IDENTIFICATION OF APNEA EVENTS USING A CHEST-WORN PHYSICAL ACTIVITY MONITOR

A thesis submitted to the University of Arizona College of Medicine – Phoenix in partial fulfillment of the requirements for the Degree of Doctor of Medicine

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Abstract

Obstructive sleep apnea (OSA) is a condition characterized by upper airway obstruction during sleep causing intermittent hypoxia and nighttime awakening. It is a common condition in the United States that is often undiagnosed. It is a significant risk factor for decreased daytime productivity, quality of life, cardiovascular disease, and death. The current gold standard for diagnosis of OSA is laboratory-based polysomnography (PSG). While PSG is necessary for the diagnosis and monitoring of OSA, many patients have limited access to PSG due to wait times at PSG laboratories or economic or geographic limitations. Portable sleep monitoring has been studied as a possible solution for patients who do not have access to timely PSG. This study aimed to use the Zephyr BioHarness 3, a chest-worn physical activity monitor that records movement and physiologic data in real-time, to detect apnea events in patients with suspected OSA undergoing single-night laboratory PSG. Twenty patients underwent single-night laboratory-based PSG while simultaneously wearing the Zephyr BioHarness 3. The Zephyr BioHarness 3 data was analyzed using three methods. First, apnea events were identified in 10-second windows of Zephyr data via support vector machine, logistic regression, and neural network (sensitivity = 76.0 ± 0.3%, specificity = 62.7 ± 0.2%, accuracy = 63.7 ± 0.1%). Second, apnea events were identified using the mean, median, and variance of the 10-second windows (sensitivity = 72.3 ± 0.3%, specificity = 69.4 ± 0.1%), accuracy 69.6 ± 0.1%). Third, apnea events were identified using phase-space transformation of the Zephyr BioHarness 3 data (sensitivity = 76.9 ± 0.3%, specificity = 77.9 ± 0.1%, accuracy = 77.9 ± 0.1%). The Zephyr BioHarness shows initial promise as a possible OSA screening tool for patients suspected of OSA but who lack access to timely laboratory-based PSG.
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Introduction

Obstructive sleep apnea (OSA) is a condition characterized by upper airway obstruction during sleep leading to intermittent periods of hypoxia and nighttime awakening. It has been identified as a major risk factor for cardiovascular disease, stroke, and sudden death\(^1\)\(^-\)\(^5\). The estimated prevalence of OSA is between 3% to 7% with the majority of patients being undiagnosed\(^6\),\(^7\). Body weight is the single largest risk factor for OSA, and the prevalence of OSA is likely to increase with the increasing prevalence of obesity\(^8\). OSA Patients with undiagnosed OSA utilize almost twice as much healthcare resources as patients who do not have OSA\(^9\). Given the burden that OSA presents to patients and the healthcare system, proper diagnosis and management of OSA presents an opportunity to reduce mortality from cardiovascular disease and stroke as well as reduce morbidity related to sleep-disordered breathing.

The current gold standard for diagnosis of OSA is the laboratory-based polysomnogram (PSG). Patients undergoing PSG spend a night in a sleep laboratory under audio and video supervision wearing sensors that record electrocardiographic, electroencephalographic, and respiratory data in addition to movement sensors placed in various locations throughout the body and face. The data from these sensors is then reviewed by a trained respiratory sleep technician who scores the study. While PSG accurately records electrocardiographic data, electroencephalographic data, respiratory, and movement data from its various sensors, it provides only a single night of data and does not replicate a patient’s typical sleep environment. In addition, many patients are not able to undergo timely PSG due to wait times, economic limitations, or geographical limitations; many patients wait at least one year between the time of their referral and the time of their PSG\(^10\). Thus, many patients are unable to undergo adequate to have OSA diagnosed or to have their disease monitored longitudinally.

Given the high prevalence of OSA and limited access to PSG, portable sleep monitoring has been studied as a possible adjunct to PSG. The American Academy of Sleep Medicine (AASM) published its first practice guideline on portable monitoring for OSA in 1994 which classified sleep monitoring technology into four categories\(^11\). The AASM subsequently published a practice guideline for portable monitoring for the diagnosis of OSA in 2007 and updated its
classification system in 2011 to classify portable sleep monitoring systems by the sensors used; namely sleep, cardiac activity, oximetry, position, effort, and respiration\textsuperscript{12,13}. Since the AASM’s first practice guideline, portable sleep monitors have improved and increasing data is showing that portable monitoring may be suitable in patients with a high pretest probability for OSA\textsuperscript{14}.

