easily scalable;
3. Appropriate to deal with big amounts and different formats of data;
4. Low complexity;
5. Short development time needed.

Further advantages of using MongoDB are the highly available documentation and tutorials, that facilitate its use.

A web server program had to be chosen from a set of open source solutions. From this set, the most used web server is Apache. Another alternative is building a web server with Node.js, a server-side JavaScript runtime built on Chrome's V8 JavaScript engine. The main difference between the two is that Apache has a synchronous architecture, while a web server built with Node.js has an asynchronous one. According to Lei et al. (2014), a Node.js web server can handle far more simultaneous requests due to its asynchronous, non blocking, event-based behaviour, making it the best choice for handling dynamic content and multiple users. A performance study, by Chaniotis et al. (2015), concludes that *Node.js offers client-server development integration, aiding code reusability in web applications, and is the perfect tool for developing fast, scalable network applications.* Node.js, a server-side JavaScript runtime environment, has one of the biggest free and shareable repository of JavaScript packages that facilitate the resolution of specific development problems, both on the server and client sides, called *npm*. One of those packages is *Express*, a web framework. One of the main feature this framework offers is routing, which defines how the server responds to a request from the client. Express has several HTTP utility methods that allow the design of a RESTful API[4]. Together with AngularJS, these three technologies combined compose the MEAN stack architecture.

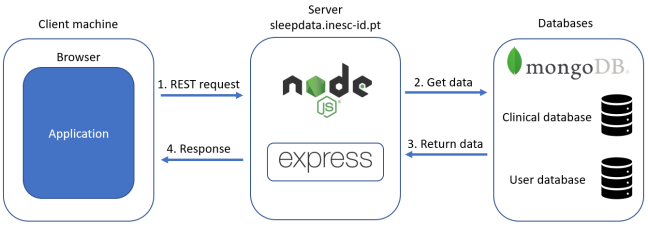


Figure 1: SleepData's software architecture

To ensure the security of the data, communication between server and client over HTTP should be done under an encrypted connection using the SSL protocol, which is the same as saying it works under a HTTPS protocol. By acquiring a SSL certificate from a Certificate Authority, the users/browsers know that no other connection is *listening*, that the data is not modified or corrupted and that the website is authentic.

4 SleepData

SleepData has an architecture similar to the MEAN stack (see Figure 1): MongoDB was chosen as the database management system, Node.js was used to build the web server and *Express* was chosen as the web framework. Considering the time available to build SleepData, it was decided not to use AngularJS and to stick to simple JavaScript and HTML.

SleepData is currently at one of FCCN/FCT's[5] data centers through the following domain: `https://sleepdata.inesc-id.pt`. This allows SleepData to be accessible to any device with an internet connection, whether it is a laptop, tablet or smartphone. We have obtained a signed SSL certificate from DigiCert[6], a Certificate Authority recognised by the most popular browsers.

4.1 Data modelling

As a database in MongoDB is comprised of collections of documents, the data modelling of SleepData consisted in specifying the JSON structures for each main concept. SleepData is composed of two databases functioning together: one for the data related with the patients and the clinic, another one for user permissions. The clinical database has collections of documents with information about the patients and their clinically relevant documents, professionals and their roles. Each document has an unique identification code. If the document is related with a patient, it also include the patient's unique ID. The same happens for documents related with other documents. For every clinical field or exam, SNOMED CT, LOINC and/or the clinic's chosen coding system codes are

[4]Express: Routing - `https://expressjs.com/en/guide/routing.html`

[5]FCCN - `https://www.fccn.pt/`

[6]DigiCert - `https://www.digicert.com/`

included. Other used coding systems include ISCED2011, ISCO and drinking levels by NIAAA. Several document types were structured as FHIR Resources [7], with their content adapted to fit SleepData needs (see Table 1).

The user database is composed of one collection where each document represents a user account. This database is essential for data privacy and security, as it is important to ensure access control in SleepData. The level of information given depends on the user's permission type. The platform distinguishes its users by giving them accounts with different types of permissions. There are three types of user accounts: Regular User, Professional User and Administrator. Regular User account is intended for patients or anyone who wants to answer to the available questionnaires. Professional User account is intended for professionals of the clinics that want to use SleepData, to manage clinical information about their patients. Administrator account is intended for administrative purposes only. Since the purpose of SleepData is to hold data from multiple clinics, it is possible to distinguish Professional User accounts from different clinics. That way, every Professional User can perform the same actions, but only related to patients associated to that clinic. Another important aspect is that Regular User accounts can be associated to a clinic.

