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A review of ECG based diagnosis support systems for obstructive sleep apnea

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Abstract

Humans need sleep. It is important for physical and psychological recreation. During sleep our consciousness is suspended or least altered. Hence, our ability to avoid or react to disturbances is reduced. These disturbances can come from external sources or from disorders within the body. Obstructive Sleep Apnea (OSA) is such a disorder. It is caused by obstruction of the upper airways which causes periods where the breathing ceases. In many cases, periods of reduced breathing, known as hypopnea, precede OSA events. The medical background of OSA is well understood, but the traditional diagnosis is expensive, as it requires sophisticated measurements and human interpretation of potentially large amounts of physiological data. Electrocardiogram (ECG) measurements have the potential to reduce the cost of OSA diagnosis by simplifying the measurement process. On the down side, detecting OSA events based on ECG data is a complex task which requires highly skilled practitioners. Computer algorithms can help to detect the subtle signal changes which indicate the presence of a disorder. That approach has the following advantages: computers never tire, processing resources are economical and progress, in the form of better algorithms, can be easily disseminated as updates over the internet. Furthermore, Computer-Aided Diagnosis (CAD) reduces intra- and inter-observer variability. In this review we adopt and support the position that computer based ECG signal interpretation is able to diagnose OSA with a high degree of accuracy.

Keywords: Computer Aided Diagnosis, Electrocardiogram, Obstructive Sleep Apnea, Classifier, Features

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1. Introduction

Obstructive Sleep Apnea (OSA) is a common disorder that affects both children and adults [1]. In 1993, the Wisconsin Sleep Cohort Study produced data which suggests that one in every 15 Americans experiences symptoms of sleep apnea, such as pauses in breathing or instances of shallow breathing during sleep [2]. OSA is associated with increased perioperative risk, hypertention and stroke [3, 4]. Kapur et al. presented evidence that medical costs almost double prior to the diagnosis of OSA [5]. The result was established by taking into account control groups matched for age, sex, residence, and in some cases, family physician as well as obesity. In a sequence of 238 cases, identified in a health-maintenance institution, in the year prior to the diagnosis of OSA, the mean yearly medical cost per patient was US$2,720, versus US$1,384 for sex and age matched controls. Regression analysis showed that the OSA severity, expressed through the Apnea/Hypopnea Index (AHI), was positively correlated with the annual medical costs, after adjusting for age, sex, and Body Mass Index (BMI) [6]. For the entire population, that increase may cause US$3.4 billion/year in additional medical costs. Unfortunately, the costs of untreated OSA are higher than just the cost incurred by health issues. Apart from diagnosis and treatment costs, there is a decrement in the quality of life, which is associated with the medical consequences, but there are also motor vehicle accidents, and occupational losses. OSA-related motor vehicle collisions in 2000 were estimated to cost US$15.9 billion [7]. Another factor, which increases the cost, is the fact that traditional OSA diagnosis requires an Polysomnography (PSG), an all-night examination in a specialized clinic, under constant medical supervision [8, 9]. That procedure is labour-intensive, time-consuming and, at times, inaccessible or even impractical [10]. Accordingly, a cost effective screening method, which allows us an early assessment of the disease severity prior to a referral for PSG [11].

As such, OSA poses a high cost to society and current diagnosis methods are expensive. These two facts are interrelated, hence it is reasonable to assume that novel methods of OSA detection can contribute to the solution of both problems. Accurate and more cost effective diagnosis will result in wider screenings where OSA is detected earlier. Early disease detection means more effective treatment can be administered, which reduces both patient suffering and social cost of the disease. Thus, there is a growing interest in alternative diagnosis approaches, such as portable holter Electrocardiogram (ECG) monitoring [12, 13]. By using modern computing machinery and state of the art algorithms, it is possible to extract respiration waveforms from ECG signals [14]. Such systems can be used in OSA analysis. In terms of medical foundations, these systems are based on the fact that there are fluctuations in both R-wave amplitude and QRS duration at the onset and termination of apnoea-bradycardia episodes [15]. However, practical holter reports are often difficult to analyze from a Heart Rate Variability (HRV) perspective, because of the nondeterministic nature of the signal, which results from underlying physiological processes that are assumed to be chaotic [16, 17, 18, 19].

Both, the amount of disability affected lifetime and the economic cost create a powerful need to diagnose OSA in an accurate and cost effective manner. ECG based screening methods hold the promise of delivering non-invasive, accurate and cost efficient diagnosis methods. However, the physiological processes, which link changes in the heart beat to OSA events are not entirely understood. Hence, we have to depend on empirical evidence to show that indeed such a link exists. The first part of our study details a comprehensive survey of papers which discuss physiological evidence that changes in the ECG signal are positively correlated with OSA events. Once that link is established, a corollary problem is to automate the detection of OSA induced changes in the ECG signal. To analyze the problem and to get an overview of the performance of automated OSA detection systems, the second part of our study reviews ECG based OSA Computer-Aided Diagnosis (CAD) systems. As such, each of these engineering papers provides evidence that there is an exploitable correlation between ECG measurements and OSA. Hence, these papers constitute valuable input to medical researchers. But, during our study, we found that the medical community forms distinct citation clusters, where research, with a biomedical background, is rarely cited. To overcome that, our review aims to provide an unbiased overview of ECG based OSA detection.

