Sleep Medicine as a Scenario for Medical Grid Application

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Abstract: Sleep medicine is gaining more and more interest and importance both within medical research and clinical routine. The investigation of sleep and associated disorders requires the overnight acquisition of a huge amount of biosignal data derived from various sensors (polysomnographic recording) as well as consecutive time-consuming manual analysis (polysomnographic analysis). Therefore, the development of automatic analysis systems has become a major focus in sleep research in the recent years, resulting in the development of algorithms for the analysis of different biosignals (EEG, ECG, EMG, breathing signals). In this study, an open source algorithm published by Hamilton et al. was used for ECG analysis, whereas the analysis of breathing signals was done using an algorithm published by Clark et al. using also variations of the intra-thoracic pressure for the detection of breathing disorders. The electromyogram (EMG) analysis was done with a self-made algorithm, whereas EEG analyses are currently under development, using both frequency analysis modules and pattern recognition procedures. Although all these algorithms have proved to be quite useful, their validity and reliability still needs to be verified in future studies. Taking into account that during a standard polysomnographic recording data from approximately 8 hours of sleep are collected, it is imaginable that processing this amount of data by the described algorithms very often exceeds the calculating capacity of current standard computers. Using Grid technology, this limitation can be transcended by splitting biosignal data and distributing it to several analysis computers. Therfore, Grid based automatic analysis systems may improve the effectiveness of polysomnographic investigations and thereby diminish the costs for health care providers.

Keywords: sleep medicine, grid computing, polysomnography

Introduction:

Sleep loss, excessive fatigue, stress and inattention constitute the social diseases of our century. Within the "24 hour society" people tend more and more to exchange sleep and serenity for gain or pleasure. This gradually leads to an excessive rate of sleep disorders, roughly 20% of the population suffer from one. One major symptom, associated with the occurrence of sleep disorders, is the excessive daytime sleepiness (EDS), showing a prevalence of 5-10% in the young and middle-aged and even 20-30% in the older-aged[1]. Furthermore, EDS and consecutive microsleep have become a major cause for hazardous car accidents over the last decades[2;3]. Taking these facts into consideration it is understandable that sleep medicine and also sleep related research is characterized by a rapidly growing interest.

Among the vast amount of different sleep disorders that are known up to now, some are well investigated with regard to prevalence, causes and treatment. This paper will focus on new investigational approaches for two sleep disorders having a considerable high prevalence and one sleep disorder with dramatic effects for the suffering patient. All three sleep disorders commonly cause excessive daytime sleepiness.

The obstructive sleep apnea syndrome (OSAS) with a prevalence of 4% in men and 2% in women[4] is a well investigated sleep disorder with regard to occurrence, associated symptoms, risk factors as well as overall consequences[5;6]. It is characterized by repetitive cessations of breathing during the night caused by endogenous obstructions of the upper airway followed by awakenings restoring ventilation. These awakenings, however, have impairing effects on the continuation of sleep but also on the cardiovascular system due to repetitive increases in blood pressure and heart rate during the night.

A second, also quite extensively investigated sleep disorder is the Restless Legs Syndrome (RLS), a sensory-motor disorder characterized by dysesthesia and leg restlessness occurring predominantly at night during periods of immobility. The sensations associated with RLS and the urge to move usually interfere with the ability to fall and/or stay asleep. A recent study by Winkelmann et al. revealed a prevalence of daily RLS symptoms of 4.2% in males and 5.4% in females[7;8].

Narcolepsy, the third sleep disorder this paper will focus on, very often has dramatic effects on the quality of life and employment status of the patient. Although the prevalence is quite low (app. 47 of 100.000), this disorder has been extensively investigated due to its dramatic effects for the patient and the immense socioeconomic impact[9].

The investigation of all three sleep disorders requires a very sophisticated overnight examination of patients in a specialized sleep centres, performing a so called polysomnography. During a polysomnography different biological signals of the human body are conducted and digitally recorded. A very important part of each polysomnographic recording is the conduction of the electroencephalogram (electrical activity of the brain) in combination with electrooculogram (eye movements) and electromyogram (electrical muscle activity) using electrodes connected to the patient's body. With the help of these signals, experienced technicians can analyze the overnight sleep of a patient with regard to sleep depth, awakenings and also sequence of sleep depths using standardized rules for the analysis[10]. This results in a sequence of so called sleep stages, allowing a sleep physician to rate a patient's sleep structure and also the effectiveness of sleep for a patient.