4.2 User interface and user experience

Upon logging in, each user is redirected to a set of web pages that can only be accessed depending on user's type of permission. Regular permission users can only answer questionnaires and manage their personal information. The user is then redirected to the chosen questionnaire. Users with Professional User permission are redirected to a homepage where they can perform the following actions:

- Perform administrative actions related to his/her clinic, like creating new patients files or map an existing patient record to a Regular User account;
- Fill in forms like Clinical Notes, Polysomnography Exam (important parameters from the raw files) and Night Diaries;
- Fill in Actigraphy and PSG reports;
- Add laboratory exams, like DLMO and Vitamin D;
- Add raw Actigraphy and PSG files;
- View patient data and populations statistics.

Administrator permission users can manage users permissions, professionals and clinics. File upload requires parsing from the original file format to JSON format, which the platform is able to do automatically. SleepData suggests the format of the file the user should upload according to the type of equipment that generated the file. To avoid mistakes, it is not possible to fill or add a clinical report/file without first choosing the patient corresponding to the document. Several forms allow the user to add information to the database. Questionnaire forms are designed to require an answer in mandatory fields. Clinical forms do not have a restricted number of parameters nor mandatory fields, as variability and subjectivity is most often present. For that reason, clinical forms have the following characteristics, which allow a better overview of the form without overloading the user with unnecessary information (see Figure 2):

1. Organised in sections by type of information;
2. Allow adding comment fields when selected;
3. Show further options when selected.

To facilitate data visualisation and the diagnosis process, two patient dashboards were created: one that highlight features related with DSPD, another one related with insomnia. Both dashboards follow the same principle: allow visualisation of specific variables and parameters relevant to the disorder, with colour cues to provide to the professional a quick understanding of the patient's state. If justified, each parameter has a colour code: normal values are highlighted in green, while abnormal values are yellow, orange or red. This allows the user a faster recognition of the patient's state. A snapshot of part of the insomnia dashboard of a random patient is shown in Figure 3. Although insomnia is not the main focus of my thesis, my colleague's thesis, Castanheira (2017), explores it in detail. Concerning DSPD, a few aspects of the dashboard should be highlighted:

1. Actigraphy often computes minimum, average and maximum values related with the days it was used. To avoid visual confusion in the dashboards, only the average values are coloured.
2. Some parameters, often lifestyle related, do not have a colour code as their values cannot be seen as "good" or "bad". Nonetheless, they are important to the process of diagnosis.
3. The sleep quality and chronotype questionnaires results presented are separated into work and free days. In patients with DPSD, these results often differ, as work/school schedules affect the desired sleep schedule, and thus sleep quality and computed chronotype.

Several charts were created to assess the existing population, based on Google Charts. SleepData allows the user to choose the type of population among three options: general, patient's diagnosed with DSPD and patient's diagnosed with insomnia. The charts include all types of clinical files and give and overview on the distribution and variance of the values of each parameter. SleepData Population Statistics charts are divided by source.

[7] FHIR: Resource Index (Consulted between March and June 2017) - `https://www.hl7.org/fhir/resourcelist.html`

Table 1: SleepData's clinical database collections and their mapping to FHIR resources

Collections	FHIR's resource	Content
Patient	Patient	Patient's data and contact information
Professional	Practitioner	Professional's data and contact information
ProfessionalRole	PractitionerRole	Information on the role of each professional and their schedule
ClinicalNotes	Observation	Parameters collected in clinical notes, with the exception of medication
Medication	Medication	Medication a patient takes, doses and active ingredients
Actigraphy	Observation	Actigraphy parameters from the automatically generated report
ActigraphyReport	Observation	Parameters of the report produced by the clinical staff concerning actigraphy results
PSG	Observation	Parameters of PSG observed by the clinical staff concerning PSG results
PSGReport	Observation	Conclusions taken out of the analysis of PSG and night diary
NightDiary	Observation	The diary produced by the clinical staff during a PSG
DLMO	Observation	Parameters of the DLMO exam

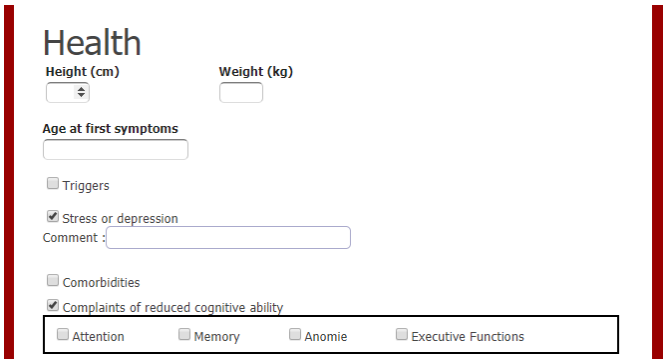


Figure 2: Partial Health section of the Clinical Notes form. The information below the selected fields does not appear in the form until the field is selected.