Portable sleep monitoring has been performed for over thirty years using wrist-worn accelerometers. Sleep-wake detection algorithms for wrist-worn accelerometers have traditionally used accumulated movement during sleep to estimate nighttime awakenings. In people with normal sleep patterns or minimal disordered breathing during sleep, sleep-wake as determined by accelerometry generally correlates well with PSG\textsuperscript{15,16}. For patients with sleep-disordered breathing, the agreement between PSG and accelerometry may be more variable\textsuperscript{17,18}.

This study aims to assess the feasibility of using the Zephyr BioHarness 3 (Medtronic; Annapolis, MD) to identify apnea events. The Zephyr BioHarness 3 is a portable activity monitor worn across the chest. It measures heart rate, respiratory rate, ECG, posture, and three-axis accelerometry. Traditionally, the BioHarness has been used for real-time physiologic performance monitoring of athletes, first-responders, and military personnel. In clinical settings, the BioHarness has was found to have high sensitivity and specificity for detecting tachypnea in patients being triaged in the emergency department\textsuperscript{19}. Because the BioHarness records physiologic parameters in addition to accelerometry, it may show promise as a possible portable sleep monitor for patients with a high pretest probability of OSA.
Materials and Methods

Participants

Eligibility criteria for the study were selected to include patients ages 35-60, BMI 27-35 kg/m², with no previous diagnosis of OSA, continuous positive airway pressure (CPAP) therapy, and no comorbid neurologic or sleep disorder. Participants meeting the eligibility criteria were recruited for the study during clinic visits with Dr. James Parrish, MD. Participants recruited for the study were informed of the aim and procedures of the study by a research coordinator and provided informed written consent before presenting to the sleep center for their PSG. The study was approved by the institutional review boards at Mayo Clinic Hospital in Phoenix, AZ and Arizona State University in Tempe, AZ.

Procedures

Participants arriving to the Sleep Disorders Center provided informed written consent prior to their arrival for PSG. During the check-in process, participants completed surveys regarding their sleep habits, dietary habits, and physical activity. After completing the check-in process, participants were brought to a bedroom fitted with an infrared camera and microphone where their PSG would take place. They were then fitted with standard PSG monitoring equipment, including electroencephalography (EEG), electrooculography (EOG), respiratory flow-sensing nasal cannula, submental electromyography (EMG), 2-lead electrocardiography (ECG), thoracic and abdominal respiratory effort sensors, finger-worn pulse oximetry, and pretibial EMG. After being fitted with the PSG equipment, patients were fitted with a Zephyr BioHarness 3 module and chest strap worn at the level of the inframamillary recess with the BioHarness module positioned at the left mid-axillary line. Data from the BioHarness module was collected simultaneously with PSG data for the night of the study. BioHarness data was logged via Bluetooth using the Zephyr OmniSense software and stored both locally on the module and on a workstation. The assessment time for the study began when the patient turned their bedroom lights off (labeled “lights out” in the data set) and laid in bed and ended when the patient arose from bed and turned their lights on the following morning (labeled “lights on” in the data set). PSG data for the single-night study was scored the following day by a registered sleep technician at the Mayo Clinic Sleep Disorders Center in Phoenix, AZ. PSG data were
imported into SAS (Statistical Analysis Institute) indicating which states were active (i.e. sleep stage, apnea, hypopnea) during a given one-second time window. Zephyr data was time-matched to the PSG data and combined with the PSG data in SAS.

Measures
The primary measures used from the PSG data were apnea/hypopnea events as defined by the American Academy of Sleep Medicine20. EEG, EOG, EMG, respiratory airflow, respiratory effort, and pulse oximetry obtained from the PSG were included in determining sleep stages and apnea/hypopnea events. The registered sleep technician interpreted the PSG data and identified apnea events as defined by the AASM Scoring Manual. Observation data from the infrared camera in the PSG rooms was used to determine “lights out” and “lights on” times. The technician further classified the apnea events as central, obstructive, or mixed depending on respiratory effort with central apneas being characterized by lower respiratory effort in comparison to obstructive apneas per the AASM Scoring Manual.

Zephyr BioHarness
The Zephyr BioHarness 3 is a chest-worn physical activity monitor that measures heart rate, breathing rate, breathing amplitude, ECG, and triaxial accelerometer. Data from the Zephyr BioHarness was recorded locally onto the module and logged to a workstation through the Zephyr OmniSense software suite. The same pulse oximetry data used in the PSG was included in the Zephyr BioHarness data files via the OmniSense software suite.
Analysis

Three methods were used to detect apnea events using the Zephyr data. The first method divided the Zephyr and PSG data into ten-second windows. Using the scored apnea events for the registered sleep technician’s interpretation of the PSG, apnea events as determined by PSG were recorded. Support vector machine learning algorithm, logistic regression, and neural network machine learning algorithms were applied to the Zephyr data to detect apnea events.

