Non-linear EEG Analysis of Idiopathic Hypersomnia

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Abstract. The electroencephalogram (*EEG*) signals are used to analyse and quantify the “depth” of sleep and its dynamic behaviour during night. In this work, we investigate a direct data-driven nonlinear and non-stationary quantitative analysis of sleep *EEG* issued from patients suffering from *idiopathic hypersomnia*. We show that the *minimum weighted average instantaneous frequency* appears to be a specific intrinsic characteristic of brain function mechanism in these patients. It could be an interesting new parameter for the quantification of sleep.

1 Introduction

The *hypersomnia* can result from a disorder of the central nervous system, what is called *primary hypersomnia*. There are two main types of *primary hypersomnia* [1,2,3]: *narcolepsy* and *idiopathic hypersomnia (IH)*. This work concerns only the automatic diagnosis of *IH*. Sleep quality and sleep duration are, in part, governed by a *homeostatic process (process S)* which increases during waking and decreases during sleep [4]. This homeostatic drive [5] can be quantified during sleep by calculating the so-called *slow wave activity (SWA)*, with Fast Fourier transform, which is the spectral power of the 0.75-4Hz band of the *EEG* corresponding to the sleep slow waves. For Sleep disorder diagnosis in routine, sleep can be analysed by the study of *electroencephalogram (EEG)* signals recorded during one night of sleep. Based on *R&K* standard rules [6], these *EEG* signals are used to quantify the “depth” of sleep and its dynamic behaviour during night. Different interesting computerized (discrete-time) automatic sleep EEG analysis approaches have been developed in the literature [7]. Among these approaches those that are based essentially on some linearity and stationarity hypothesis such as the use of *FFT* spectrum in short time of a segment of data. However, the accuracy of the *FFT* calculation is closely related to the choice of the the duration of the signal segment [7]. The main disadvantage of Fourier analysis in signal processing is that it extracts only global features of signals and does

not adapt to analysed signals. Different drawbacks of *FFT* for *EEG* analysis are given by Penzel et al. [7].

In the framework of automatic diagnosis of *IH*, the calculation of homeostatic drive during sleep with *SWA* has been widely used since Borbely's work [4], and is unquestionably a robust parameter to study *process S* regulation in response to experimental conditions such as sleep deprivation in intra-individual study design. However, the calculation of *SWA* using *FFT* has some limitations and caveats that have to be kept in mind. First, as already stated supra, *FFT* calculation relies on the assumption that sleep *EEG* is a stationary signal, which is likely not the case. Second, and more importantly, *SWA* analysis with *FFT* supposes the choice a priori of the band-width of interest. The lower limit of *SWA* band has never been strictly defined and varies across studies from 0.25Hz [8] or 0.5Hz [9] to 0.75 [10]. However, this could be of physiological importance since the *SWA* results in the combination of two distinct *EEG* generators, the cortical slow oscillation (around 0.7 Hz) [11] and the thalamic delta clock rhythm (around 2Hz) [12]. Such combination is supported by the fact that the dynamics across the night of *SWA* in response to sleep deprivation, has been showed to be significantly different for the lower part of the *SWA* ($< 1\text{Hz}$) and the upper part (1-4Hz) in both animals and humans [13] -[14]. Thus it is interesting to search for a non linear and non stationary decomposition without a priori choice of frequency bands. In Wavelet Transform (*WT*) [15] more generalized functions may be used. These functions are characterized by the frequency as well as by the time scales. Although these approaches are more effective than the *FFT*, they show at the same time much bigger ambiguity in signal decomposition. In this work, we use a more fairly recent technique called the *empirical mode decomposition* (*EMD*) [16] for nonlinear and non-stationary time series data analysis such as *EEG*. The *EMD* behaves like a bank of filters. However, the significant difference with a standard bank of filters is that the modes can be modulated in amplitude and especially in frequency. The advantage of *EMD* is that it is a data driven approach, i.e. one does not need to define a mother wavelet beforehand. In this work, we are motivated by a direct nonlinear and non-stationary quantitative analysis of sleep *EEG* issued from healthy subjects and patients suffering from *idiopathic hypersomnia* based on the *instantaneous frequency* (*IF*) using the *EMD* algorithm. The rest of the paper is organized as follows. Section 2 briefly recalls the principle of the *EMD*. In section 3 we introduce the *IF* estimation approaches. Section 4 introduces our methods for *hypersomnia* analysis. Section 5 is devoted to the results. Finally, section 6 gives some discussion and conclusions on this work.

