Apneas induced Arousals characterization

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1. ABSTRACT

In this work, we characterized the encephalographic responses before, during, and after apnea and hypopnea (AH) events, using polysomnographic data of three individuals and the respective annotations of the respiratory events and sleep stages. Variance, entropy, and absolute and relative power features were extracted for the 5 EEG bands of interest in C3 and C4 channels: delta (δ, 0.5-4 Hz), theta (θ, 4-8 Hz), alpha (α, 8-12 Hz), sigma (σ, 12-16 Hz) and beta (β, 16–30 Hz). The mean, minimum, and standard deviation of SAO_2, and the sleep stage were also added to the feature set. The entire feature set was tested in the classification of types of AH events, and the EEG features set was tested in the identification of respiratory events, using LDA, SVM, and KNN classifiers.

We found there were significant differences in the EEG characteristics depending on the severity of the respiratory event, with the most relevant features being the variance and absolute power of the δ, θ, and α bands, but further research with larger datasets is needed to reach a definitive conclusion.

2. PROBLEM AND MOTIVATION

Arousals are defined by the American Sleep Disorders Association (ASDA) as an "abrupt shift in EEG frequency, which may include theta, alpha and/or frequencies greater than 16 Hz, but not spindles, and are subject to several other rules and conditions for scoring [1]. However, scoring EEG arousals in long polysomnography records is difficult, labor-intensive and time-consuming [2]. Looking at EEG features during apnea and hypopnea events could void the need for scoring arousals, while providing a more complete picture of the relationship between the respiratory and central nervous systems.

Therefore, the main goal of this study was to characterize the electroencephalographic responses of different types of apneas and hypopnea events (AH), by exploring C3 and C4 EEG characteristics in 3 periods: before, during, and after each respiratory event.

3. BACKGROUND AND RELATED WORK

Apnea is a very common sleep disorder characterized by pauses in breathing or shallow breaths that cause sleep deprivation and can lead to headaches, daytime sleepiness, diminished cognitive performance, and cardiovascular diseases [3]. There are three types of apnea: Obstructive Sleep Apnea (OSA), Central Sleep Apnea (CSA), and Mixed Sleep Apnea. The OSA is the most prevalent and dangerous, since it causes a complete blockage of upper airways and relaxes the throat muscles to block airflow during sleep [4], and a respiratory effort is recorded throughout the event [5]. Conversely, in CSA, the brain stops sending signals to the muscles that control breathing [4] and there are pauses in breathing due to a lack of a respiratory effort during sleep. Finally, Mixed Apnea is a combination of both, where there is an absence of respiratory effort during the beginning of the event followed by increasing respiratory effort during the second half [5].

Apneas are defined as a reduction in airflow greater than 90% of the baseline, while hypopneas (as a respiratory effort) are defined as a reduction in airflow greater than 50% of the baseline. Both these events must have a duration greater than 10 seconds, and a reduction of airflow during at least 90% of the event [5].

According to ASDA, an arousal is defined as a sudden change in EEG frequency consisting of alpha and theta activity, and duration 3-15 seconds, and normal sleep must be recorded for at least 10 seconds before the event [1]. Arousals are "forced" wakings of the brain as the result of a respiratory disturbance, and they are needed for upper airway opening during hypopneas and apneas to reestablish airflow. It is also believed that they disturb the sleep homeostatic process and cause the damage from sleep apnea. The dominant symptom seen in respiratory sleep clinics is excessive daytime sleepiness, which is often due to sleep fragmentation secondary to repetitive arousal from sleep [6] and can lead to reduced alertness and attention, along with other serious effects.

Current sleep diagnosis counts the average number of apneas and hypopneas per hour during the night, using the Apnea-Hypopnea Index [5] to determine the severity of a person's sleep apnea. However, since any respiratory event that causes an arousal can cause damage, the counting of respiratory effort related arousals (RERA) has been considered to evaluate sleep apnea using the Respiratory Disturbance Index (RDI), that is, the average number of apneas, hypopneas and RERAs per hour of sleep, confirmed by EEG [5].

Therefore, arousal quantification is important to evaluate apnea severity and identify patients who might benefit from treatment, and there have been considerable efforts to find robust methods to quantify arousal frequency [6]. Manual arousal scoring is currently the most used method, with the 3-second definition from ASDA being the most widely used, though there are other more sensitive definitions. However, this process is very labor-intensive, and different definitions of arousals can lead to different results. More sensitive definitions have been shown to increase the correlation between sleep fragmentation severity and the measurable daytime consequences, but shortening the duration of EEG alpha activity required for the presence of an arousal makes it progressively more difficult to separate pathological events from normal high frequency EEG characteristics [6].

