Electrocardiogram Based Evaluation of Children with Sleep Related Upper Airway Obstruction

A Baharav[1,2], Z Shinar[1], Y Sivan[2], M Greenfeld[2], S Akselrod[1]

[1]The Abramson Center for Medical Physics, Tel-Aviv University, Israel
[2]Pediatric Sleep Disorders Center, Dana Children Hospital, Tel Aviv, Israel

Abstract

Sleep disordered breathing became an important health issue. It remains under diagnosed due the complexity and cost of the standard overnight polysomnography. The ECG signal contains important information concerning sleep and autonomic function. In the present study we reassessed the behavior of several HRV parameters during sleep stages. In addition we developed an algorithm, able to discriminate between different sleep stages. This classification algorithm was based on phase space of HRV parameters that have proved to be significantly different between different sleep stages in children with sleep related breathing disorder and in normal children. The algorithm was then validated on 21 children using the "leave-one-out" technique. The sensitivity of the classification was 59%-69% for different sleep stages, and its specificity between 51%-66%. The overall accuracy was 66%, less than inter-expert agreement and better than automatic PSG analysis.

1. Introduction

Sleep related upper airways obstruction cause significant compromise of breathing during sleep in children as in adults. There is increasing evidence that the resulting Sleep Related Breathing Disorder (SBD) have important impact on many aspects of childhood health, behavior and cognition. However the disorder remains under diagnosed, partly due to a certain degree of unawareness as to the signs, symptoms and impact of SBD in childhood. The main barrier to improved diagnosis rate is the complexity and cost of the standard diagnostic procedure: the overnight polysomnography (PSG) performed in an expensive medical environment. The development of new, simple, reliable and cost effective tools of assessment and diagnosis of SBD in children is of great importance. Based on previous studies performed both in our laboratory and by other investigators [1-4], we hypothesized that crucial information concerning sleep quality and architecture, SBD and its relationship with cardiovascular control can be reliably derived from a single and robust signal recorded during sleep: the electrocardiogram (ECG).

The objectives of the present study were:

To evaluate the effects SBD in children have on autonomic cardiovascular regulation during sleep

To estimate the differences in Heart Rate Variability between different sleep states in normal children and in children with various degrees of SBD

To develop a method of sleep evaluation based on information extracted from the ECG and to validate this method in normal children and in children with SBD

2. Methods

2.1. Subjects

The study population included 11 children referred to our sleep clinic for suspected SBD and diagnosed to have SBD after overnight polysomnogram. The control group included 10 volunteers, with normal sleep habits, no symptoms of SBD and normal results of the sleep study. Subjects in the control group were older than subjects in the SBD group.

2.2. Procedures

All participants underwent standard overnight PSG which included 4 electroencephalographic, 2 eye movement, 3 electromyographic channels, ECG, oxygen saturation and saturation pulse wave, end tidal CO2, oro-nasal airflow, respiratory effort by means of impedance plethysmography of chest and abdomen movement and continuous simultaneous audio-video recording. All signals were continuously monitored, digitized and stored on PC for off line analysis.

The sleep studies were scored by a sleep expert to obtain sleep stages, arousals according to gold standard criteria [5]. Each epoch (a 30 second period) was assigned a sleep stage that was used as the gold standard result for the further statistical analysis and classification procedure. Data from the respiratory parameters were analyzed according to criteria widely accepted for pediatric age.

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2.2.1. ECG derived information and parameter selection

R waves were detected from the ECG recordings sampled at 100Hz, and RR Interval (RRI) series were obtained. The following parameters were extracted from these series in the time and frequency domains:

Time-Domain:

- RRI –inter beat interval.
- Same-RR – this parameter counts the number of RR intervals that are different from the previous RR interval by no more than 1/100 second. A moving window of 3 epochs was used over the RRI series. The counter counts the number of values in the series that are different from their adjacent previous value by no more than one hundredth second:

  if $|RR_i - RR_{i-d}| <= 0.01sec$,
  then counter=counter+1

  where RR_i is the current RR value, RR_{i-d} is the RR value that precedes the current by d heartbeats. We used $d=2heartbeats$.
  Note that due to the limited sampling rate of 100Hz, R-waves timing has a temporal resolution of hundredth second. Thus, a difference of 0.01sec was used as a limit for equal RR intervals.

Time-dependant spectral components [6,7] of the RRI series:

- VLF power – Very Low Frequency power in the frequency range 0.005-0.04Hz
- LF power – Low Frequency power in the frequency range 0.04 – 0.18Hz
- HF power – High Frequency power in the frequency range 0.18-0.7Hz
- LF/HF
- (VLF+LF)/HF power

Due to a large inter-subject variability in time-dependant RRI parameters, we considered absolute as well as normalized values of VLF, LF, and HF. Two methods of normalizations were used:

- Percent normalization – for each subject, each of the parameters at each specific moment in time was normalized by the total energy **at that time**. The obtained value represents the relative power in the corresponding spectral band as a function of time.
- Level normalization – for each subject, each of the parameters was normalized by **the average total energy of the subject**. The obtained value represents the power in each spectral band relative to the average power of the subject.