2 Empirical Mode Decomposition (EMD)

The traditional *EMD*, recently introduced by Huang et al. [16], is simply defined by an algorithm based on empirical framework. The *EMD* can be used to decompose adaptively a signal into a finite number of mono-component signals, which are known as intrinsic mode functions (*IMFs*) or *modes*. It considers signals at

their local oscillations, but they are not necessarily considered in the sens of Fourier harmonics. Their extraction is non-linear, but their recombination for exact reconstruction of the signal is linear. The *IMFs* admit well-behaved *Hilbert transforms* (*HT*) [19] and they satisfy the following properties: they are symmetric, different *IMFs* yield different instantaneous local frequencies as functions of time that give sharp identifications of embedded structures. The decomposition is done linearly or non-linearly depending on the data. This complete and almost orthogonal decomposition is empirically realised by identifying the physical local characteristic time scales intrinsic to these data, which is the lapse between successive extrema. For more details on the *EMD* algorithm, see [16].

3 Instantaneous Frequency Estimation (*IF*)

The *IF* was originally defined in the context of FM modulation theory in communications. Ville [17] unified the work done by Carson and Fry [18] and Gabor [19] and noted that since the *IF* was time-varying, there should intuitively be some instantaneous spectrum associated with it-with the mean value of the frequencies in this instantaneous spectrum being the *IF* [20]. The importance of the *IF* concept stems from the fact that in many applications, like our *EEG* signal analysis, spectral characteristics (in particular the frequency of the spectral peaks) are varying with time, i.e. nonstationary. In this case, the *IF* is an important characteristic; it is a time-varying parameter which defines the location of the signals spectral peak as it varies with time. Conceptually it may be interpreted as the frequency of a sine wave which locally fits the signal under analysis. Physically, it has meaning only for monocomponent signals, where there is only one frequency or a narrow range of frequencies varying as a function of time [20]. The *IF* has been applied with success to *EEG* signal analysis [21]. The *EMD* method is not itself a time-frequency representation. The use of the concept of *IF* is here interesting since the (*IMFs*) are mono-component signals. This implies that there is a single frequency at any time. There are several techniques to estimate the *IF* using the derivative of the phase of a signal. *Hilbert-Huang transform* (*HHT*) method [22] is an empirically based data-analysis method based on *EMD* and *Hilbert transform* *HT* [19] which is the most common method to estimate the *IF*. Its basis of expansion is adaptive, so that it can produce physically meaningful representations of data from nonlinear and non-stationary processes. . The results indicate that both these two methods can abstract the main characters of the *EEG*. But *HHT* can more accurately express *EEG* distribution in time and frequency domain. Thats because it can produce a self-adaptive basis according to the signal and obtain local and instantaneous frequency of *EEG*. However, the determination of this instantaneous quantity is based on the integration of the signal, which is a global operation on signal duration with the same weight for the past and for the future. Moreover, the definition of this instantaneous quantity is based on a non-causal and non-instantaneous filter and on the *FT* of the analytical signal. The estimation of instantaneous quantities requires the values of the signal that are not yet observed. Thus, we can not do that before

that the signal has been fully observed. To avoid this constraint, there are other approaches privileging essentially the notion of instantaneity to estimate the *IF* and the *IA* of a signal. These approaches use only the amplitudes of the signal and, if necessary, its derivative at the given instant [23].

3.1 Teager-Kaiser Energy Operator (TKEO)

Kaiser [23] proposed a very simple and fast algorithm to estimate the energy. That operator is called *Teager-Kaiser Energy Operator* (*TKEO*), provided that the restriction related to the signal bandwidth (narrow-band signal) is respected. In the following, the discrete version of this algorithm is presented.

Consider a discrete real value signal $x(n)$. The discrete *TKEO*, $\Psi_d[x(n)]$, may be written as $\Psi_d[x(n)] = x^2(n) - x(n-1)x(n+1)$. This operator requires no assumption on the stationarity of the signal. Its formulation shows that it is local and easy to implement. Indeed, only three samples are required to calculate the energy at each moment. The estimation of the *IF* and *IA* of a discrete signal $x(n)$ sampled at a frequency f_e is inspired by the *discrete-time energy separation algorithm - 1* noted (*DESA₁*) developed by Maragos et al. [24]-[26]

$$|a(n)| = \sqrt{\frac{\Psi_d[x(n)]}{1 - (1 - \frac{\Psi_d[y(n)] + \Psi_d[y(n+1)]}{4\Psi_d[x(n)]})^2}}, \quad (1)$$

$$\Omega_i(n) = \arccos(1 - \frac{\Psi_d[y(n)] + \Psi_d[y(n+1)]}{4\Psi_d[x(n)]}), \quad f_i(n) = \frac{\Omega_i(n)}{2\pi} f_e, \quad (2)$$

with $y(n) = x(n) - x(n-1)$. Finally, the *IF* is estimated by Potamianos et al. [27] have concluded on the interest of this operator for the estimation of the *IF* for demodulation in speech compared to the approach based on the analytical signal.

