AUTOMATIC DIAGNOSIS OF ADHD BASED ON NONLINEAR ANALYSIS OF ACTIMETRY REGISTRIES

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ABSTRACT

Attention-Deficit Hyperactivity Disorder (ADHD) is the most common mental health problem in childhood and adolescence. Its diagnosis is commonly performed in a subjective manner since current objective measurements are either expensive or time-consuming. However, subjective methods tend to overestimate the severity of the pathology. In this paper, we propose a novel methodology for automatic diagnosis of ADHD based on signal processing methods. The method is constructed in two stages: 1) An automatic activity/rest detection filter which allows for a separate analysis of both types of periods and 2) A feature extraction module based on nonlinear regularity quantification of either the global signal or the detected epochs. Results on real data show that the proposed methodology can discriminate between patients and controls with sensibility and specificity values approaching 80%

Index Terms— ADHD, Automatic Diagnosis System, Activity/Rest Detection, Regularity Assessment, Central Tendency Measure.

1. INTRODUCTION

Attention-Deficit Hyperactivity Disorder (ADHD) is the most common mental health problem in childhood and adolescence with a prevalence reaching 5% of this population [1]. Currently there exist several ways to address the ADHD diagnosis which can be classified into two groups: those methods relying on subjective considerations such as parental reports or clinical interviews and those based on the observation of objective measurements (polysomnographic –PSG– and actimetry sleep reports, etc.). Subjective methods are cheaper and easier to apply than objective ones. However, higher degrees of severity than the actually existing have been reported with parental reports, even when parents are instructed for the observation task [2]. On the other hand, methods based on objective measures provide higher reliability in the diagnosis, being the PSG, the standard technique. Nevertheless, this technique has to be performed in a hospital or clinic center with the consequent temporal and economic impact.

Actimetry registries constitute a simple and economic alternative for the objective diagnosis of ADHD. A number of studies, most of them synthesized in [2], report important differences in the sleep parameters (onset latency, number of awakenings, etc.) between ADHD diagnosed (cases group) and healthy (control group) children. However, these studies are focused on the observation of specific amplitude patterns in the sleep registries, which require logs of at least, 7 days duration [3]. In addition, these studies only consider rest (sleep) epochs, which involves discarding meaningful information related to normal activity.

In this paper, we propose a novel signal-processing-based methodology for automatic ADHD diagnosis based on 24h actimetry registries. In order to assess if activity and sleep epochs can separately provide useful information for the identification of patterns related to ADHD, a first stage of our method provides automatic detection of activity/rest epochs overcoming the limitations of so far proposed approaches [4, 5, 6]. Then, we propose a nonlinear regularity measurement of the actimetry signal in order to identify meaningful patterns in either the detected periods or the whole registry. As a regularity quantifier, we have chosen the Central Tendency Measure (CTM) [7] due to its low computational cost and simplicity of the parameter setting stage in comparison with other non-linear methods.

The paper is organized as follows: Section 2 presents the proposed approach with specific subsections describing the different stages of the method. Section 3 includes the experimental evaluation of the method together with a discussion on the presented results. Finally, Section 4 closes the paper with the main conclusions obtained from the developed work.
2. METHODS

2.1. Identification of Activity/Rest Epochs

The first stage of the proposed approach aims at the automatic detection of activity/rest intervals over the actimetry logs. We have tried to overcome several drawbacks appearing in so far proposed approaches. The method in [4] is widely used to generate sleep reports in nighttime and hence, is commonly implemented in the software accompanying actimeter devices. However, it is not completely automatic, since it needs the sleep onset and finish time as inputs. In addition, the main parameters involved in the method are empirically calculated and thus, make the method device dependent. Jean-Louis et al. [5] proposed a similar method which presented the same limitations except from the fact that in this case sampling frequencies higher than 1 Hz can be dealt with. In [6] we proposed a wavelet-based full-automatic method overcoming the limitations of [4, 5]. In this case, we propose a very simple iterative filter which avoids the parameter selection issues of the wavelet-based approach, leading to a more accurate epoch identification thanks to its iterative nature.