1.1. Sleep apnea survey

Before we introduce CAD systems for OSA detection, it is beneficial to briefly review the scientific literature that relates to sleep-disordered breathing and Heart Rate (HR). In general, sleep disordered breathing, known as sleep apnea, is further classified as mixed, central, or obstructive. The classification is based on whether effort to breathe is present during the event [20]. With approximately 84% of all cases, OSA is the most common form of sleep apnea [21, 22]. In 1984, Guilleminault et al. published the first paper about the effects of sleep apnea on the electrical activity of the human heart. To be specific, they noted that OSAs were often correlated with a bradycardia during apneic periods, followed by a tachycardia as breathing resumes [23]. These patterns were termed cyclical fluctuations in HR. Typical apneas have a duration of 10–20 seconds and that is the time when the effect on the heart beat is most profound. More specifically, the apnea periods introduce a frequency component to the Respiration Rate (RR) interval tachogram, which corresponds to the apnea duration. Hence, the apnea induced frequency component has a value in the range of 0.05 Hz to 0.1 Hz. It is difficult to detect these additional frequency components in the time domain. However, transform domains, like the spectrum, reveal both frequency and amplitude of the sleep apnea induced signal component. Stein et al. established a useful graphical representation of this observation [24]. In adult patients, they were able to detect episodes of OSA solely through visual inspection of the RR-interval tachogram by detecting the characteristic cyclical variations in HR patterns. Other research groups noted the low-frequency fluctuations which were introduced by apneas as well. In response, they developed a range of possible systems for using HR to detect apneas [25, 26]. Even healthy subjects can influence their heart beats by holding their breath [27]. Erdem et al. demonstrated the pure effect of OSA on the cardiac autonomic function with HR turbulence parameters [28]. Impaired HR turbulence may be an important factor which causes arrhythmia and sudden cardiac death in patients with OSA [29]. By monitoring the Q wave/T wave (QT) interval, computed from ECG signals during sleep, it is possible to create a link between the ventricular repolarization and sleep stages [30]. Uznańska et al. found that there is a significant correlated between OSA and cardiovascular diseases [31].

That concludes our brief review of the medical evidence which underpins all attempts to construct ECG based diagnosis support systems for OSA. In the next section, we review scientific articles, which were published on that subject. Our focus is on CAD systems which help practitioners to detect OSA. Section 3 relates these systems to the wider research in the field of OSA detection and CAD. The paper concludes with Section 4, where we highlight again the systemic aspects of creating ECG based diagnosis support systems for OSA.

2. Materials

The previous section outlined that there is a link between OSA and the beating pattern of the human heart. That link is important, because these beating pattern can be measured with the non-invasive and cost effective ECG method. However, OSA induced changes on the ECG signal are minute and the data needs to be observed over a long time interval. Hence, human based interpretation is error prone and there is inter- and intra-observer variability. As a consequence, computing technology is used to detect OSA induced changes in ECG signals.

Such computing methods form the backbone of CAD systems. These systems benefit patients through diagnosis support and treatment monitoring. In this part of our study, we review research on ECG based CAD systems for OSA.

The data for our study were retrieved in November 2015 from the Scopus Database (DB) [32]. In the time frame from January 2002 to October 2015, a total of 85 articles on the topic of sleep apnea and ECG were found. A citation analysis of the 85 scientific articles reveals that the majority of these publications falls into one of two groups. The first group of articles provides physiological evidence that sleep apnea affects the heart and indeed these sleep apnea induced changes can be captured with ECG measurements. These articles have a medical nature. The second group of articles describes automated sleep apnea detection systems. Hence, the second group of articles has an engineering nature. All engineering articles focused on OSA. Figure 1 shows the citation cluster visualization. The clustering was done with the VOSviewer [33].

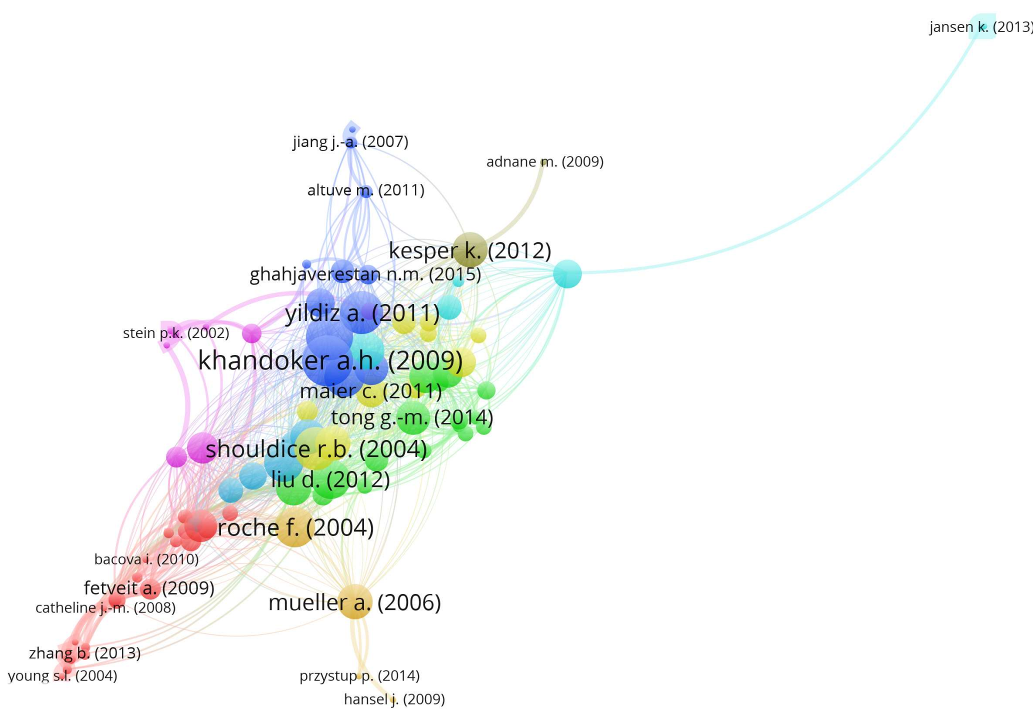

Figure 1: Citation network visualization for papers on ECG based sleep apnea detection from the Scopus DB. All research articles were published within the time period from January 2002 to October 2015.