The second method also divided the data into ten-second windows. Features such as mean, median, and variance within the ten-second windows of PSG and Zephyr data to detect apnea events.

The third method applied to the Zephyr data was phase-space transformation. Phase-space transformation enables an analysis that accounts for all independent variables within a system and their interactions with each other. Phase-space transformation take a time series signal $x(t)$ and shifts the signal by a multiple of $\tau$, generating signals $x(t), x(t-\tau), x(t-2\tau), x(t-3\tau), \ldots x(t-m\tau)$, each creating an additional dimension of the initial time signal $x(t)$. The value of $\tau$ is determination as the first zero crossing of the graph of the time series $x(t)$. The embedding dimension $m$, or the number of dimensions to be used, is determined empirically. This converts the one-dimensional signal $x(t)$ into a multi-dimensional signal that represents the state space of that system.

After the phase space transformation, a window was obtained of the vectors in the state space. The window analysis represents a time period in which the vectors of the independent variables are used to predict an event in the next time instant. In this analysis, five-second windows of the variables captured by the Zephyr data were used to determine if an apnea would occur in the following five-second window.
Results

Sample population

Twenty-seven participants were recruited for the study. Data from twenty patients was included in the analysis. Of the twenty participants included in the analysis, ten were male and ten were female. Average age was 58.0 ± 7.3 years with an average of BMI of 29.6 ± 3.0 kg/m². Average neck circumference in the sample population was 38 ± 3 cm. Six patients were being treated for hypertension, and mean STOP-BANG and Epworth Sleepiness Scale were 4.6 ± 1.9 and 8 ± 5.4, respectively (see Table 1). STOP-BANG is a well-validated questionnaire for detection of OSA\textsuperscript{21}. The Epworth Sleepiness Scale is a questionnaire used to evaluate daytime sleepiness and has been found to correlate with decreased oxygen saturation during PSG\textsuperscript{22}. Eighteen of the twenty patients included in this study were at increased risk for moderate to severe OSA. All participants in this study underwent single night polysomnography at the Mayo Clinic Sleep Disorders Center in Phoenix, AZ. Zephyr BioHarness data was collected simultaneously with PSG data.

Three methods were used to develop prediction algorithms. The first used support vector machine, logistic regression, and neural networks. The data was analyzed in ten-second windows. This first prediction algorithm yielded sensitivity of 76.0 ± 0.3%, specificity of 62.7 ± 0.1%, and accuracy of 63.7 ± 0.1% (see Table 2).

The second prediction algorithm was based on the mean, median, and variance within the ten-second windows used for the previously mentioned algorithm. This algorithm yielded sensitivity of 72.3 ± 0.3%, specificity of 69.4 ± 0.1%, and accuracy of 69.6 ± 0.1% (see Table 3).

The third method used was phase-space transformation. The first algorithm used a $\tau$ of 70 and window size of 5 seconds. This yielded sensitivity of 76.9 ± 0.3%, specificity of 77.9 ± 0.1%, and accuracy of 77.9 ± 0.1%. The values for $\tau$ and window size were determined empirically (see Table 4).
Table 1. Patient Characteristics

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<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
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<tr>
<td>Male</td>
<td>10</td>
</tr>
<tr>
<td>Female</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>58.0 ± 7.3 years</td>
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<tr>
<td>BMI</td>
<td>29.6 ± 3.0 kg/m²</td>
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<tr>
<td>Neck circumference</td>
<td>38 ± 3 cm</td>
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<td>Number of patients</td>
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<tr>
<td>receiving HTN treatment</td>
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<tr>
<td>STOP-Bang</td>
<td>4.6 ± 1.9</td>
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<tr>
<td>ESS+2</td>
<td>8 ± 5.4</td>
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</table>

**BMI** = Body Mass Index. **HTN** = Hypertension. **ESS+2** = Epworth Sleepiness Scale +2. **STOP-Bang** = Stop-Bang questionnaire for obstructive sleep apnea.
Table 2. Detection of Apnea Events Using Support Vector Machine, Logistic Regression, and Neural Network with Window Size of 10 Seconds

<table>
<thead>
<tr>
<th></th>
<th>PSG Apnea</th>
<th>PSG Not Apnea</th>
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<tbody>
<tr>
<td>Zephyr Apnea</td>
<td>15479</td>
<td>90917</td>
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<tr>
<td>Zephyr Not Apnea</td>
<td>4880</td>
<td>152751</td>
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<tr>
<td>Sensitivity</td>
<td>76.0 ± 0.3%</td>
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</tr>
<tr>
<td>Sensitivity</td>
<td>62.7 ± 0.1%</td>
<td></td>
</tr>
<tr>
<td>Accuracy</td>
<td>63.7 ± 0.1%</td>
<td></td>
</tr>
</tbody>
</table>