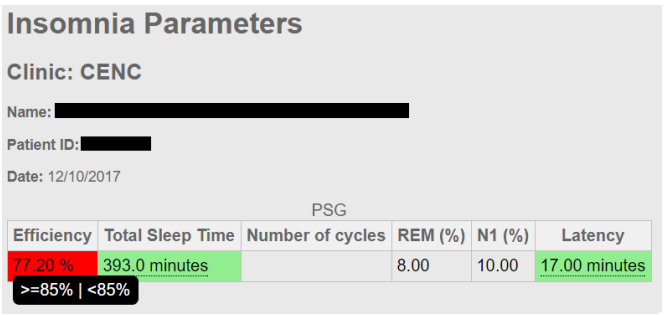


Figure 3: Insomnia Patient dashboard (partial snapshot, only PSG parameters)

4.3 Overview on SleepData's features

To have a good understanding of the status of SleepData platform, it's useful to look at each requirement and how they were met:

FAIR data Unique identifiers, standardised FHIR Resources to structure clinical documents, SNOMED CT, LOINC, ISCED2011, ISCO and NIAAA.

Logical separation between data Health documents do not have personal information and vice-versa.

Different access levels and controlled access Different account permissions give access to different documents. Password authentication implemented, but stronger authentication methods in library possible.

Update and delete users Administrator is able to delete accounts and change permissions.

Prohibit access to unauthorised people Authentication of platform by x509 certificate in SSL connections. Validation of users.

Encrypted transmission HTTPS connections enforced.

Access to servers restricted Platform hosted in secure data centre (FCCN).

Frequent backups SleepData host managed by data centre professionals.

Professional secrecy IST students and faculty signed confidentiality agreements before having access to the CENC data.

Scalable DBMS MongoDB.

Scalable web server Node.js.

Web framework that handles RESTful API *express*

Multi-clinic platform SleepData is able to handle information of several clinics. It is possible to create new clinics.

Integrate clinical information from different sources Clinical notes, sleep questionnaires, actigraphy reports, PSG reports and DLMO exams.

Automatic update and processing of the data Clinical forms, questionnaires and parsing methods prepared to receive information and update database.

Tools for statistical analysis Several charts.

Diagnostic tools Colourful dashboards.

Considering the topics above, SleepData is a fairly consistent prototype for a more advanced and better platform for integrating sleep medicine data. SleepData already has information about CENC patients. The personal information of over 5000 patients was uploaded, together with the clinical information of two selected sets:

- 145 patients previously diagnosed with DSPD;
- 100 patients previously diagnosed with insomnia.

These two sets were used to test SleepData's capacity to deliver the intended information of population statistics and to work as a support diagnostic tool for DSPD (and for insomnia, in Castanheira (2017)).

5 Characterisation of the DSPD population

The characterisation of the DSPD population was conducted using the data set provided by CENC. This data set is comprised of patients that were or are being treated for DSPD. All charts and results used in this characterisation were provided by SleepData's statistical analysis tools.

5.1 Characterisation

Out of 123 patients being treated with DSPD, more than 25% have between 20 and 30 years old, and that more than 65% of patients have between 20 and 50 years old. Regarding distribution of the age at first symptom reported by 75 patients, 52% report having the first symptom between the ages of 6 and 20 years old. These values show that, although children and teenagers suffer from DSPD the most, they don't seek treatment until they reach adulthood. There are three possible explanations behind these results:

1. Increased difficulty in dealing with the disorder when confronted with certain responsibilities associated with adulthood – like work schedules – leads to increased search for medical treatment;
2. Parents believe the symptoms in children and teenagers are age related and do not think medical advice is needed;
3. Cumulative effects of an untreated disorder leads to higher demand for medical treatment in older age groups.