As such, ECG based sleep apnea detection was never a hot topic, but over

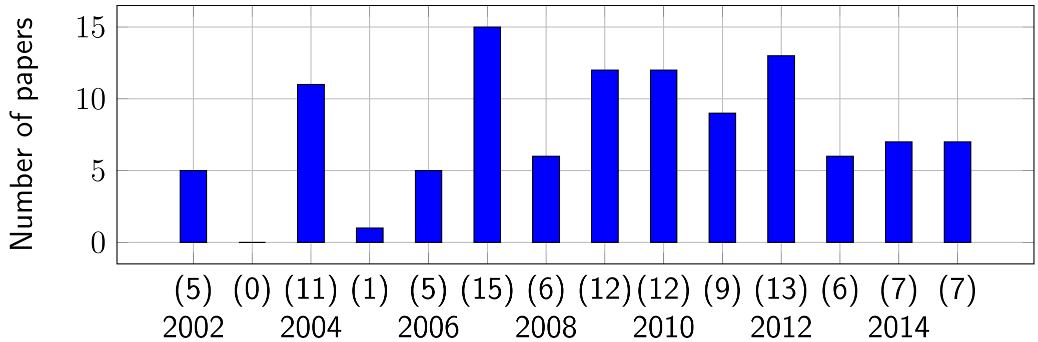

Figure 2: Distribution of papers on ECG based sleep apnea detection over the observation period from 2002 to 2015.

the last 10 years there was a steady stream of high quality research articles which focused on that subject. Figure 2 details the yearly distribution of these research articles over the time span from January 2002 to October 2015. Within the observation period, 2007 saw the largest number of research articles (15) on ECG and sleep apnea. In contrast, there were no articles in 2003. From 2006 onwards, there were at least five articles a year on that topic.

Having outlined both the need for CAD systems and the way in which that need sparked research publications, we move on to discuss CAD systems for ECG based OSA detection.

2.1. Computer aided diagnosis systems

The steady stream of research articles indicates that there is a link between respiration and ECG signals. Hence, it is necessary to translate that link into tangible improvements for patients as well as cost savings for society. CAD systems are a well-known strategy to realize the diagnostic potential of physiological measurements, such as ECG [34, 35].

CAD systems apply data mining techniques to reach a decision on whether or not a particular ECG signal sequence shows signs of OSA [36, 37]. Interpreting CAD systems as data mining machines leads to a clear design pattern which structures the system creation [38]. Figure 3 shows an overview block-diagram of the individual processing steps which establish the CAD functionality. In terms of systems design, each of these steps poses a particular problem. As long as these problems are well defined, they can be addressed with standard solutions. In exceptional cases, it is possible to find novel and innovative problem solutions. The next sections detail the individual steps, by introducing the problem and

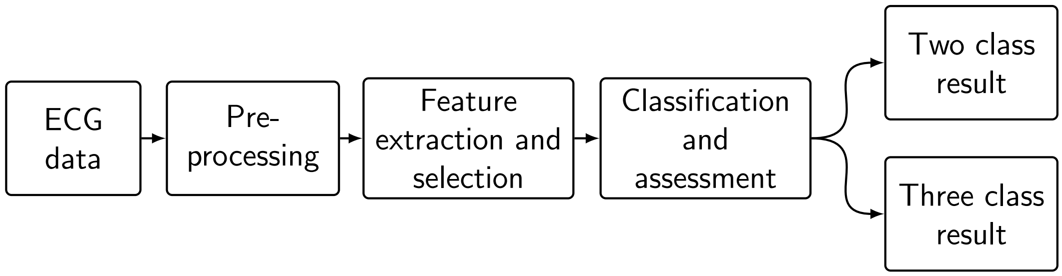

Figure 3: Block diagram of computer aided sleep apnea detection systems based on ECG signals.

discussing standard solutions.

2.1.1. Electrocardiogram data

The first problem of ECG based OSA detection is data. There are a number of requirements for the ECG recordings, some of them are even conflicting. First and foremost, the data should represent the variety and veracity of OSA induced changes in ECG signals [39]. In general, that requirement can only be adequately met with large datasets taken from a wide range of specimens. However, there is problem with the group of heart patients. Their heart beat, hence also their ECG signal, is already altered by an underlying heart disease [40, 41, 42]. Routinely, such datasets are not considered as a basis for the design of OSA detection systems. As a consequence, all automated OSA detection systems under-perform for patients with an underlying heart disease.

Another important requirement for ECG data, which is used for OSA detection, is concerned with availability and competition. As such, availability is prerequisite for competition, because competition means to compare the performance results of different studies and that comparison is only valid if the underlying data is the same. When the studies, under scrutiny, were based on different datasets, researchers tend to regard larger datasets to be more difficult, i.e. good performance results are harder to achieve, then smaller datasets or datasets from selected individuals.