*PSG Apnea* = events identified as apneas on PSG. *PSG Not Apnea* = events not identified as apneas on PSG. *Zephyr Apnea* = events identified as apneas using Zephyr data. *Zephyr Not Apnea* = events not classified as apneas using Zephyr data.
Table 3. Detection of Apnea Events Using Mean, Median, and Variance Within 10-Second Windows of Zephyr Data

<table>
<thead>
<tr>
<th></th>
<th>PSG Apnea</th>
<th>PSG Not Apnea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zephyr Apnea</td>
<td>14714</td>
<td>74624</td>
</tr>
<tr>
<td>Zephyr Not Apnea</td>
<td>5645</td>
<td>169044</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>72.3 ± 0.3%</td>
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</tr>
<tr>
<td>Specificity</td>
<td>69.4 ± 0.1%</td>
<td></td>
</tr>
<tr>
<td>Accuracy</td>
<td>69.6 ± 0.1%</td>
<td></td>
</tr>
</tbody>
</table>

PSG Apnea = events identified as apneas on PSG. PSG Not Apnea = events not identified as apneas on PSG. Zephyr Apnea = events identified as apneas using Zephyr data. Zephyr Not Apnea = events not classified as apneas using Zephyr data.
Table 4. Detection of Apnea Events Using Phase-Space Transformation of Zephyr Data with $\tau$ of 70 and Window Size of 5 Seconds

<table>
<thead>
<tr>
<th></th>
<th>PSG Apnea</th>
<th>PSG Not Apnea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zephyr Apnea</td>
<td>15262</td>
<td>92853</td>
</tr>
<tr>
<td>Zephyr Not Apnea</td>
<td>4587</td>
<td>327974</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>76.9 ± 0.3%</td>
<td></td>
</tr>
<tr>
<td>Specificity</td>
<td>77.9 ± 0.1%</td>
<td></td>
</tr>
<tr>
<td>Accuracy</td>
<td>77.9 ± 0.1%</td>
<td></td>
</tr>
</tbody>
</table>

$PSG$ Apnea = events identified as apneas on PSG. $PSG$ Not Apnea = events not identified as apneas on PSG. Zephyr Apnea = events identified as apneas using Zephyr data. Zephyr Not Apnea = events not classified as apneas using Zephyr data.
Discussion

OSA has become an increasing public health concern and will continue to impact the health of the general population as obesity rates increase. With widespread efforts seen to improve primary prevention of cardiovascular disease including myocardial infarction and stroke, proper sleep health remains an understudied and often undervalued modifiable risk factor, especially for patients who suffer from OSA. Improving the quality of sleep in patients with OSA is key to reducing cardiovascular mortality and improving daytime quality of life.

Proper detection and management of OSA requires PSG not only to confirm the diagnosis, but also to properly titrate positive airway pressure treatment modalities and monitor response to treatment. Unfortunately, however, many patients lack access to PSG, either due to limited financial resources, geographic limitations, or wait times at PSG facilities.

Portable sleep monitoring presents a crucial opportunity to gather sleep data in free-living environments and can serve as an important adjunct to PSG. While portable sleep monitoring has been studied most extensively in wrist-worn accelerometers, the Zephyr BioHarness shows potential as a portable sleep monitor due to the physiologic data that it gathers in addition to accelerometry.

The results of this study show that a phase-space transformation model with $\tau$ of 70 and window size of 5 seconds yielded the best sensitivity, specificity, and accuracy. This is the first known study that uses phase-space transformation analysis of Zephyr BioHarness 3 data for detection of apnea events in patients with suspected OSA. While the sample population was small, the many data points collected over a night of sleep in a PSG provide meaningful data concerning each individual patient. Due to its portability, the Zephyr BioHarness 3 offers the possibility of free-living sleep monitoring over multiple nights, allowing for collection of more robust patient sleep data in their typical sleep environment.
Future Directions
While these initial results show that the Zephyr BioHarness 3 may be of use in screening patients for OSA in circumstances where access to PSG is limited. Further studies are needed, especially in a free-living environment, to assess if the Zephyr BioHarness has utility for detecting apnea and hypopnea events in home settings.
Conclusions

The Zephyr BioHarness 3 shows initial promise as a portable sleep monitor capable of independently predicting apnea events in patients of OSA. Before it is used as a screening tool for OSA, more studies should be done, especially in a free-living environment or with multiple nights of sleep data. The potential of successful screening for OSA with the Zephyr BioHarness 3 is an important opportunity for detecting OSA in patients who otherwise may not have access to PSG.
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