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Estimating Sleep disordered Breathing Based on Heart Rate Analysis

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***Abstract*— Heart rate variability and the analysis of the ECG with ECG derived respiration has been used to diagnose sleep disordered breathing. Recently it was possible to distinguish obstructive sleep apnea and central sleep apnea. This can be achieved by analyzing both, heart rate variability and the more mechanically induced ECG derived respiration in parallel. In addition the analysis of cardiopulmonary coupling facilitates to predict the personal risk factor for cardiovascular disorders. The analysis of heart rate, ECG and respiration goes beyond this analysis. Some studies indicate that it is possible to derive sleep stages from these signals. In order to derive sleep stages a more complex analysis of the signals is applied taking into account non-linear properties by using methods of statistical physics. To extract coupling information supports the distinction between sleep stages. Results are reported in this review.**

I. Introduction

Sleep disorders are a common problem. Among sleep disorders sleep related breathing disorders are of high importance due to their cardiovascular consequences. The prevalence of sleep disordered breathing has been reported to be between 1% and 10% of the population depending on definitions and cohorts. Sleep disordered breathing is categorized into nine subcategories according to the International Classification of Sleep Disorders (ICSD). These are (a) primary central sleep apnea (b) central sleep apnea due to Cheyne-Stokes breathing pattern (c) central sleep apnea due to high altitude periodic breathing (d) central sleep apnea due to medical condition not Cheyne-Stokes (e) central sleep apnea due to drug or substance (f) primary sleep apnea of infancy (g) obstructive sleep apnea (h) idiopathic sleep related non-obstructive alveolar hypoventilation (i) congenital central alveolar hypoventilation syndrome. These categories are separate entities according to the International Classification of diseases ICD-9. Obstructive sleep apnea is the most common type of sleep disordered breathing. It is characterized by cessations of breathing of at least 10 seconds duration, called apnea events. If there is a reduction of airflow by at least 30% with a reduction of oxygen saturation by more than 3% then a hypopnea is counted. The severity of the disorder sleep apnea is rated according to the number of apnea and hypopnea events during the time asleep, the apnea-hypopnea index (AHI). The disorder sleep apnea is diagnosed with an AHI of 5 /hour or greater. Moderate sleep apnea is diagnosed with an AHI > 15 /hour. Severe sleep apnea is diagnosed with an AHI > 30 /hour. In some countries in Europe treatment is reimbursed by health insurances without negotiations if severe sleep apnea had been diagnosed.

It is now recognized that more men suffer from sleep apnea and that sleep apnea presents an independent risk factor for cardiovascular disorders such as hypertension, myocardial infarction, ischemic stroke, atrial fibrillation and for metabolic disorders as well.

Sleep apnea occurs during sleep only. If apnea events are found during wakefulness they are not taken into account for the disorder. This is why sleep has to be recorded in parallel. At the end of each single sleep apnea event, concomitant with the drop in oxygen saturation, a large increase in sympathetic tone occurs. This goes along with an increase in heart rate and blood pressure. The apnea event is then terminated by a central nervous activation (arousal) which re-coordinates the respiratory activity and thereby opens the upper airways to deliver full airflow to the lungs and the body.

Sleep apnea is modulated by the different sleep stages. The sleep stages themselves do show a considerable variation of sympathetic tone from stage to stage. During non-REM sleep sympathetic nervous activity decreases. Sympathetic nervous activity is lowest during slow wave sleep. At the same time the vagal component is highest during slow wave sleep with a decreased heart rate and blood pressure under normal / healthy conditions. During REM sleep instead sympathetic activity is very variable with high surges of neural activity followed by cessations of activity as recorded by sympathetic nerve activity. The average sympathetic activity recorded by neurography on the nervus perineus is similar to wakefulness and higher than during non-REM sleep. Vagal activity during REM sleep is not as high as during slow wave sleep. For vagal activity only indirect parameters (e.g. derived from heart rate variability) are taken and no direct continuous variable was assessed so far.

Sleep disordered breathing is accompanied by cyclical variation of heart rate. This cyclical variation of heart rate had been described very early, shortly after the description of sleep apnea [1]. This cyclic heart rate variation is so typical, that it can be used to diagnose sleep apnea from the heart rate

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pattern alone [3]. Combining the results of previous studies it is even possible to distinguish sleep stages and severity of sleep apnea to some degree [4].

II. Methods of Sleep Apnea Recording

Before classifying sleep apnea the different types of events are depicted with recording examples in the following figures.