As a consequence of the interrelatedness between performance and data used, we have to be extra careful when comparing different OSA detection methods. For example, the plentiful and diverse measurements very useful for validating methods for diagnosing sleep disorders, however researchers must be careful when comparing their algorithms with those implemented by other authors. The same algorithm my yield significantly different results, if the DB employed to test the algorithm is not the same, due to differences in methodologies of processing, thus leading to confusing conclusions in the outcomes obtained [43].

One way to overcome the lack of data for and to foster competition amongst researchers is to establish publicly accessible DBs. For the special field of ECG based OSA detection, the PhysioNet sleep apnea ECG DataBase (PNDB) is such a publicly accessible resource. The DB contains 70 nighttime ECG measurements from sleep apnea patients [44]. The data is annotated based on visual scoring of disordered breathing during sleep. Both annotation quality and amount of data make the PNDB a prime resource for research on OSA induced changes of the ECG signals.

2.1.2. Preprocessing

The second problem, we have to deal with for ECG based OSA detection, arises from unwanted disturbances in the signal. The electrodes, used for ECG measurements, pick up ambient and power line noise as well as muscle movement artifices. These undesired signal components have a degrading effect on the CAD system performance. For example, artifacts in electrocardiographic recordings lead to the spurious quantification of RR intervals and these effects can result in substantial biases in studies of the chronotropic state of the heart [45]. The problem of artefact contaminated ECG signals is well documented in scientific literature, and a number of artifact detection methods were developed to help in identifying of suspicious heart periods [46]. Also the problem of noise is well understood and there are numerous noise filtering approaches. Wavelet methods have gained a good reputation for their ability to differentiate between information bearing signal components and noise [47, 48].

Once the ECG signals are cleaned, the practitioner, who is designing the OSA detection system, phases a choice between using ECG or HR based features. Both approaches are equally valid and they have been used for ECG based OSA detection. As such, a HR signal captures the main activity of the heart, but information about the particular shape of the QRS complex is lost. For ECG based OSA detection, that loss of information is acceptable if we limit our investigations to the influence of OSA on the heartbeat. Accepting that limitation has the advantage that the feature extraction becomes simpler and more transparent. In terms of systems design, HR extraction is considered to be a pre-processing technique. Conceptually, HR is based on the time between two R peaks known as the RR interval. Pan and Tomkins developed a widely used ECG based QRS detection algorithm [49].

2.1.3. Feature extraction and selection

The third problem for ECG based OSA detection is to find methods which extract relevant information from ECG signals. In this case, information is relevant if it helps to discriminate between OSA and normal berating periods. The process of extracting relevant information from a physiological signal is usually referred to as feature extraction. In the past years, we have seen the application of machine learning or pattern recognition. As a consequence, the feature domain has expanded from tens to hundreds of features that can be used in those applications [50]. ECG based OSA detection is no exception. In the reviewed research articles, we found a diverse range of feature extraction algorithms. The following text describes the most common feature extraction methods with a bias towards nonlinear feature extraction.

A number of researchers used statistical methods to extract relevant information from either ECG or HR. The statistical methods included basic first order quantities, such as mean and variance as well as more advanced approaches such as ST-segment deviation. In general, these statistical approaches assume that the signal is predictable and that the signal is stationary. However, the human heart is a non-stationary oscillator and there is good evidence that it is even a chaotic system. Statistical methods are prone to failure, because they are not robust to nonlinear events. Indeed such nonlinear events can be caused by OSA, i.e. such events cause a significant but unpredictable alteration of the heartbeat.

The main idea behind domain transformation algorithms, such as Fourier, Spectrum estimation and wavelets, is to compare the measured ECG signal with known signals. In the case of spectrum approaches, the known signals are sine waves of different phase angles and frequencies. As a consequence, the spectrum method yields information about the frequency content of the ECG signal and the phase angle. The phase angle is rarely used, but the frequency content is an important signal feature. Similarly, the continuous wavelet transform compares the measured ECG signal with scaled versions of the so called mother wavelet. The discrete wavelet transform compares the measured signal with the filter transfer functions. The wavelet transform results show location and quality of the comparison. Both parameters hold valuable information for ECG based OSA detection, because they reveal the nature of an OSA induced abnormality and when that abnormality happened.

The reviewed papers describe a number of novel time domain feature extraction methods. These methods aim to extract relevant information for either HR or ECG to OSA periods. They were proposed by scientists with expertise in both algorithm design and wide ranging medical knowledge on either ECG or HR [51]. For example, Kalman filter can be used to measure the predictability of the ECG signal. OSA events are not predictable, hence the Kalman filter will do poorly for OSA affected ECG signals. As a consequence, the Kalmen filter performance can be used as feature, for OSA detection.

Nonlinear features were also used for ECG based OSA detection. The features were extracted with algorithms from the domain of the chaos theory [52]. These algorithms deal with strange signals. In this case 'strange' means that the signals are predictable if and only if we understand all the physiological processes in the human body. Clearly, that is impossible, hence the ECG prediction is also impossible. However, it is possible to quantify the strangeness or indeed the self-similarity of the signal. Such quantifications reveal lots of hidden information about the underlying processes. One of these underlying processes is the effect OSA has on the human heart. A common test to support the idea that ECG signals result from strange attractors can be constructed with a surrogate data test [53]. The test is established as follows. The Fast Fourier Transform (FFT) algorithm is used to calculate the spectrum of the ECG signal. Subsequently, the phase is randomized before the inverse FFT is used to transform the signal back into the time domain. The resulting signal has the same statistical properties as the original ECG signal. If a nonlinear parameter shows a difference between the original and phase randomized signal, then we cannot rule out that the underlying process, which generates the signal, is nonlinear. So far, there are no records that the test has failed for ECG signals, at least not for all nonlinear parameters.