4 Methods

4.1 EEG Records

EEG-records obtained from healthy females as well as females suffering from *IH* were collected by the team at "Sleep Laboratory, Department of Physiology - Functional Explorations at Henri Mondor Hospital (Créteil-France)" for about 8 hours of sleep. There are two types of collected *EEG*-records. The first records were obtained from healthy volunteers: 9 healthy females aged 25 - 35 years while the second records were obtained from age-matched females that suffering from *IH* diagnosed with polysymptomatic form of *IH*: 11 females aged 25 - 35 years. Diagnosis of *IH* were established using the *International criteria* [5]. All the *EEG* signals, issued from the placement of electrodes C4 - O2 according to the *International 10-20 system*, were sampled at 200 Hz, with 16-bit resolution. The studied *EEG* signals were scored with 30-second epochs based on R&K standard criteria. The *hypnograms* corresponding to these signals were also used in our work.

4.2 Application of *EMD* to our EEG records

In our work, the *EMD* algorithm is used to calculate the *IMFs* or *modes*. Five modes were generated. Then, the instantaneous frequencies (*IFs*) were calculated using Equations (1-2). Analysing all night sleep necessitates analysing each of the *modes* on all night. To do that, the *EMD* is applied on each epoch (30 seconds) of the *EEG* signal to retrieve the mode of interest. For each epoch of the calculated mode, we calculate the mean of *IF* and the *energy* of the *EEG* signal of the epoch. Finally, we calculate and Plot the *IF* and the *energy* as a function of the time. To reduce noise, the values are smoothed using *median* filter for the *energy* and *Savitzky and Golay* filter [28] for the *IF*. This will provide the evolution of *IF* and *energy* during all night sleep.

5 Results

We started by applying first the *EMD* algorithm on one epoch (30 seconds) of the *EEG* signal corresponding to a healthy female “ab”. In our analysis, each *mode* reveals predominantly a certain range of frequency and that the frequency of *mode* 1 is nearly two times greater than that of *mode* 2 and so on.

5.1 Identification of the Descriptive Parameter of Slow Deep Sleep by the Study of 9 Healthy Females

The *IFs* of the different modes during a night’s sleep were calculated. We observe that the *IF* of stage 4 is always lower than the other stages. Besides, the evolution of the *IFs* during the night is almost the same for all 5 *modes*, only the amplitude of the variations decreases more and more from mode 1 to mode 5. This led us to calculate the *weighted average instantaneous frequency* (*WAIF*) [29] which has a linear relationship to the individual instantaneous frequencies. This weighting will take into account the amplitudes of the different *modes*.

Let $x(t)$ a signal decomposed by the *EMD* algorithm to N modes. The *WAIF* at time t is given by

$$WAIF(t) = \frac{\sum_{n=1}^N a_n^2(t) f_n(t)}{\sum_{n=1}^N a_n^2(t)}, \quad (3)$$

where $a_n(t)$ and $f_n(t)$ are the *IA* and the *IF* at time t respectively. The *weighted average instantaneous frequency* (*WAIF*) of one epoch is the average of the *weighted averages instantaneous frequency* (*WAIFs*) of all its points. For the nine healthy females, we noted that, whatever the stage, the *WAIF* is lower during sleep than in awakening state and it reveals very well the slow deep sleep (stages 3 and 4), particularly the very deep sleep (stage 4). Indeed, during stage 4, the *WAIF* decreases significantly. In addition, the stage-4 periods are well localised in terms of time and duration. A statistical analysis using repeated *analysis of variance* (*ANOVA*) showed a significant effect of sleep stages (wake, stage 1, stage 2 to 4, and REM) on *WAIF* for all sleep epochs ($F = 62.5$ and $p < 0.0001$). Post hoc Fisher test also

Fig. 1. The *minWAIF* of the episodes of deep sleep for the healthy female “ab”. The different *minWAIF* are indicated by red dots.

showed that *WAIF* in each sleep stage significantly differs from the three others ($p < 0.006$ for all pairs). We noticed that the most interesting parameter could be the *minimum weighted average instantaneous frequency* (*minWAIF*) reached during deep sleep episodes (one episode is a series of 30-second epochs). These episodes of deep sleep contain inevitably stage 4 (or stage 3 in case of a new type of *scoring* in which stages 3 and 4 are grouped) and possibly stages 2 and 3. Hence, we developed a simple algorithm to obtain *minWAIF* of deep sleep episodes. Fig. 1 shows that the *minWAIF* could be considered as a new parameter for quantification of sleep EEG.