2.2.2. Statistical tests for differences between sleep stages

The manual sleep scoring was scanned and periods of at least 3 consecutive minutes in the same sleep stage were chosen. For each subject the average and standard deviation of each parameter was calculated separately for SWS, LS, REM, and wake. Next we tested for significant difference between sleep stages by comparing the average values of the subjects using paired t-test. This test was applied to each pair of sleep stages for each parameter, to examine whether the values during a sleep stage differ significantly from the values of the other sleep stages. Parameters that had significant different values in different sleep stages were chosen for the classification algorithm.

2.2.3. Classification algorithm based on phase space and Mahalanobis distance

We used the "Leave-One-Out" technique to build a phase space and classify the sleep stages of the subjects. Each time we left one subject out and constructed a phase space from the parameters calculated for all other subjects.

The parameters found to have significantly different values for different sleep-wake states in the previous step of analysis served as axes of the phase space. For any given sleep study epochs from all other studies were represented as points in the described phase space: the coordinates of each point were the values of the chosen parameters during the corresponding epoch. Points with the same gold-standard stage constituted a group in phase space.

Classification of epochs from the one left-out sleep study was performed by representing each epoch as an additional point in the phase space and calculating its Mahalanobis distance to each group of points obtained from all other sleep studies. The nearest distance determined the classification of that epoch (point).

We repeated the above procedure for each subject: the phase space was reconstructed without a different study, and the given missing study was classified according to the above procedure.

3. Results

Time in bed, Total Sleep time and sleep architecture (percentage of sleep time spent in different sleep stages) were similar in both groups. Arousal index was similar in both groups indicating that sleep fragmentation was not significantly higher in the SBD group although the SBD

Table 1

	VLF	LF	HF	VLF/TOT	LF/TOT	HF/TOT	LF/HF	same rr	RRI
SWS	0.003^{LRW}	0.006^{LW}	0.021	0.183^{LRW}	0.202^{LRW}	0.613^{LRW}	0.574^{LRW}	0.617^{LRW}	0.779
LS	0.011^{SW}	0.009^{SW}	0.021^{RW}	0.310^{SRW}	0.219^{SRW}	0.460^{SRW}	1.195^{SRW}	0.745^{SRW}	0.778^{W}
REM	0.010^{SW}	0.008^{W}	0.011^{L}	0.412^{SLW}	0.254^{SLW}	0.326^{SLW}	1.590^{SLW}	1.399^{SLW}	0.743
wake	0.025^{SLR}	0.015^{SLR}	0.013^{L}	0.508^{SLR}	0.269^{SLR}	0.181^{SLR}	9.671^{SLR}	1.867^{SLR}	0.756^{L}
Sleep only	0.009	0.008	0.020	0.287	0.217	0.488	1.076	0.920	0.776
Sleep+wake	0.009	0.009	0.019	0.302	0.223	0.465	1.613	1.157	0.772

Table 2

	VLF	LF	HF	VLF/TOT	LF/TOT	HF/TOT	LF/HF	same rr	RRI
SWS	0.0022^{LRW}	0.0034^{LRW}	0.0233^{LRW}	0.1426^{LRW}	0.1435^{LRW}	0.7080^{LRW}	0.4139^{LRW}	0.6166^{LRW}	0.6636^{LRW}
LS	0.0077^{SW}	0.0061^{SW}	0.0152^{SRW}	0.3185^{SRW}	0.1925^{SW}	0.4742^{SRW}	1.0694^{SRW}	0.7448^{SRW}	0.6353^{SRW}
REM	0.0093^{S}	0.0053^{SW}	0.0090^{SLW}	0.4995^{SL}	0.1993^{SW}	0.2888^{SLW}	1.4812^{SLW}	1.3988^{SLW}	0.6209^{SL}
wake	0.0133^{SL}	0.0093^{SLR}	0.0058^{SLR}	0.5309^{SL}	0.2850^{SLR}	0.1644^{SLR}	10.454^{SLR}	1.8668^{SLR}	0.6170^{SL}
Sleep only	0.0063	0.0051	0.0159	0.3042	0.1789	0.5052	0.9565	0.9201	0.6399
Sleep+wake	0.0068	0.0053	0.0151	0.3271	0.1882	0.4731	1.5957	1.1567	0.6359

group displayed a significant respiratory disturbance index (number of obstructive events per hour of sleep: 12.54±5.6 versus 0.12±0.25). Most obstructive events were REM related. The overnight mean oxygen saturation and average REM saturation were significantly lower in the SBD group (95%+1.40% versus 97%+1.04%, $p<0.05$ and during REM: 96%+2.89% versus 98%+1.02%, $p < 0.002$, no significant difference during SWS).

Comparisons between spectral parameters in the two groups revealed no significant differences in autonomic activity during any sleep stage in contrast with previous results in children and in adults (age matched). The most likely explanation to the above result is the significantly higher age of the control group.

Comparison between parameters during different sleep stages revealed valuable results which allowed to continue with a classification algorithm.