Having such a wide range of possible feature extraction methods requires feature selection. Fundamentally, feature selection is necessary because the classification step can only deal with a limited number of features. Plenty of feature selection methods are documented in literature due to the availability of data with hundreds of variables leading to data with very high dimension. As such, feature selection methods provide us with a way of reducing computational complexity, improving prediction performance, and a better understanding of the data in machine learning or pattern recognition applications. There is no way of knowing a priori which feature combination works best for a given OSA detection task. Hence, the strategy must be to try out as many features as possible. With that approach, the problem reduces to the simple task of feature selection, i.e. we have to select the features which are used for classification. To find the best possible combination, the experimenter has multiple options. The first of these options is to use statistical performance evaluation methods, such as students t-test and Analysis Of Variance (ANOVA) [54, 55]. Once the statistical test results are established, the best features are selected, to form the basis for classification. Another method is to process all permutations of a feature set with strong classifier. However, even with state of the art processing facilities, such a brute force approach is very time consuming, because running classification algorithms for all feature permutations is computationally complex. The final method relies on dimension reduction through algorithms, such as Principal Component Analysis (PCA), Kernel PCA, Neighborhood Preserving Embedding (NPE), Locality Sensitive Discriminant Analysis (LSDA), Independent Component Analysis (ICA) [35, 56, 57]. The idea, behind that method, is to establish an ordered sequence of parameters from a feature set. The parameters are ordered in terms of their ability to represent the important properties (not noise) of the feature set [58]. Hence, the feature vector, which is used for classification, is composed from the most signification parameters.

2.1.4. Two class results

The forth problem of ECG based OSA detection centres on finding ways of using the extracted information. In general, the extracted features do not reassemble the ECG waveform. Hence, it is difficult for humans to relate the features to particular diseases. To overcome that difficulty, threshold values are introduced. For example, Roche et al. state that a threshold value of -11.1 for a statistical feature (Δ[D/N] SDNN index) results in a sensitivity of 86.5% and a specificity of 55% [59]. However, such thresholding methods can only be used on a single scalar value. One way to overcome that drawback is to incorporate multiple features into one index value and to present the resulting value to the threshold classifier [60]. However, the creation of such index values is based on the intuition and experience of the experimenter. Hence, such indexes are highly subjective, which makes it difficult to evaluate them. To be specific, a different way of combining the features might yield better results. In many cases it is impossible to analyze all features combinations, therefore we cannot proof that a particular index is the most performant for a given feature set. To find the right threshold value, the Receiver Operating Characteristic (ROC) method can be used [61]. The ROC curve reflects the fact that a lower threshold value increases the sensitivity, but decreases the specificity, under the assumption that a larger feature value indicates OSA.

A much better approach, then to combine individual features to form an index value and to specify a threshold value, is to automate the classification of a feature vector. An automated classification algorithm will find the best way of reaching a classification decision. For supervised learning algorithms, the best way is found with decision strategies based on a known dataset. By extraction relevant information from a known dataset, the Support Vector Machine (SVM) algorithm establishes a hyperplane which separates two signal groups [62, 63]. Repeating the process of establishing the hyperplane, with a reduced dataset, will lead to the classification of more than two classes. The classifier has been used for five of the surveyed OSA detection systems, as shown in Tables 1 and 2.

The Artificial Neural Network (ANN) classifier is one of the oldest decision making algorithms [64]. It models the way a human brain works. The ANN structure is application specific, i.e. different ANN structures show different performance for the same OSA detection task [65]. There is no way to predict which structure works the best. Hence, trial and error is required to find the best ANN configuration for a given task. As part of our survey, we found four ANN based OSA detection systems.

The most common application for Linear Discriminant (LD) in medicine is disease severity assessment [66]. However, the technique, which characterizes two or more signal classes, can also be used for classification [67]. In the surveyed scientific articles, LD was used twice as classification method.

AdaBoost is a modern meta classification algorithm, which employs a potentially large number of weak decision making methods to reach a strong decision [68]. For biomedical problems, AdaBoost is always a strong contender for the best classifier, but it is usually outperformed by other classification algorithms, such as SVM. Hence, AdaBoost was used only once in the surveyed research articles.

Just like feature extraction, also the classification step needs internal competition as well. There is no way of knowing which classification algorithm works best for a given feature set. Therefore, empirical science is called upon to find the best classification algorithm. The best classification algorithm is chosen based on performance parameters which reflect various aspects of making a correct decision [69]. For classification problems, the correct decision constitutes the true value and the classification. Accuracy (A) is inversely proportional to the degree of closeness of the classification achieved by an individual algorithm. Another important performance measure is Sensitivity (Se), which describes the proportion of different samples that are correctly identified. For ECG based OSA detection, Se represents the percentage of ECG samples that were correctly identified as showing signs of OSA [70]. Specificity (Sp) is the last measure which was widely used in the surveyed papers. As such, Sp determines the proportion of normal ECG signals that were correctly identified. The formal definition of all three performance measures is based on the confusion matrix [71]. That four quadrant matrix contains: true positive – ECG segments correctly identified as showing signs of OSA, true negative – normal segments correctly identified as normal, false positive – normal segments identified as showing signs of OSA, and false negative – incorrect identification of ECG signal segment showing signs of OSA.