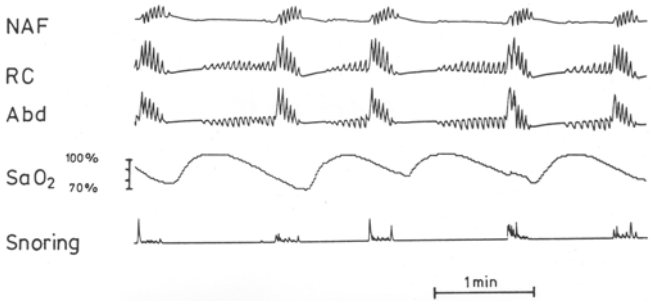

Figure 1. Example of obstructive sleep apnea events. Sleep apna events are characterized by cessations of breathing for at least 10 seconds lasting usually 40 to 60 seconds. Snoring is seen in parallel during the period of hyperventilation. In this example there is no respiratory effort in the beginning of each event and therefore these events are called 'mixed apnea events'. NAF = nasal airflow. RC = ribcage respiratory movement, Abd = abdominal respiratory movement, then pulse oximetry and snoring shows the integrated activity of a tracheal microphone. The example shows a 5-minute recording period.

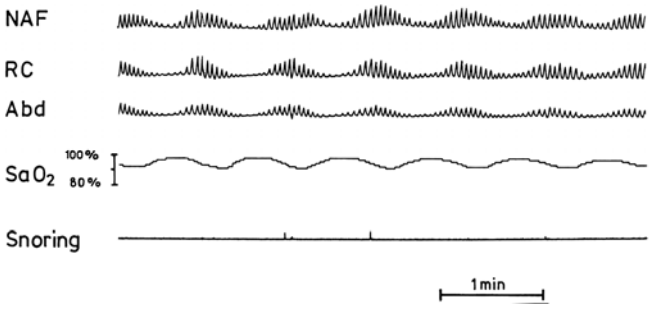

Figure 2. Example of periodic breathing with no upper airway obstruction and no snoring in parallel. The labels of the signals are the same as fig. 1.

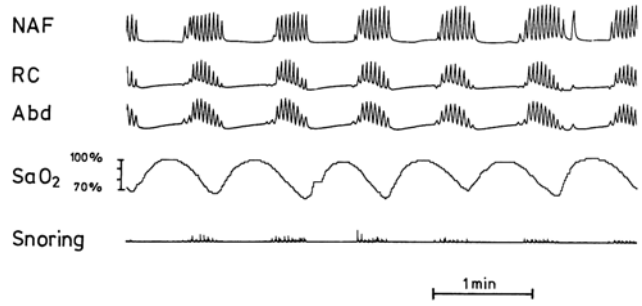

Figure 3. Example of central sleep apnea events. Central sleep apnea events are often short in duration. The respiratory effort shows a waxing and waning pattern in the two respiratory movement signals. There is no snoring noise recorded because there is no obstruction of the upper airways. Sometimes low amplitude breathing noises can be recorded – as observed in this example. Labels of the signals are the same as fig. 1.

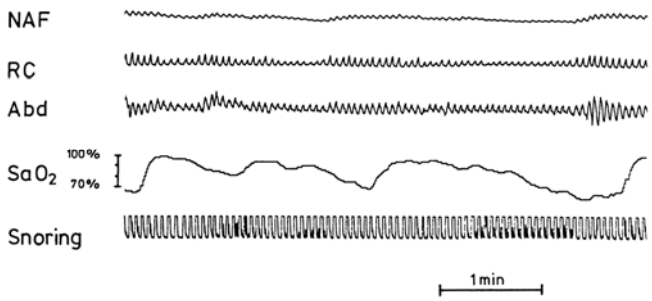

Figure 4. Example of hypoventilation periods with heavy snoring. With obstructive hypoventilation, periods were observe much snoring due to upper airway obstruction. This results in flow limitation. Respiratory effort is increased but respiratory flow and respiratory movements are often decreased – as seen in this example. Sometimes it is not easy to separate one event from the next event in order to count the total number of events. The labels in this figure are the same as fig. 1 and this is a 5-minute recording period.

This outlines the recordings obtained with cardiorespiratory polysomnography in a sleep laboratory according to international standards [5].

The different types of events depicted in Fig. 1 to 4 do show that the distinction between them depends much on the time course of respiratory signals and the time course of oxygen saturation. The amplitudes of respiratory flow and respiratory effort are evaluated. These signals are used to classify the underlying pathophysiology of upper airway obstruction and of limited air exchange leading to intermittent or sustained hypoxia and nocturnal hypercapnia. Central apnea and periodic breathing do not show upper airway obstruction but other pathophysiologies impair the breathing. This can be heart failure, prolonged cardiocirculatory times, impaired chemoreflex responses, or damages to the respiratory center in the brain stem. With that sleep disordered breathing can result from completely different pathophysiological pathways which need to be distinguished when preparing a diagnosis.