More than a third of the 145 examined patients complain about family conflicts, while at least 10% report traumatic experiences, academic underachievement or feeling stress or depressed. While these features may not be the reason behind DSPD, they might be some of the main triggers, as they provoke stress and worry in the patients, leading to difficulty falling asleep, delaying the sleep phase of the patients.

Among the studied comorbidities, the most common is anxiety, affecting about 60% of the population, followed by insomnia and depression, with 54% and 48% respectively (see Figure 4(a)). It is possible to see that more than 73% of the patients have between two and four comorbidities (see Figure 4(b)). Given the common triggers to these disorders include the stressors mentioned above, it is expected that each patient develops more than one disorder. This supports the fact that DSPD is not easily diagnosed, as it is associated with many other comorbidities, thus leading to the its misdiagnosis.

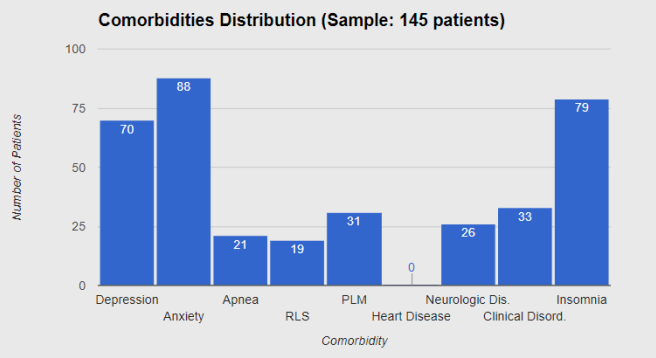
Regarding sleep schedules, about 80% of the patients go to bed between 1 and 4 AM and wake up between 9 AM and 12 PM, showing a phase delay of one to four hours. Out of 75 patients, 27 have an average total sleep time of 420 minutes (7 hours). This indicates that these patients are getting enough sleep. However, about 30 (out of 75) patients are getting six or less hours of sleep. Looking into sleep efficiency, 65.8% of the patients have reduced sleep efficiency (efficiency lower than 85%). The distribution of average sleep latency perceived by actigraphy shows that 60 out of 75 patients fall asleep is 30 minutes or less. However, most of those patients experience maximum latency of up to two hours (120 minutes). These results support the hypothesis that the patients are either trying to follow a sleep schedule that is not on their sleep phase, probably sooner than that, or patients are taking a long time to fall asleep, a probable indicator of insomnia.

Figure 5 compares the average bed time hour as reported by the patient in a sleep diary and as perceived by the actigraphy, and the bed time hour when the patient did a PSG. Looking at the chart it is possible to verify that the bed time hour perceived by the actigraphy is often much later than the one reported by the patient or even later than the bed time hour of the PSG exam of the patient. This tendency is more notable for later hours. The results of computing the difference between the average bed time hour of the actigraphy and other two sources show that:

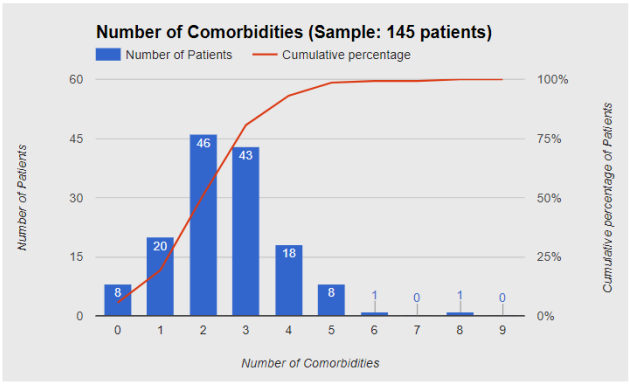
- The bed time in actigraphy is nearly one hour later than the one reported by the patient in their sleep diary;
- The bed time in actigraphy is nearly two hours later than the one perceived by PSG.

Looking at these results it is possible to point out two things:

1. Patient's often report their bed time hour to be



(a)



(b)

Figure 4: (a) Distribution of main comorbidities and (b) Distribution of number of comorbidities per patient with cumulative percentage

sooner than it actually is: either it is misjudged by the patient or misreported on purpose;

2. PSG is often conducted earlier than the usual bed time hour of the patient.

Bear in mind that PSG is conducted in a clinic's sleep lab, where patient have a lot less stimuli than at home: calm environment, no access to television or bright screens and dim-light conditions. The fact that patients are able to fall asleep earlier and that their sleep efficiency and sleep latency show improvements in this type environment leads to an interesting hypothesis concerning this set of patients with DSPD: the disorder may be mainly caused by behavioural aspects rather than physiological, since patients present a good and earlier sleep pattern when the stimuli are reduced.