2.1.5. Two class results

In between January 2002 to October 2015, there were 29 engineering papers, which discussed OSA detection systems. In technical terms, sleep apnea detection comes down to a two class problem: either there are sleep apnea events in a given ECG signal or not. In general, the research articles in Table 1 describe system designs which follow the block diagram shown in Figure 3. However, the methods used in the individual steps vary significantly. From an engineering perspective, the feature extraction methods are the most important and indeed the most creative step. During this step, a designer is confronted with the task of selecting the best feature extraction methods, for a given task, from a wide range of existing algorithms. Some designers push the envelope by proposing new and innovative feature extraction methods which are specifically tailored to ECG based OSA detection.

From the 29 research articles, listed in Table 1, 17 detail threshold classification, in some cases supported by ROC analysis. Even with such basic classification methods, the researchers achieved good classification accuracy, $>= 79\%$. The lowest reported classification accuracy came from Cohen and de Chazal [72]. They reported an accuracy of just 67% based on the LD classifier. However, their system had to deal with infant ECG signals which have a much smaller knowledge base when compared with adult ECG.

Table 1: Summary of study conducted on classification of normal and apnea. The term features to the feature extraction method used. The column labelled 'Perf. in %' details the CAD system performance in A, Se, and Sp. Some researchers did no publish all three performance measures. Primarily, the table entries are ordered in terms of data used. Within the resulting subgroups, the entries are ordered in terms of classification performance.

Name, year	Features	Classifier	Data used	Perf. in %
Khandoker et al. [73], 2009	Wavelet	SVM	PNDB	A = 100

Table 1: (continued)

Name, year	Features	Classifier	Data used	Perf. in %
Bsoul et al. [74], 2014	Time and spectral	SVM	PNDB	Se=96
Oussama et al. [75], 2016	11 time domain and PCA	ANN	PNDB	A=96
Khandoker et al. [76], 2009	Wavelet	SVM	Sleep Research Unit DB, PNDB	A=93
Thomas et al. [77], 2007	Spectrograms	Threshold	PNDB	Se=86, Sp=95
Maier et al. [78], 2014	Time-domain feature	Threshold	PNDB in addition data from 121 patients	Se=86, Sp=86
Varon et al. [79], 2015	Wavelet and HRV statistics	Threshold	PNDB and KU Leuven sleep lab	A=85, Se=85, Sp=85
Liu et al. [80], 2012	HilbertHuang transform	ROC threshold	PNDB	A=79, Se=73, Sp=71
Dickhaus and Maier [81], 2007	Amplitude modulation	ROC, threshold	PNDB	ROC areas
Xie and Minn [82], 2012	HRV	AdaBoost	UCD DB	A=83, Se=79, Sp=85
O'Brien and Heneghan [83], 2007	Statistics and spectral	LD	UCD and Computers in Cardiology challenge 2000 DB	A=82, Se=78, Sp=85

Table 1: (continued)

Name, year	Features	Classifier	Data used	Perf. in %
Akşahin et al. [84], 2011	HRV cross power spectrum density	ANN	10 patients and 10 control	A=99
Cohen and de Chazal [72], 2015	HRV statistics and PSD	LD	National Collaborative Home Infant Monitoring Evaluation dataset	A=67, Se=67, Sp=58
Tong et al. [85], 2014	Mean cardiac electrical axis	ROC, thresh-old	32 control, 88 patients	A=88
Jiang et al. [86], 2014	ST-segment deviation	Threshold	105 patients and a control group	Se=65, Sp=89
Monasterio et al. [87], 2012	20 linear measures	SVM	Multi-Parameter Intelligent Monitoring for Intensive Care II	A=90, Se=86, Sp=91
Roche et al. [59], 2002	HRV statistics	Threshold	124 sets	Se=87
Maier et al. [88], 2007	Local recurrences	ROC thresh-old	140 sets	Se=81, Sp=86
Shouldice et al. [89], 2004	Statistics and PSD	Quadratic dis-crimi-nant	25 sets	A=88, Se=86, Sp=91
Roche et al. [90], 2007	HRV statistics and spectrum	ROC	150 sets	Se=91, Sp=34
Kesper et al. [91], 2012	HRV, EDR	Threshold	SIESTA DB	A=81

Table 1: (continued)

Name, year	Features	Classifier	Data used	Perf. in %
Poupard et al. [92], 2012	HRV statistics	Threshold	118 patients	Se=97, Sp=72
Yilmaz et al. [93], 2010	HRV statistics	SVM	17 subjects	A=87
Singhathip et al. [94], 2010	HRV statistics	ROC threshold	26 subjects	A=93
Roche et al. [95], 2004	Spectral	Threshold	28 subjects	Se=78, Sp=70
Tong et al. [85], 2012	Not reported	ROC threshold	120 subjects	Se=85, Sp=94
Maier and Dickhaus [96], 2010	Time-delay Embedding	Threshold	26 recordings	Se=84
Ghahjaverestan et al. [97], 2015	Kalman filter	Threshold	Not reported	Se=95, Sp=94

2.1.6. Three class results

There were only five research articles, which discriminated the ECG signals in three classes, in the Scopus DB on ECG and sleep apnea between January 2002 to October 2015. Table 2 lists these five papers. Most of the three class CAD systems discriminate between normal, apnea and hypopnea ECG segments. In general, three class problems are more difficult than two class problems. Therefore, the performance measurements are lower as compared to two class problems. The work by Acharya et al. stands out, because they achieved a classification accuracy of 90% on a large dataset [98]. The key to that classification performance lies in the feature extraction methods. The authors have used a range of nonlinear methods, from the domain of chaos theory, to extract features which represent the complexities of the electrical activity of the human heart well.

Table 2: Summary of study conducted on classification of normal, hypopnea and apnea.