Which physiological pathways may have higher importance for pathological consequences remains an open question to be answered by future studies on mortality in these disorders.

III. Methods of Sleep Apnea Estimating

To estimate sleep disordered breathing from other signals, which are not respiratory signals but surrogates, one has to reflect how the surrogates are linked to respiration and changes in respiration.

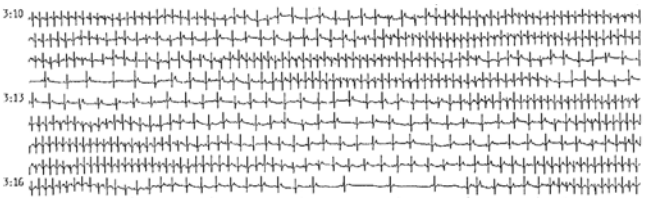

Figure 5. The recording example of ECG in a patient with sleep apnea shows the characteristic cyclical variation of heart rate which accompanies the apnea events. During each apnea there is a relative bradycardia and during the following respiration there is a relative tachycardia.

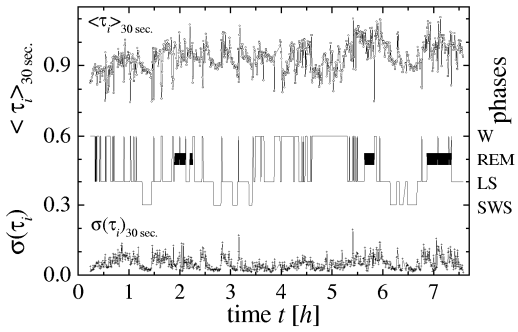

Figure 6. The entire eight hour recording a patient with obstructive sleep apnea is shown here. The time course of sleep shows a disturbed sleep pattern over the night with little slow-wave sleep (SWS) and many wake (W) periods. Labels are on the right side. 30-second mean values of heart rate (top trace) vary much due to sleep apnea. Thestandard deviation of heart rate (bottom trace) is high and very variable throughout the recording. Labels for RR-mean values and standard deviation (both in seconds) are on the left side. Apnea events in terms of number of events or apnea severity in terms of an apnea index cannot be derived from this condensed heart rate variability analysis.

With heart rate variability one is close to sympathetic tone and not to airflow. Heart rate is modulated with each single breath and is even stronger modulated by sleep disordered breathing. A simple analysis of heart rate during sleep could be a calculation of mean values and standard deviation per selected time window. In sleep medicine, the recording is scored for sleep stages visually in 30 second epochs. For each epoch a sleep stage is assigned. Fig. 6 shows the recording of one night with heart rate mean values at the top and standard deviations at the bottom calculated for the same 30-second epochs. In between the two traces are the sleep stages of this person plotted. Sleep stage characteristics cannot be recognized in this way.

Several methods can be used to derive sleep apnea events from heart rate analysis. Based on the pattern observed in fig. 5, one approach is to use frequency domain methods to extract the cyclical variation of heart rate. Applying methods for this, it has to be considered that the cyclical pattern is not very regular, because apnea events vary in duration and type. Appropriate methods for time frequency analysis must be selected. According to a method comparison it does not matter too much which method is chosen [3].

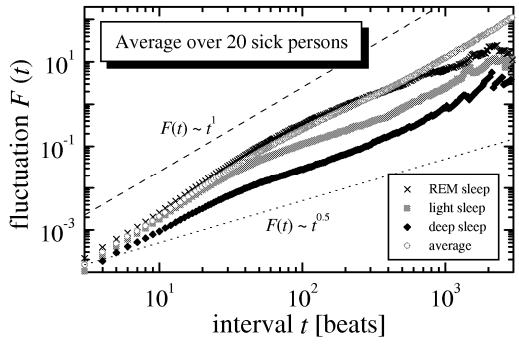

Figure 7. Detrended fluctuation analysis averaged over the heart rate of 20 patients with obstructive sleep apnea. On the slopes it is possible to distinguish sleep stages. The effect of sleep apnea is also visible by the buckle at the time scale of 40 to 60 beats.