5.2 Comparison of the *minWAIF* for the Two Female Groups

We compared the *minWAIF* for the two female groups (9 healthy females and 11 females suffering from *IH*). We realize two types of In this section, we compare the *minWAIF* for the two female groups (9 healthy females and 11 females suffering from *IH*). We realize two types of interpretation: visual interpretation and statistical interpretation.

Visual interpretation. In Fig. 2, one can already see that the mean of the *minWAIF* value in healthy females never drops below 0.6 Hz, while that of females suffering from *IH* drops as low as 0.45 Hz. In addition, the range of the

Fig. 2. The mean of the *minWAIF* of the first four deep sleep episodes of 2 groups

mean of *minWAIF* values in healthy females is more narrow than that of female patients.

Statistical interpretation. For all tests, the level of significance, α , was set to 5%. In order to find possible differences between healthy females and females suffering from *IH*, we compared the *minWAIF* values in both groups (9 healthy females vs. 11 female patients) using the *Mann-Whitney* nonparametric test. The test result shows that the *minWAIF* value was significantly lower in patients than in healthy females 0.7172; [0.6787 – 0.7635] (median; 25th percentile - 75th percentile) for the 9 healthy females vs. 0.6524; [0.5640 – 0.7761] for the 11 female patients ($p < 0.05$, Mann-Whitney test).

6 Conclusions

In this work, we studied a new approach for nonlinear and non-stationary quantitative analysis of sleep *EEG* signals issued from healthy females as well as females suffering from *idiopathic hypersomnia*. This approach is based on the *empirical mode decomposition* (*EMD*) algorithm and the *instantaneous frequency* (*IF*) of the *intrinsic mode functions* (*IMFs*). The *IF*, which is generated by the *Teager-Kaiser energy operator* (*TKEO*), is motivated by the objective of seeking a relevant descriptive parameter of the *neurological hypersomnia*. Our study has been validated on sleep *EEG* data issued from healthy females and patient females suffering from *IH*. Because of the similarity in the evolution of the (*IF*) in the five relevant modes, the *weighted average instantaneous frequency* (*WAIF*) was then calculated by weighting with the amplitudes of the different

modes. The results showed that the *WAIF* reveals well deep sleep (especially stage 4). However, it should be noted that the physiological interpretation of these quantities is difficult and delicate because their values do not represent in themselves the "true" physiological frequencies that are normally observed. We are interested only by their variation over time since it reflects the evolution of physiological frequencies of brain waves. Unlike the *IF*, the evolution of the signal energy is more discriminating with only modes 2, 3 and 4. The reduction of energy at the end of the night can be explained by the fact that in general the amount of deep sleep gradually decreases during a night sleep. A physiological explanation could be attributed to the decrease in frequency and increase in energy during deep sleep. The deeper the sleep is, the more brain activities slow down and become synchronised, resulting in the slower and bigger brain waves observed during deep sleep. Finally, we decided to go further by examining the *minimum weighted average instantaneous frequency (minWAIF)* reached during deep sleep episodes. Statistical tests showed that *minWAIF* is stable during the night and significantly lower among patients suffering from *IH* than among healthy females. The *minWAIF* appears to be a specific intrinsic characteristic of brain function mechanism in patients suffering from *IH*. It could be an interesting new parameter for the quantification of sleep *EEG*. Most of patients have a *minWAIF* in the range of the healthy subjects. However, the three patients who have a *minWAIF* clearly below the lowest healthy's *minWAIF* also suffer from severe difficulties to awake in the morning. Further studies will be necessary to determine if this low *WAIF* is specific to these awakening difficulties.

The results of the analysis of the *minWAIF* seem interesting and promising. However, it remains to verify in a future study the reproducibility of this parameter from one night to another in order to study the *first night effect*. This study needs *EEG* records of two consecutive nights for the same healthy females. In order to obtain a more statistically significant results, several *EEG* records issued from a sufficient number of healthy subjects as well as patients suffering from *IH* will also be required.

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