In addition to the investigation of brain waves, also ECG waves (electrocardiogram, electrical activity of the heart), respiratory related signals and electrical activity of leg muscles are recorded and analysed in polysomnographic investigations. For example, the number of breathing cessations occurring during the night helps to diagnose the OSAS. For the diagnosis of RLS, periodically occurring leg movements are counted. And one new approach for the investigation of narcolepsy is the determination of short muscle activations, the so called twitches, during the night.

The acquisition of all described biological signals during a whole night (usually app. 8h) produces a huge amount of digital data. For an interpretation of this data with regard to recognition of sleep disorders, usually a time consuming manual analysis of the recorded signals is performed. Furthermore, the quality of the manual analysis depends mainly on the expertise of the scoring technician despite there exist specific rules for most scoring procedures. Furthermore interindividual differences between human scorers make scoring results sometimes barely comparable between different sleep centres.

Automated analysis systems, being independent from human expertise and interindividual differences, have therefore become a major research focus in sleep medicine over the past decades. One major problem has always been the vast amount of data that needs to be processed by automated analysis systems, very often exceeding the calculating capacity of standard computers.

As each biological signal is stored in a single channel of the digital recording, all recorded data can be easily split and analysed separately. Thinking of GRID technology and its primary objective to split and distribute data in small packets for analysis on many different connected computers, digital polysomnographic investigations turn out to be the ideal area for the implementation of GRID based automated analysis systems.

1. Methods:

For the automated analysis of polysomnographic recordings to diagnose the above described sleep disorders, our group has developed different algorithms. The first algorithm automatically analyzes the ECG signal and detects the different waves and spikes and calculates the heart rate (time interval between R waves). The second algorithm performs automated analyses of respiratory signals (nasal airflow and esophageal pressure changes) and detects inspiratory airflow limitations. A third algorithm was created for the analysis of the electromyogram signal, determining the muscle tone as well as intermittent activations like periodic leg movements or short muscle activations (twitches).

The analysis of the ECG consists of a fully automated analysis of the ECG wave and automatic detection of QRS complexes (electrical innervation of the heart muscle) within the ECG wave, calculation of R-R-intervals and thereby calculation of heart rate and also heart rate variations during the night. For this purpose, an algorithm developed and published by Hamilton et al. has been used[11]. In Figure 1 the results of the automatic detection of QRS complexes of one example recording are shown. Using this detection algorithm, the width of QRS complexes and the interval between the R-waves can be calculated.

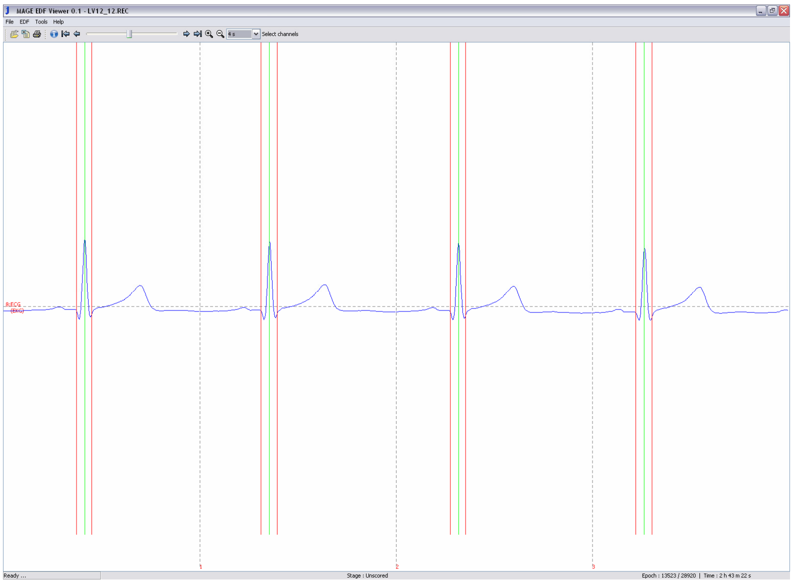

Figure 1: Automatic detection of QRS complex within the ECG signal.

As shown in figure 2, the distribution of R-R interval duration (y-axis) throughout a whole night recording, which is typically around 8h, can be calculated from this algorithm (time on x-axis), thereby compressing the ECG signal data to values ready for further sophisticated analysis.