Name, year	Features	Classifier	Data used	Perf. in %
Acharya et al. [98], 2011	Approximate entropy, fractal dimension, correlation dimension, largest Lyapunov exponent and Hurst exponent	ANN	450 apnoea sets, 130 hypopnoea sets and 130 normal sets	A=90, Se=100, Sp=95
Khandoker et al. [99], 2009	Wavelet	ANN	17 sets	A=77
Babaeizadeh et al. [100], 2011	Peak-to-trough QRS amplitude and HRV based method	ROC thresholds	Sleep health center in Boston	A = 71, Se=60, Sp=82
Boyle et al. [101]	Wavelet	Statistical analysis	10 one hour recordings and six overnight recordings	ECG method comparable with respiratory monitor.
Lado et al. [102], 2012	HRV STFT	Threshold	46 patients	Not reported

3. Discussion

The human heart beat is influenced by both internal and external factors. Therefore, electrical measurements of the heart, in the form of ECG signals, can provide a holistic assessment of health [103]. However, a fundamental problem with such general indicators of health is the complexity of interpretation. As a consequence, it is necessary to focus on one disease or disease class. The prime candidates for such a focus are the heart diseases [104, 105]. For this disease class, ECG signals are the reference physiological measurement. OSA is another application area where ECG abnormalities can be used to support a diagnosis, despite the fact that the ECG signal changes are just a secondary measure of breathing problems [101]. In this case, secondary means that the ECG signals are influenced by both autonomous and non-autonomous activities of the human body, and respiration events are just one amongst many influencing factors. Fortunately, sleep describes a rather predictable state of the human body, hence other factors, which shape the ECG signals are less prominent, at least they are more predictable. Therefore, external influences on the ECG signal are minimal. Hence, it is possible to link abnormalities in ECG signals with berating disorders without the need for restricting or controlling external influences. For example, during sleep, there is no need to enforce a specific posture when taking the ECG measurement. As a consequence, ECG based OSA detection is practical, it can be done with autonomous machines, such as holter or even cost effective HR monitors [106].

There is dependable physiological evidence that OSA events cause changes in the ECG signal. As a consequence it is possible to build automated systems which detect OSA induced ECG signal changes and through that provide diagnosis support for practitioners. Building these systems is a creative process, because there is no standard way of extracting information from nonlinear signals, such as ECG measurements. In this review, we focused on the creative process and the fact that it is difficult to compare individual OSA detection systems. Tables 1 and 2 detail features, classifier, data as well as performance of OSA detection systems. The data used, together with the classification performance, indicate the system quality. To be specific, accuracy alone is insufficient to determine the system quality, because the accuracy depends on the dataset used for testing. In general, the performance measures, A, Se and Sp, are more dependable when obtained in huge quantity from varied dataset. Hence, the first step in evaluating the system performance is to look at the datasets used. According to our review, for two class problems, the most widely used data comes from the PNDB. The eight studies, which were based on PNDB, are highly competitive, because the performance results are comparable. Therefore, we have ordered the entries in Table 1 according to the data used. Within the resulting subsets, the order was established by the system performance. That ordering allows us to compare the feature extraction and the classification methods. The most relevant observations come from the largest subset, namely to the detection systems based on the

PNDB. For that subset, the adopted element ordering reveals that classification algorithms are superior to simple threshold methods, because the four classifier based systems outperform the five threshold based systems. There is not such a clear result for the features used. Time and frequency domain as well as wavelet features seem to be sufficient to discriminate two classes.

Some researchers describe the effects of obstructive sleep hypopnea as indistinguishable from apnea events [107]. Gould et al. introduced the idea of a sleep hypopnea syndrome as an alternative to the AHI [108]. Their index lists minimal breathing difficulties on the lower end of the scale and OSA is listed as most severe event. Another aspect, which makes it worthwhile to study hypopnea, comes from the fact that hypopnea periods usually precede apnea events. Hence, hypopnea periods can be used to predict and, with more advanced systems, prevent OSA events. Future CAD systems should have the ability to discriminate between hypopnea periods and apnea events, because hat will improve patient monitoring. With such improved patient monitoring, it is possible to individualize treatment. The ability to administer individualized treatment, together with constant patient monitoring, can lead to self-optimizing patient control systems with feedback through monitoring and activation through individualized treatment.

ECG based OSA detection is not the only novel method to diagnose breathing disorders during sleep. Pulse oximetry is another non-invasive tool which is often applied in modern medicine to evaluate both arterial oxygen saturation and HR. In recent years, pulse oximeters shrank, the smaller size has broadened their application spectrum. In terms of medical evidence, it was found that OSA is frequently accompanied by repetitive oxygen desaturation that can be useful in its detection [109]. For diagnosis and treatment of sleep-disordered breathing, overnight pulse oximetry helps us to determine the severity of disease and is used as an economical means to detect OSA [110, 111, 112].

The prevalence of specific sleep disorders increases with age. For example, the number of patients with phase advance in the normal circadian sleep cycle increases with age, so does the restless legs syndrome. Especially, OSA is increasingly seen among older individuals and it is significantly correlated with cardio- and cerebrovascular diseases as well as cognitive impairment [113]. OSA increases corrected QT dispersion, that is the difference between the maximum and minimum QT intervals and is a strong risk factor for cardiovascular mortality [114]. Solaimanzadeh et al. identified ECG based predictors of mortality in patients with familial dysautonomia [115].