Let \( x[n], \ n = 1, 2, \ldots, N \) be the actimetry signal acquired during a 24h period. In order to deal with the same dynamic range for each patient, and considering that in the next step we are going to obtain variability measurements instead of absolute amplitude values, we define the unitary signal as

\[
x_{unit}[n] = \frac{x[n]}{\max\{x[n], \ n = 1, 2, \ldots, N\}}
\]  

(1)

The rationale of the proposed filter is that epochs related to high global activity can be associated to normal activity while those with less activity can be assigned to sleep periods. The problem with this type of signals (see Fig. 2) is that both activity and rest periods contain high frequency variations from no activity to actual movement values so that a simple thresholding cannot be applied. In order to overcome this limitation, the step following normalization consists in low-pass filtering \( x_{unit}[n] \) by a 30 min windowed moving average yielding the filtered signal

\[
x_{av}[n] = x_{unit}[n] * h_{30}[n]
\]  

(2)

where we have selected an inverted triangle shaped window \( h_{30}[n] \) in order to give higher relevance to distant samples.

Final classification of the activity/rest epochs is performed by thresholding the filtered signal, so that the mask identifying the activity epochs is constructed as

\[
m_a[n] = \begin{cases} 
0 & \text{if } x_{av}[n] < th \\
1 & \text{otherwise.}
\end{cases}
\]  

(3)

where \( th \) is the comparing threshold. The mask identifying the rest periods is constructed as \( m_r[n] = 1 - m_a[n] \). A suitable value of the threshold value was found to be \( th = 0.025 \) since during activity epochs the filtered signal values spread over the entire dynamic range of the signal, while during rest epochs, the major part of the values are below this threshold. To illustrate this issue, we present in Fig. 1 the histograms of a filtered signal during activity and rest epochs.

![Fig. 1. Histograms of a signal \( x_{av}[n] \) during activity and rest epochs. The histograms are done with 20 intervals and scaled by the number of samples. The delineation of the signal was manually done.](image)

In order to improve the performance of this classifier, we have included an iterative stage that consists on the iterative computation of \( m_a[n] \) from an iterative signal defined as \( x_{av,\text{iterative}}[n] = x_{av}[n] * m_a[n] \). This stage is implemented in order to decrease the noise influence. By performing this iterative filtering, the histogram corresponding to the rest epochs tends to accumulate more values in the first bin leading to a better detection of these epochs. The iteration process stops when no difference between two consecutive computations of \( m_a[n] \) exists. An example of the performance of the iterative process is presented in Fig. 2 for the two iterations needed for a specific signal. Note that errors existing in both activity and rest epochs in the first iteration, disappear after the second one.

2.2. Central Tendency Measure (CTM)

The CTM is a non-linear magnitude based on a second-order difference plot whose axis are —for a signal \( y[n], \ n = 1, 2, \ldots, N \)— \( y[n+2] - y[n+1] \) and \( y[n+1] - y[n] \). According to [7], CTM is defined as the number of points that fall inside a circle of radius \( \rho \) around the origin, divided by the total number of points:

\[
CTM = \frac{1}{N-2} \sum_{i=1}^{N-2} \delta_i,
\]  

(4)

where

\[
\delta_i = \begin{cases} 
1 & \text{if } \sqrt{(y[n+2] - y[n+1])^2 + (y[n+1] - y[n])^2} \leq \rho \\
0 & \text{otherwise.}
\end{cases}
\]  

(5)
Higher CTM values are obtained from regular signals, while signals with high variability yield lower values of the CTM measure. The computation of the CTM requires only one parameter to be set: \( \rho \geq 0 \). It should be chosen as small as possible in order to be sensitive to little amplitude events, but large enough to exclude noise. A common choice is \( \rho = 0 \) though previous explorations can also be made for optimal results.

### 3. RESULTS AND DISCUSSION

In order to evaluate the performance of the proposed method for automatic ADHD diagnosis, we carried out an study on a group of 6 years-old children. The study was presented as a case-control, where the case (positive ADHD diagnosis by DSM-IV protocol [1]) and the control group contain logs from 31 and 35 children, respectively. Each log was obtained with an ActiGraph GT3x device (Actigraph LLC, Pensacola, FL, USA) which was placed on the non-dominant wrist and sampled at 1Hz during 24h for the following 3 channels: global activity, horizontal plane activity, and third axis activity.