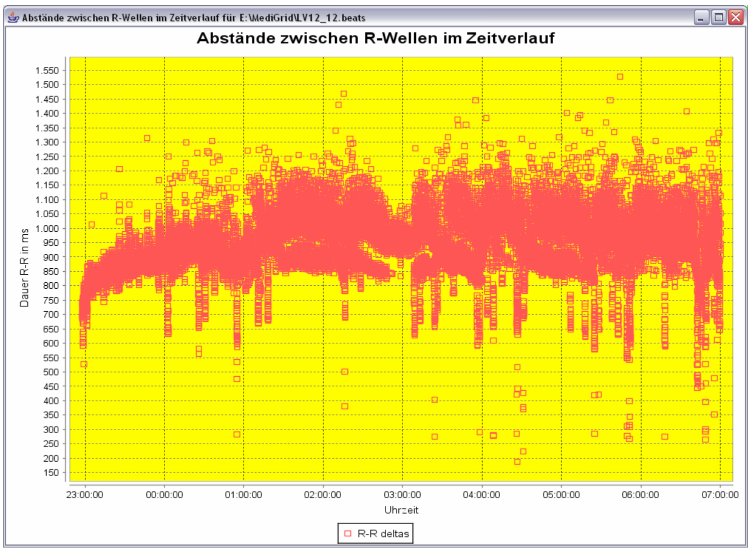

Figure 2: R-R-Intervals throughout the night recording. Although the mean heart rate during the night can be clearly identified, there is a remarkably high variance during some periods of the night. These extreme values may be due to body movements of the patient, very often interfering with the recorded biological signals.

Figure 3 shows the results of a percental distribution of R-R intervals during the whole recording. Thereby the physician can get an overview of the heart rate during the night but also detect frequent variations in heart rate, being a possible indicator for sleep disorders like OSAS or RLS. Furthermore, the analysed data can be used for Fourier transform calculations, calculations of QT-interval (activity phase of the heart).

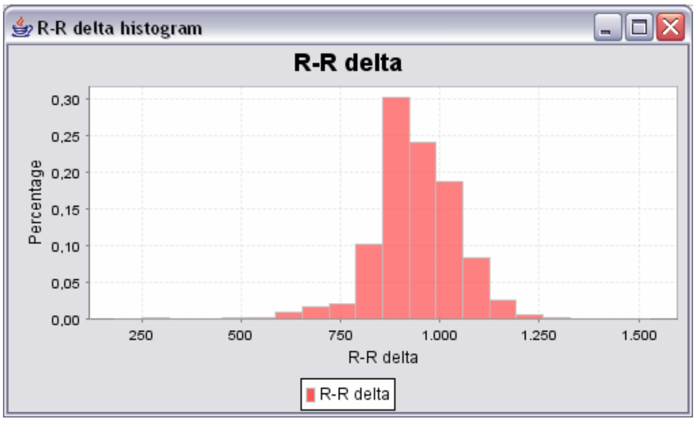

Figure 3: Histogram of the R-R-intervals during the night.

As described in the Introduction, OSAS is accompanied by breathing cessations during the night and consecutive awakening reactions. Usually these breathing cessations (apneas) and also hypoventilations (hypopneas) are sought and counted, using standardized criteria[12;13]. The amount of events during sleep is then one parameter of the treatment decision.

However, not only complete cessations of breathing can cause such awakening reactions and associated increases in nightly blood pressure and heart rate. Even a limited inspiratory airflow can cause such events during the night[14]. The detection of a limited inspiratory airflow, however, represents a difficult task even for experienced technicians. For this reason, the developed algorithm uses not only the nasal airflow signal (amount of air flowing through the nose/min) but also pressure variations in the esophagus for the detection of those inspiratory flow limitations. Usually, this esophageal pressure decreases when we breathe in and increases when we breathe out. Excessive decreases in esophageal with lacking increases in nasal airflow can be a possible sign for inspiratory flow limitations. The algorithm used for this purpose analyzes both signals for the occurrence of the inspiratory flow limitations[15].

Figure 4 shows exemplary results of the developed algorithm. It first detects the inspiratory and expiratory part of the recorded signal. Then esophageal pressure swings and nasal airflow signals are analysed to detect inspiratory flow limitations. The red dot in the lower part of the picture indicates that the marked breath was identified to be flow limited.