OSA is associated with hypertension and diabetes. The combination of these diseases puts patients at high risk of developing cardiovascular disease. Appropriate screening routines are important to detect cardiovascular risk factors in patients with OSA [116]. Unfortunately, very little data is currently available about the incidence of OSA in patients examined for cardiac arrhythmias [117, 118]. Another important problem is heritability of abnormalities in cardiopulmonary coupling in sleep apnea [119]. Mauser et al. predicted that ECG based sleep apnea detection methods could become a simple tool for cardiologists to screen for Sleep Apnea/Hypopnoea Syndrome (SAHS) in clinical routine [120]. In patients with arrhythmias, coincidence with sleep-related breathing disorders is high and of clinical relevance [121]. To investigate the cardiac activity further, Czopek combined acoustic and ECG measurements to monitor sleep [122].

Morbidly obese patients have a high prevalence of known and unknown cardiopulmonary diseases [123]. Catheline et al. evaluated the impact of surgically-induced weight loss on obstructive SAHS electrocardiographic changes, pulmonary arterial pressure and daytime sleepiness in morbidly obese patients [124].

Adnane et al. developed a cardiorespiratory belt sensor [125]. Their system is used for unobtrusive night-time ECG and HRV monitoring. Furthermore, they present data analysis methods by comparing bed sheet HR and HRV values with corresponding parameters obtained by a reference measurement. ECG derived RR[1]-interval data can be used to calculate HRV parameters, these parameters can be used to analyze the sleep quality as well as other wellness-related topics, which include sleep apnoea detection [126].

Traditionally, sleep staging is based on Electroencephalogrphy (EEG) signals [127]. Redmond and Heneghan found that cardiorespiratory signals deliver moderate sleep-staging accuracy [128]. The features exhibit significant subject dependence which is a limitation to use these signals in a general subject-independent sleep staging system. Parée et al. discuss the design of a new sleep staging system for ambulatory situations [129]. Cardiorespiratory-based sleep staging can be used as an adjunct tool in home sleep apnea monitoring [130].

We predict that the complexity of ECG based CAD systems will increase, because that is the dominant way of increasing accuracy, sensitivity and specificity of such mature systems [131, 132, 133]. The increased complexity creates its own unique set of problems. The increased system complexity is addressed with divide and conquer design methods [134]. Individual design teams create functional entities which communicate with one another. On the system level, complex networked problem solutions are susceptible to cyber vandalism and cybercrime.

[1]R-peak to R-peak in the QS complex.

The only way to overcome these difficulties is through well thought out design strategies which take into account the increased levels of system complexity [135].

4. Conclusion

Over the last decades, ECG based OSA detection has attracted lots of interest from the research community. One measure for that interest is the number and diversity of the research articles on that topic. In the current review, we have analysed papers from a range of medical and engineering backgrounds. During the review we found that ECG based OSA detection is difficult, because ECG signals are complex and the OSA induced signal changes are varied and subtle. Such complex detection tasks are best handled with computer algorithms. Indeed, none of the surveyed research relied on human interpretation of ECG signals. Even though all relevant studies involved computer support, there was a wide range of topics covered. Fundamental studies established the link between OSA and ECG. Scientific articles, from the engineering domain, described how to exploit such a link for diagnostic purposes to complete descriptions of physical system implementations. Our review focused on papers which aim to automate OSA detection. From these papers, we distilled the design pattern for the data mining systems which deliver effective physical problem solutions for the challenging task of ECG based OSA detection. These physical problem solutions take the form of CAD systems. It is of eminent importance to establish and improve the CAD system performance through internal and external competition. Most of the reviewed articles establish the concept of internal competition by comparing different feature extraction and classification methods. That competition leads to optimal CAD systems within the search space, which was established through the tested methods. External competition is established through citing the performance and data used by other published research work. As a direct consequence of the requirement for external competition, the surveyed research papers also published their performance and the dataset used. In turn, that information should be used by future ECG based OSA detection systems for future external competition.

Our survey shows that there is a link between changes in the ECG signal and OSA events. Hence, it is time to realize the cost saving potential of ECG based OSA detection by designing CAD systems. During our survey, we discovered 29 two class and 5 three class OSA diagnosis support systems. Most of the three class studies discriminated between normal, hypopnea and OSA events. We found that, based on the same data, classification algorithms outperform threshold methods. Another observation is that for simple two class detectors time and frequency feature extraction methods yield good results. However, for three class problems nonlinear feature extraction methods were used with great success. Hence, even two class systems might benefit from nonlinear feature extraction methods. These features could help to extend the detector performance for larger and more varied datasets.

5. Acronyms

A	Accuracy
ANN	Artificial Neural Network
AHI	Apnea/Hypopnea Index
ANOVA	Analysis Of Variance
BMI	Body Mass Index
CAD	Computer-Aided Diagnosis
DB	Database
ECG	Electrocardiogram
EDR	ECG-Derived Respiration
EEG	Electroencephalogrphy
FFT	Fast Fourier Transform
HR	Heart Rate
HRV	Heart Rate Variability
ICA	Independent Component Analysis
LD	Linear Discriminant
LSDA	Locality Sensitive Discriminant Analysis
NPE	Neighborhood Preserving Embedding
OSA	Obstructive Sleep Apnea
PCA	Principal Component Analysis
PNDB	PhysioNet sleep apnea ECG DataBase
PSD	Power Spectrum Density
PSG	Polysomnography
ROC	Receiver Operating Characteristic
RR	Respiration Rate
SAHS	Sleep Apnea/Hypopnoea Syndrome
Se	Sensitivity
Sp	Specificity
STFT	Short Time Fourier Transform
SVM	Support Vector Machine

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