5.2 The role of DLMO in the diagnosis of DSPD

One way to determine if the melatonin circadian cycle is in phase with the sleep cycle, is to compute the phase angle between the time at sleep onset and the time at DLMO:

$$\text{Phase angle} = \text{Time at sleep onset} - \text{Time at DLMO}$$

Only 8 out of 55 patients present a normal phase angle presents values (between 120 to 180 minutes, see Figure 6). Considering the set of patients who have values nearly normal (1-2 hours and 3-4 hours of phase angle), this represents only 40% of patients with the production of melatonin in phase with the sleep cycle. This does not mean that the other 60% were mistakenly diagnosed with DSPD, as the production of melatonin in phase is not a mandatory criterion to diagnose this disorder. About 45% of these patients present a delay of the production of melatonin higher than the delay in sleep phase (phase angle between -4 to 1 hours). These results are not consistent with the studied bibliography (Fahey and Zee, 2008). By comparing these results with the ones presented in the literature, we can point out two aspects:

1. There is a high variation of phase angle, which can be explained by individual differences;

2. DSPD can be often caused by behavioural aspects and not physiological.

Both these aspects point to same conclusion: DLMO may not be a good marker for DSPD, considering the data set available.

The results of DLMO are not consistent with the disorder, possibly due to individual differences. Additionally, DSPD can have behavioural and not physiological causes, leading to the conclusion that DLMO is not a good marker of DSPD for this set of patients.

6 Conclusions and Future Work

This paper presented the design and development of SleepData, a clinical platform oriented for sleep medicine.

The use of standard protocol for information exchange, FHIR, for modelling the most common information resources, such as patient and clinical notes, together with nomenclatures like SNOMED CT and LOINC, make the integrated clinical data more FAIR. The guidelines provided by CNPD to ensure data protection were also taken in consideration. SleepData software architecture resembles the MEAN stack: MongoDB was chosen as a DBMS due to its scalability, its capacity to store structured and unstructured data and to deal with big amount of heterogeneous data. On the server-side, Node.js, a JavaScript runtime environment, was chosen to build the server, together with *express*, a web framework. The transmission of data between server and client is done under an encrypted connection by a SSL. The chosen tools proved to be appropriate for the type of platform we intended to build.

SleepData can be used to support the the daily activities of any sleep medicine clinic. Clinics can manage their patients and fill in clinical forms. Patients can answer sleep medicine questionnaires. SleepData has analysis tools that support the diagnosis of DSDP and insomnia

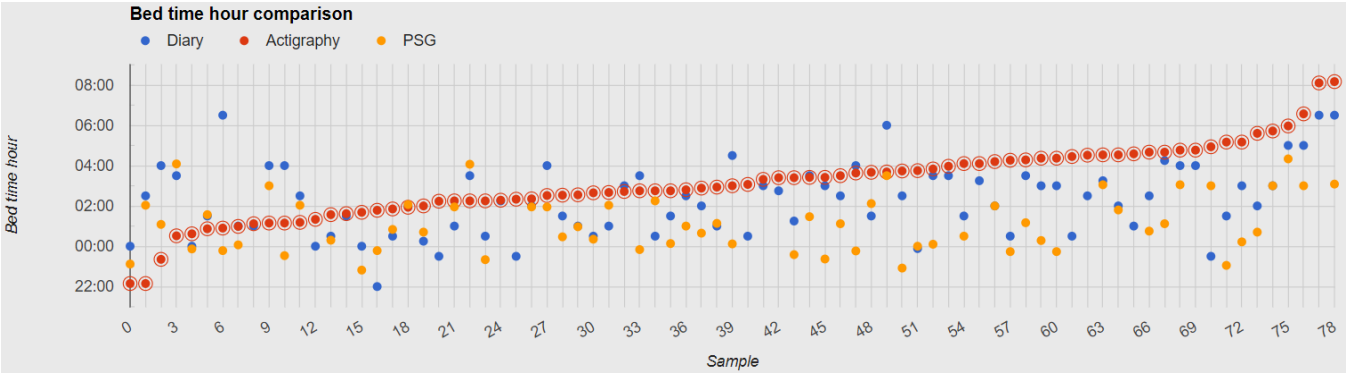


Figure 5: Average bed time hour reported in a sleep diary (blue), actigraphy (red) and PSG (yellow). Each vertical line (sample) represents the average values for the same patient. The samples are sorted in ascending order by bed time hour (actigraphy).