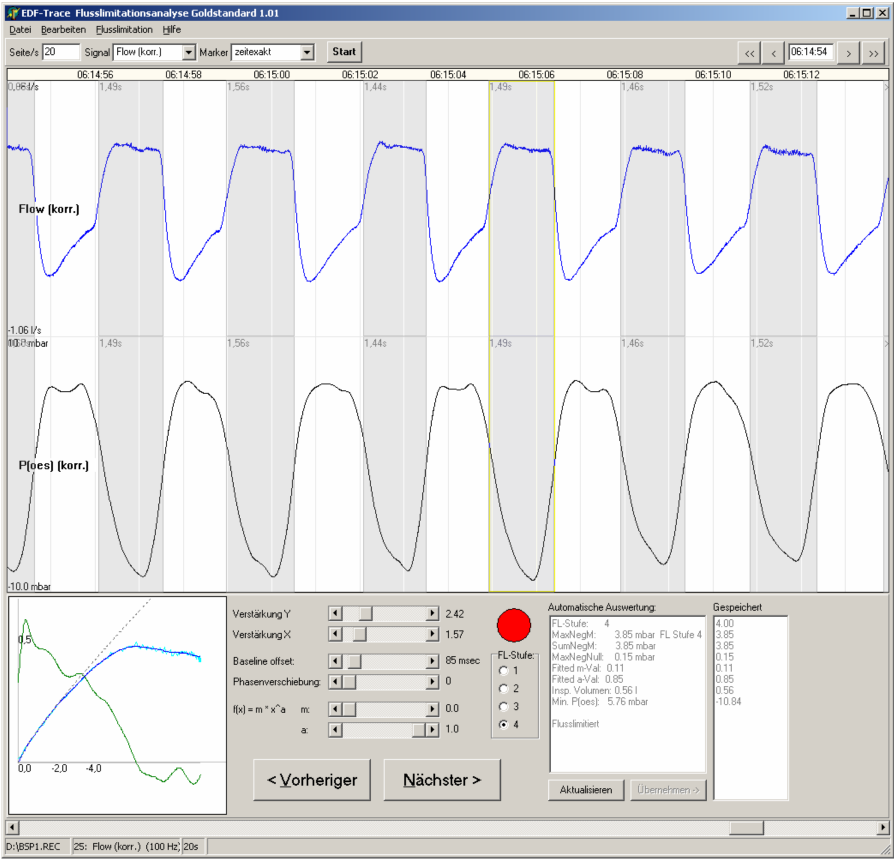

Figure 4: Automatic detection of inspiration (grey background) and expiration (white background), automatic detection of flow limited inspirations

Apart from breathing disorders that may have impairing effects on sleep, there also exist neurologic disorders that can affect sleep. The other two sleep disorders described in the Introduction (narcolepsy, restless legs syndrome) represent such neurologic disorders.

For both disorders, the analysis of muscle activity with the help of the electromyogram (EMG) during sleep can alleviate the finding of the correct diagnosis. The algorithm described here was developed to analyse the overall muscle tone of the recorded EMG signal and search for the occurrence of periodic leg movements during sleep, which can be an indicator for the restless legs syndrome or the periodic leg movement syndrome. Short muscle activations during sleep (so called twitches), which frequently occur in narcolepsy, can also be detected.

Similar to the diagnosis of sleep disordered breathing, periodic leg movements are also scored according to standard criteria and then counted in order to get an estimate of the severity of the disease[16;17].

The analysis is done by calculating upper and lower envelopes for the EMG signal, thereby calculating the amplitude. EMG activations with an interval smaller than 1 second between the amplitude peaks are considered as one activation. Thereby short activations (twitches) can be distinguished from longer activations.

In Figure 5, the results of the automated amplitude calculation using upper and lower envelopes are shown.

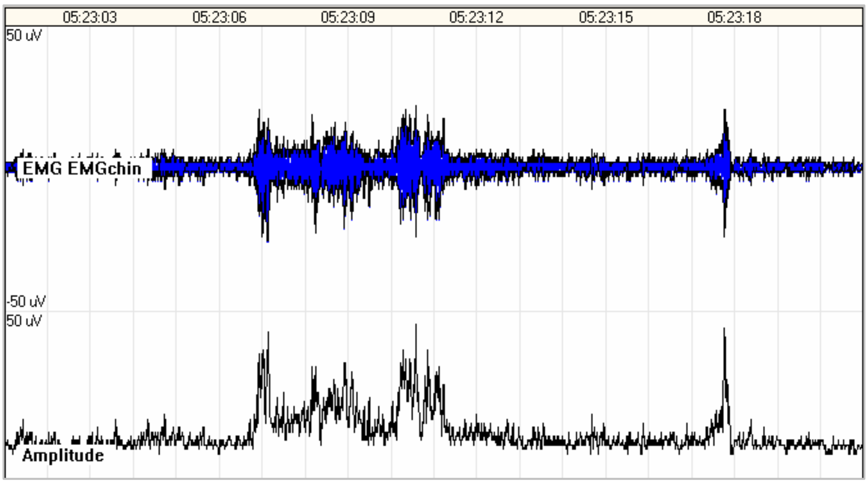

Figure 5: Automated analysis of EMG activations by calculation of an upper and lower envelope and consecutive calculation of the amplitude.

In Figure 6, the detected events are shown in the upper trace. The middle trace shows the described summarization of events. In the lower trace, the original EMG signal is shown.