The activity/rest filter was applied to each channel at the original sampling frequency (1 Hz). After the activity and rest epochs were identified, the CTM was evaluated for each signal in three different cases respectively involving the whole global signal, and the activity and rest epochs independently. In order to avoid noise effects due to the excessive number of non activity measurements in signals sampled at 1 Hz, joint information on 10 seconds epochs was collected for CTM calculation by time averaging, yielding a filtered signal sampled at 0.1 Hz. The distance parameter \( \rho \) was set to the common null choice, although we also present results for the optimal choice \( \rho = 2.28 \) obtained from separability analysis.

After applying the method to the different channels and epoch selections, we have 9 CTM values with potential ADHD diagnostic utility. Their discriminative capability was evaluated in two steps. First, a separability analysis was performed by means of a nonparametric Mann-Whitney test [8]. Then, we developed a linear discriminant analysis [9] in order to obtain discriminant functions able to differentiate between cases and controls. The performance of each classifier was evaluated in terms of specificity and sensitivity by constructing the corresponding Receiver Operating Characteristic (ROC) curves. Since not many subjects are available—to establish representative training and test sets—we carried out a leave-one-out test [10] for evaluation.

Fig. 3 summarizes the \( p \)-values obtained from the Mann-Whitney test for each one of the nine CTM-based indexes calculated for different \( \rho \) values varying in the interval [0, 300]. Three axes have been represented, each one corresponding to a different channel. For each channel, the \( p \)-values obtained for the different epochs are independently represented. By observing the figures, one can easily infer that the best results are obtained from low values of the parameter \( \rho \) and, though optimal figures are obtained for \( \rho = 2.28 \), the common value of \( \rho = 0 \) is a good choice.

In addition, it can be noticed that a separate analysis of the activity and rest epochs leads in general to an index with lower discriminative capability than the analysis of the global signal. By analyzing only activity epochs we have obtained \( p \)-values close to one for all the values of \( \rho \) for each channel (see blue lines in Fig. 3). Results are much better when analyzing the rest epochs (see red lines in figure 3). In all the channels there are several values of \( \rho \) whose associated \( p \)-value is much lower than the significance level \( \alpha = 0.05 \). However, the lower \( p \)-values are always obtained for the global signal (green lines in Fig. 3), which involves that considering only the sleep epochs discards meaningful information that can be very useful for ADHD diagnosis.

This is an important contribution of this work, since previous approaches only pay attention to sleep periods [2]. A possible explanation of this issue is the following: by making an independent analysis of each part of the signal, there is no information, for example, about the amount of time that a subject is resting, information that is present into the global signal. Finally, we present in Fig. 4 the ROC curves obtained from the CTM calculated over the whole global activity signal with two different values of the parameter \( \rho \). In both cases the Area Under Curve (AUC) values are near to 0.9, which reveal a high classification performance.
Fig. 3. Results of the separability analysis (Mann-Whitney test) of the CTM values in terms of $p$-value in semilog scale (vertical axis). CTM values have been computed over the activity-related part (blue), the rest-related part (red) and the global signal (green). (a) Global Activity, (b) Horizontal Plane Activity and (c) Third Axis Activity. Significant differences are considered for $p < 0.05$.

Fig. 4. ROCs for (a) $\rho = 0$ and (b) $\rho = 2.28$ for the global activity of the global signal.

4. CONCLUSIONS

We have introduced a novel method based on signal processing of 24h actimetry registries which constitutes a low-cost objective diagnosis tool for ADHD in children. Experimental results have shown that the joint analysis of activity and rest epochs by regularity assessment can provide better results than so far proposed methods based on separate analysis of rest periods. However, for applications requiring independent analysis of activity/rest periods (or for evaluation purposes as in this study), automatic detection of the different type of epochs may be necessary. A fully-automatic detection filter has also been proposed within the method. The proposed filter overcomes the limitations of those commonly used for this application.

5. REFERENCES