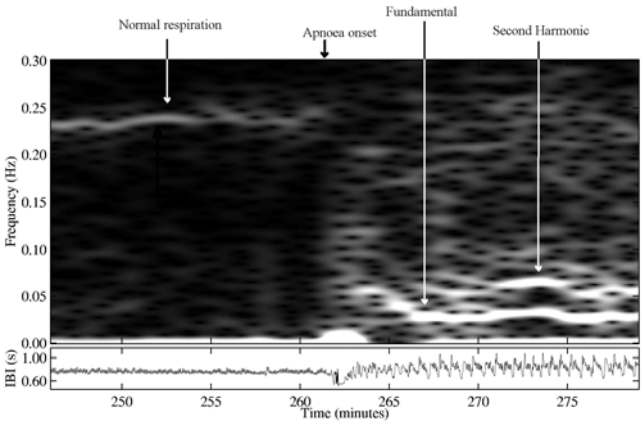

Figure 8. A time-frequency map of heart rate representing a part of the sleep recording of a patient with sleep apnea The figure had been taken from [4]. The modulation of heart rate by the normal respiration is shown in the left half and the modulation of heart rate by sleep apna is shown in the right half. The lower trace shows the inter-beat-intervals (IBI).

Detrended fluctuation analysis, a technique derived from statistical physics methods reveals short and long term correlations of successive heart beat intervals. This property depends strongly on the sleep stage. This had been shown both in healthy subjects and in patients with sleep apnea [2]. The DFA analysis for sleep apnea subjects is shown in fig. 7.

Respiration modulates heart rate as explained previously (compare fig. 8). In addition to this respiration modulates properties of the ECG itself. The amplitude of the R-wave and of other waves in the ECG are modulated due to the movement of the heart inside the chest with each single breath. This is a mechanical interaction between breathing efforts and the electrical waveform of the ECG. This modulation is independent from the autonomous nervous system and sympathetic tone. The analysis of the mechanical interaction in addition to heart rate variability allows to characterize sleep apnea. If both methods are combined the detection of sleep disordered breathing can be optimized [4].

IV. Results

The results of the studies specified do show that sleep apnea and sleep stages can be recognized if the methods used focus on the different properties influenced by sleep disordered breathing and sleep stage changes.

A number of devices which use the ECG analysis techniques mentioned here try to link this analysis technique to previous techniques for identifying sleep apnea. Already early in the portable diagnosis of sleep apnea pulse oximetry had been used. Pulse oximetry alone has large limitations in patients with arrhythmias or with additional lung diseases such as COPD when quantifying the number of oxygen desaturations (compare fig. 4). COPD with a lower oxygen baseline makes drops in oxygen saturation difficult to detect. In contrast to that subjects with a large lung capacity may experience 30 second apnea events with minor oxygen desaturation events (2 to 3% only) because their drop in oxygen partial pressure going along with the apnea event may occur in the upper flat portion of the oxygen binding

curve. As a consequence apnea events are not well reflected in the oxygen saturation curve.

Combining ECG based sleep apnea analysis and oximetry is therefore a very promising approach [7]. Earlier studies used heart rate (more precisely: pulse rate) in addition to oximetry successfully to improve the detection of sleep apnea. One retrospective study did show the advantage over pulse oximetry alone when using ECG analysis in addition. There ECG from a parallel polysomnography was analyzed. Based on these results a combined long-term ECG recording system with oximetry was tested in a prospective study and provided very convincing results in terms of sleep apnea detection [7].

Cardiorespiratory coupling in addition to this analysis can be analyzed to distinguish sleep stages [8]. The coupling information represents additional physiological regulation processes, which are independent of the previous described effects as had been proven recently. The coupling analysis results are independent from respiratory sinus arrhythmia and apnea / hypopnea events.

V. Discussions

With new analysis methods it is possible to recognize sleep stages and sleep disordered breathing by the analysis of heart rate and ECG from nocturnal recordings. This analysis provides good estimates in normal subjects and in patients with sleep disorders. In how far this is possible in patients with additional cardiac or autonomous nervous system disorders needs to be studied. The estimates for sleep stages and for sleep disordered breathing are not as good as more direct recording methods, such as polysomnography with sleep EEG or direct recording of respiratory flow and effort. Still they can serve the purpose of risk identification to initiate appropriate further testing. The methodology does not require expensive or complicated hardware.

One good improvement of the heart rate recording and analysis is the addition of a pulse oximetry as indicated by several other studies.

The aim of these approaches is to improve a portable monitoring of sleep apnea. This is useful to identify patients at risk to fall asleep, at monotonous tasks such as driving a truck on long distance roads or on supervising chemical or power plants in industry. The aim is not to provide a full differential diagnosis and to distinguish the respiratory patterns explained in the methods section of this presentation.

A second important aim is the therapy follow up of patients with already diagnosed sleep disordered breathing and being treated with either CPAP ventilation or with other devices. Those patients need to receive annual controls whether their therapy is still effective or may be even reduced. Those patients should not go to sleep centers and should not block the capacity needed for a full diagnosis. These patients could use simpler devices because then the underlying problem is recognized and needs to be quantified only.

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