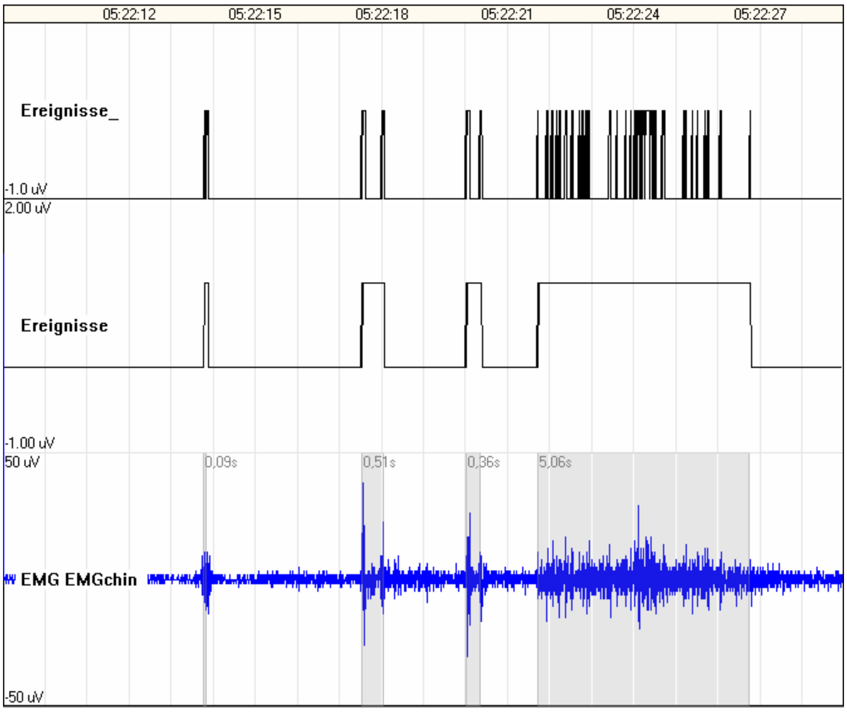

Figure 6: Summarization of coherent EMG activations (interval between activations < 1 sec) to distinguish between short twitches and longer muscle activations.

2. Results and Discussion

First results regarding the automated ECG analysis showed a good detection rate of QRS complexes with an exact calculation of R-R-intervals compared to manual analysis. Using this method, changes in heart rate that may be associated with sleep related disorders seem to be detectable with sufficient precision.

Comparative tests of the algorithm for the analysis of breathing signals showed a precise and thorough detection of inspiration and expiration. Furthermore, the detection algorithm for inspiratory flow limitations in combination with esophageal pressure changes led to a good automatic recognition of flow limited breaths compared to expert opinion. However, further studies investigating the validity of the detection of inspiration and expiration have to be performed, while the validity of the detection of inspiratory flow limitation has been investigated in a study by Clark et al. in a small population of 7 patients [15].

Comparing the manual and automatic scoring of periodic leg movements, the accordance between both methods appeared to be good both for the detection of periodic leg movements and for the detection of short twitches appearing in RBD patients. However, there are no objective scoring criteria for EMG twitches as they exist for periodic leg movements. Further studies are necessary to confirm the reliability and validity of the algorithm. In future publications, the underlying procedures for EMG analysis have to be described in detail.

Limitations with regard to the estimation of usefulness of the presented approaches are lacking information about consumed resources and computational power.

Automatic detection algorithms for sleep stages, as described in the introductory section, are currently in preparation. They will be based on the analysis of frequencies of the EEG waves with regard to alpha, theta, delta and sigma activity. Furthermore, detection of features like sleep spindles and K-complexes in combination with a detection of slow and rapid eye movements from the EOG signal will be integrated in this algorithm. This will allow the correct classification of sleep stages according to the current Rechtschaffen and Kales rules [10].

3. Conclusion:

All developed algorithms for the analysis of biosignals from overnight recordings showed a good accordance to expert opinion ratings. Furthermore, all algorithms are written in standard programming languages (Delphi, Java) and can therefore be easily implemented into GRID environments.

All data needed for the analysis can be split into small packets, as polysomnographic data is recorded in separate channels from different sensors. We therefore believe that in short future, Grid based analysis of polysomnographic recordings will be available using the described scenarios. In combinations with different approaches, e.g. to use the ECG changes for the detection of sleep related disorders, it may be possible to have a Grid based polysomnographic analysis. As this can have improving effects on the effectiveness of the analysis of overnight recordings, costs for polysomnographic investigations that have to be raised by health care providers can possibly be diminished.

Further studies are necessary for the assessment of validity and reliability of the different presented approaches.

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