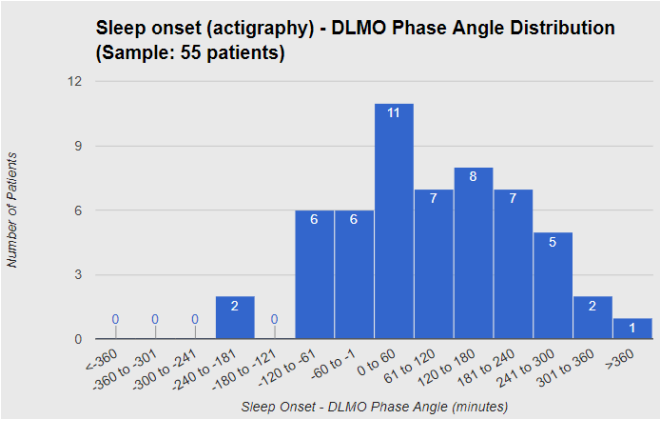


Figure 6: Distribution of phase angle between time at sleep onset (as computed by actigraphy) and time at DLMO, in minutes

and statistical tools to assess sets of patients. The platform was loaded with DSPD and insomnia patients from CENC.

To ensure the usability of SleepData's tools, the clinical outlines of sleep disorders were taken into consideration. There was a detailed study about the diagnostic tools used in clinical practice and about DSPD. In this analysis we saw that the diagnostic tools present high variability of format and size and that the relevance of DLMO to the disorder's diagnosis needs further investigation.

SleepData is a consistent basis for a more developed platform for integrating sleep medicine data. It should not be considered as a final product for clinics, as many features still need to be implemented. Additionally, it was decided not to use AngularJS. Although this did not affect the goals intended for SleepData, AngularJS could have provided a more consistent and dynamic interface. Additionally, SleepData data would benefit from Encryption at Rest in MongoDB.

This paper also included a characterisation of a set of patients diagnosed with DSDP, using the SleepData tools for statistical analysis. Most patients present a delay in sleep phase of 1-4 hours, poor sleep quality and comorbidities associated with psychological disorders. One of the most relevant features that CENC patients with DSPD present was the ability to fall asleep earlier in environments with reduced stimuli. This may show that DSPD, in this set of patients, is caused by behavioural aspects. Regarding DLMO, it was found that, contrary to the literature, the melatonin production cycle did not present the same phase delay as the sleep cycle. This supports studies that show that DLMO should not be used as a marker for DSPD. It would have been relevant to study parameters like light exposure and schedules of physical activity. However, this was not possible due to the structure of the data set provided.

6.1 Future work

SleepData is a consistent prototype and has the potential to become a more developed and advanced product. It is possible to foresee what improvements on interface, infrastructure and security would make SleepData a better platform for integrating sleep medicine data:

Managing exams Allow visualisation of files inserted, such as clinical notes and reports. Allow Professional User to compare different versions of the same file, to assess evolution of the patient.

Dynamic content Allow the user to choose what fields to see, what data set to study and what type of charts in dashboards and statistics pages.

Filters for other sleep disorders Design dashboards and statistics pages to analyse specific data considering other sleep disorders than DSPD and insomnia.

Multilingual interface Provide translation in other languages.

Sleep diary Allow patients to fill in their sleep diaries in SleepData.

Bulk inserts Allow clinics to import data to sleep data in bulk.

Add option to associate patient with diagnosis Allow physicians to a patient's data to the statistical analysis of a disorder.

Universal account Create a universal account type that allows access to anonymised clinical information, to conduct clinical studies.

Machine learning algorithms An integrated analysis of a patient's clinical data and other universal data available could ease the physicians burden of diagnosis by notifying or alerting them to certain parameters.

Email authentication Allow users to authenticate with their email address.

Two-factor authentication Confirm a user's claimed identity by using two different components combined.

Allow password change In case the user needs to recover the password or simply wants to change it.

Regarding DSPD and the use of DLMO as a marker, further studies with larger and more detailed data sets are still needed. It is important to understand how relevant light exposure, physical exercise and other stimuli are, as they clearly affect the circadian sleep cycle. It is also relevant to study how these factors may have no effect on other circadian cycles, such as the production of melatonin.

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