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Mathematical modelling of sleep fragmentation diagnosis

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ABSTRACT

Polysomnography (PSG) is the recording during sleep of multiple physiological parameters enabling to diagnose sleep disorders and to characterize sleep fragmentation. From PSG several *sleep characteristics* such as the micro arousal rate (MAR), the number of sleep stages shifts (SSS) and the rate of intra sleep awakenings (ISA) can be deduced each having its own *fragmentation threshold value* and each being more or less important (*weight*) in the clinician's diagnosis according to his specialization (*pulmonologist*, *neurophysiologist* and *technical expert*). In this work we propose a mathematical model of sleep fragmentation diagnosis based on these three main sleep characteristics (MAR, SSS, ISA) each having its own *threshold* and *weight* values for each clinician. Then, a database of 111 PSG consisting of 55 healthy adults and 56 adult patients with a suspicion of obstructive sleep apnoea syndrome (OSAS), has been diagnosed by nine clinicians divided into three groups (three *pulmonologists*, three *neurophysiologists* and three *technical experts*) representing a panel of *polysomnography experts* usually working in a hospital. This has enabled to determine statistically the *thresholds* and *weights* values which characterize each clinician's diagnosis. Thus, we show that the *agreement* between each clinician's diagnosis and each corresponding mathematical model goes from *substantial* ($\kappa > 61\%$) to *almost perfect* ($\kappa > 81\%$), according to their specialization and so, that the mean value of the *agreements* of each group is also *substantial* ($\kappa > 73\%$) despite the existing variability between clinicians. It follows from this result that our mathematical model of sleep fragmentation diagnosis is *a posteriori* validated for each clinician.

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1. Introduction

Polysomnography (PSG) consists in study of concurrent biophysiological electric signal shifts such as the electroencephalogram (EEG), electro-oculogram (EOG) and electromyogram (EMG) that occur during sleep. The PSG is commonly used as a diagnosis tool for the investigation of the sleep disorders and to characterize sleep fragmentation and sleep-disordered breathing such as sleep apnea (Obstructive Sleep Apnea/Hypopnea Syndrome, OSAHS). At the end of the sixties, Rechtschaffen and Kales [1] established a system of standardized rules and a scoring system for sleep stages of human subjects which enables the visual recognition by clinicians and technical experts of different sleep stages. Very recently, the American Academy of Sleep Medicine has updated these rules and technical specifications [2,3] up to five: wakefulness, non-rapid eye-movement (NREM) sleep stages 1, 2 and 3, and rapid eye-movement (REM) or paradoxical sleep (PS). Thus, the sleep stages are subsequently scored by sleep specialists every 30-s epoch. This graphic representation of the variations of the stages of sleep as a function of time leads to a temporal distribution called *hypnogram* (see Fig. 1).

Because the PSG depicts the micro and macro-architecture of sleep, it has enabled to define many indicators called *sleep characteristics* used to assess sleep quality and so, to quantify sleep

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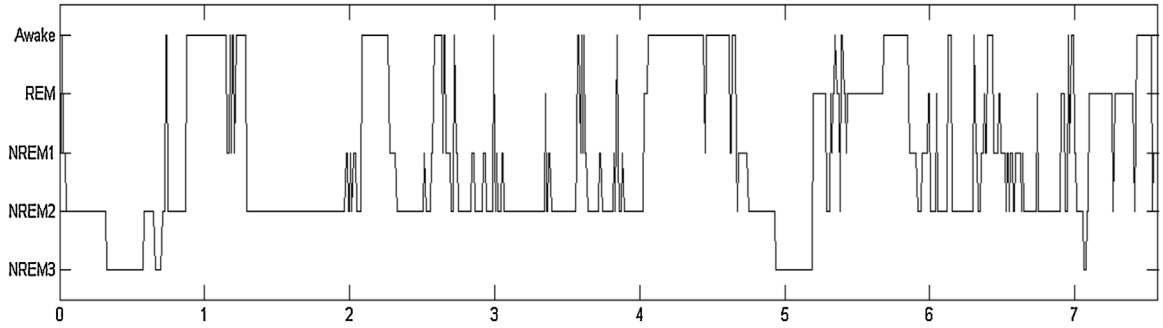

Fig. 1. Hypnogram of a patient with a suspicion of OSAS.

fragmentation. Then, from these characteristics and from their corresponding *thresholds*' values, clinicians decide whether the patients' sleep is *fragmented* or not. So, for mathematically modelling the sleep fragmentation diagnosis, a questionnaire has been sent to nine clinicians (three *pulmonologists*, three *neurophysiologists* and three *technical experts*) asking them to answer the following questions:

- What are the three main sleep characteristics enabling to diagnose a fragmented sleep?
- What are the *thresholds values* for each of them?
- What is the importance (*weight*) of each of them in their diagnosis?