Table 1 shows the average values for each parameter and each sleep stage for the Control group. The superscripts (^{S,L,R,W}) above each value indicate whether it is significantly different from the value of the same parameter during SWS, LS, REM and Wake correspondingly. Table 2 summarizes the same results for the SBD group.

Significant differences in a number of parameters were found in both groups. This finding is of great importance, since it allowed using the same classification parameters in all children studied, with no a priori knowledge on their respiration at night. An example of the results of the classification procedure along with all relevant parameters used by the classification algorithm for one subject appears in Figure 1. The first panel represents the Hypnogram as determined by the gold standard manual scoring. The next panel is the Hypnogram as determined by the classification algorithm. The following panels display the different parameters as a function of time (in epochs).

Classification results are summarized for all epochs in all 21 sleep studies (Controls and SBD) in Table 3.

As can be noted from the table, of the 4430 epochs that were scored as SWS by the gold standard manual scoring system, 3044 were classified as such by our algorithm, 1253 were classified as LS and only 133 were classified as REM. Similarly, of the 7758 epochs of LS, 4517 were classified correctly, and 1699 and 1542 epochs were erroneously classified as SWS and REM correspondingly. As for REM epochs, 1776 epochs were scored correctly, 1091 were mistakenly classified as LS and only 20 as SWS.

Note that the majority of errors are between LS and other sleep stages, only (133+20=) 153 epochs were classified as REM instead of SWS or vice versa.

Table 3

		Gold Standard Results		
		SWS	LS	REM
Classification Results	SWS	3044	1699	20
	LS	1253	4517	1091
	REM	133	1542	1776

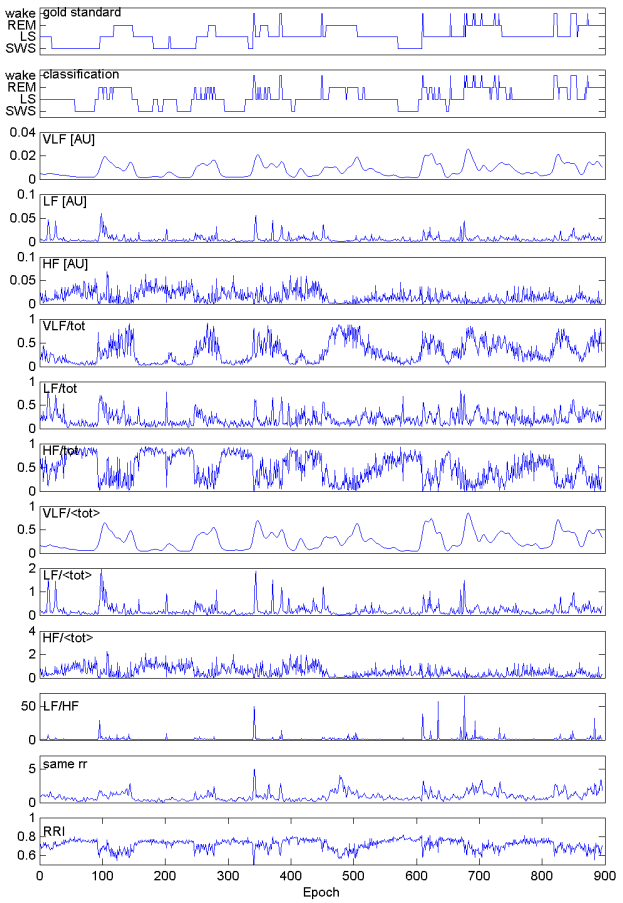

Figure 1: An example of the sleep stages and the parameters calculated along a sleep study of one subject. Abscissa is time in epochs (30 seconds periods). Top panel shows the sleep stages as determined by an expert according to gold standard criteria. Second panel shows the results of our classification according to the parameters calculated from a single lead ECG. Third-Last panels show the different parameters calculated from the ECG channel as described in the text.

4. Discussion and conclusions

The present study reconfirmed previous results concerning autonomic function during sleep in children, regardless if they suffer of upper airway obstruction or not. No difference in sleep time sympatho-vagal balance was detected between normal children and children with diagnosed SBD. This last finding does not corroborate with previous results [1], and is most probably due to the lack of age matching between subject groups.

We developed and validated a sleep stage classification algorithm based on HRV derived parameters only. This algorithm yielded accurate results for any epoch checked at a rate of 66%. Although this hit rate is less than the agreement ratio between manual expert scorings, it is much better than expert-automatic scoring based on standard PSG recordings.

The accuracy can be improved by using higher sampling rates for the ECG signal. Information derived from the ECG signal, besides HRV, such as EMG activity, body position and respiration pattern may enhance the performance of the described algorithm.

The fact that our new classification method works for normal children and for children with SBD, regardless their breathing pattern is of great importance, since it enables us to use it with no need for a priori information on the individual subject.

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Address for correspondence

Dr Armanda Baharav
Faculty of Exact Sciences
Medical Physics Department
Tel Aviv University
Ramat Aviv, Israel
e-mail: armanda@netvision.net.il