It seems to be a consensus for the following three main sleep characteristics:

- the micro arousal rate (MAR),
- the number of sleep stages shifts (SSS) during the night recording,
- the number of intra sleep awakenings (ISA) by hour of total sleep time (hTST).

Concerning the *thresholds values* and the *weights* of these sleep characteristics from which the sleep can be considered as fragmented we observe some differences depending on each clinician's specialization (*pulmonologist*, *neurophysiologist* and *technical experts*). So, the clinician's diagnosis can be modelled according to three sleep characteristics (MAR, SSS, ISA) each having its own *threshold* and *weight* values.

In their seminal works, Lusted and Ledley [4–6] proposed many models from symbolic logic, probability, and value theory as a mathematical basis for logical analysis and in the use of machine aids to diagnosis. In the beginning of the eighties, Lezotte and Scheinok [7] discussed "The Role of Modelling Methods in Medical Diagnosis" using mathematical approaches which include cluster analysis, discriminant analysis, Bayesian methods, computer approaches, game theory, information theory, stochastic representations, stepwise procedures, decision analysis, and pattern recognition techniques. They pointed out some limitations of modelling methods in health care due to the complexity of the proposed model and also due to the sensitivity of the methodology to extract the informational content of the input parameters. Though mathematical models have been used in medical diagnosis since the sixties, it was only in the early nineties that they have been applied for analyzing the human sleep as exemplified by the article of Achermann and Borbély [8] who proposed a mathematical model for sleep regulation based on a continuous time dynamical systems. More particularly, it wasn't until the last decades that several indicators of sleep quality were defined including the sleep fragmentation index (SFI) [9], the weighted-transition sleep fragmentation (WSFI) [10] and the sleep diversity index (SDI) [11]. Very recently, Swihart et al. [12] proposed a modelling of sleep fragmentation in sleep hypnograms based on the extension of current approaches of multivariate survival data analysis to clustered, recurrent event discrete-state discrete-time processes. Along with these mathematical approaches, the computational modelling of human sleep using *Artificial Neural Networks* for sleep stage scoring has been also developed since the nineties [13]. Thus, it appears that mathematical models of medical diagnosis and mathematical models of sleep fragmentation have been performed with the help of probabilistic methods, statistical methods, dynamical systems, artificial neural networks and sleep indicators. However, it does not seem, to our knowledge, that there exists any mathematical model of sleep fragmentation diagnosis. Actually, the modelling of a clinician's diagnosis is not an easy task if we take into account all the factors involved in such a process. Nevertheless, following the remark concerning the limitations of modelling methods highlighted by Lezotte and Scheinok [7], the aim of our work is to propose the most simple and consistent model of sleep fragmentation diagnosis. Our model, presented in Section 3, involving three sleep characteristics (MAR, SSS, ISA) each having its own *threshold* and *weight* values is thus based on the definition of a *weighted arithmetic mean* that we call below *Mathematical Diagnosis' Index*. Statistical methods are then used for these parameters' estimation. Thresholds are deduced from Receiver Operating Characteristic (ROC) curves [14,15] while weights are computed with the help of Principal Component Analysis (PCA) [16,17], while. Hence, from a database of 111 PSG, a mathematical model of sleep fragmentation diagnosis is built for each clinician while taking into account its own specialization and which is *a posteriori* validated.

2. Material

2.1. Presentation of the PSG database

This retrospective and observational study (Protocol No. CH-2013-02) was conducted with the sleep laboratory of the Centre Hospitalier Intercommunal de Toulon la Seyne (CHITS). One hundred and eleven PSG under spontaneous breathing were selected in the sleep laboratory of the CHITS database: 55 from healthy adults and 56 from adult patients with a suspicion of obstructive sleep apnea syndrome (OSAS). The signals were recorded by a polysomnograph (Medatec®, Belgium). All the recordings were analyzed by nine clinicians (three *pulmonologists*, three *neurophysiologists* and three *technical experts*) and the sleep stages were encoded according to the *American Academy of Sleep Medicine recommendations* [2,3].

2.2. Sleep characteristics extracted from the PSG recordings

Starting from our database, each polysomnographic (PSG) signal recording leads to the representation of the temporal distribution of

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