These complexities in the development of definitions of arousal for manual scoring have led to attempts to improve this process using automated signal processing techniques, that are often based on the analysis of the EEG spectrum [6]. A number of studies have been published in recent years, that perform arousal

detection using a single EEG derivation [7], or multichannel data [8], using several methods for time-frequency analysis and feature extraction. However, most of these studies also use the ASDA definition for arousals, so the problem with the development of an accurate and universally accepted arousal definition remains.

We hypothesize that the lack of agreement on a single definition may result from the inadequacy of such a strict definition to fully describe the complex EEG responses which are triggered by the referred respiratory events, and that contribute to restoring the normal breathing pattern.

Thus, a broader characterization of the relevant EEG features for each type of respiratory event could provide a more complete picture of the relationship between the respiratory and central nervous systems, and possibly surpass the need for a definition-based arousal classification. These features could be used for apnea detection and classification, and to gain a better understanding of sleep arousals for proper assessment of sleep fragmentation.

Several studies have also approached this topic through EEG feature extraction. The variance, energy, power, or entropy of EEG sub‑bands can be used for classification of apnea and normal breathing events or arousal characterization [4,9,10]. Band separation can be done using Infinite Impulse Response Butterworth Band pass filter or Hilbert Huang Transform techniques [4]. Other studies also used inter-band feature ratios for a more complete qualitative characterization of the changes in EEG [3,10].

These features are often used in classification of sleep apnea or arousals. EEG based classification and characterization of sleep apnea is most commonly done using Support Vector Machine (SVM) and K-nearest neighbor (KNN) classifiers [4,9]. Other classification methods have been used, such as Random Forest (RF), Artificial Neural Networks (ANN), or Linear Discriminant Analysis (LDA) [4,9,11].

4. APPROACH AND UNIQUENESS

4.1 Material

For this study, we used three whole night EDF raw polysomnography files, with data on EEG, Thorax and Abdominal effort belt, Oro-Nasal thermistor, Cannula, ECG, EOG, and Oxygen Saturation. The signals were annotated by professionals with respect to sleep stages and respiratory events (obstructive apnea, central apnea, mixed apnea, or hypopnea). EEG signals were sampled at 250 Hz. In total, there were 778 respiratory events, with 1 central apnea, 375 hypopneas, 362 obstructive sleep apneas and 40 mixed apneas.

The channels used in this study were C3, C4, since they are the most commonly used in PSG studies, and SAO2 (oxygen saturation). The results presented in Section 5 were obtained taking together the data from the three PSG recordings (in order to obtain statistically significant results). We then analysed the results for each recording individually to confirm their agreement with the general results obtained.

One of the goals of this study was to evaluate EEG features in intervals before, during and after the annotated events. The results presented in this paper were obtained using time-windows before and after the events of 10 seconds. Besides, we decided to avoid overlap of the windows after and before two consecutive events, so that the EEG features measured were not significantly influenced by the neighboring events. Accordingly, we excluded all the events that had less than 20 seconds between each other. This yielded a total of 511 events, with 263 hypopneas, 225 obstructive sleep apneas, 21 mixed apneas, and 1 central apnea. The single central apnea event was also excluded, since its results wouldn't be statistically significant.

4.2 Pre-Processing of the EEG signals

In this analysis, we were only concerned with EEG rhythms in the frequency band of 0.5 - 30 Hz (α to β bands), since higher frequencies aren't common in PSG records. Thus, according to the Sampling Theorem, a sampling frequency of 100 Hz should be enough to avoid loss of information. For that reason, and in order to increase the computational speed, we downsampled the EEG data to 100 Hz.

We started by designing a Infinite Impulse Response (IIR) Butterworth bandpass filter, with cutoff frequencies of 0.5 and 40 Hz. This filter had three main purposes: to attenuate possible high-frequency noise; to limit the bandwidth of the signal in order to avoid aliasing upon downsampling; finally, to remove the slow trends that commonly affect surface EEG recordings (they originate at the interface between the electrodes and the skin, and may be due, for instance, to heterogeneities of the skin surface or to the presence of sweat [12]).

Since the high-frequency attenuation slope of the Butterworth filter wasn't very high, we first applied an IIR Notch filter with half-power frequencies 59 and 61 Hz to better remove the powerline interference noise (which was strongly marked in the Fourier spectrum of some EEG channels).

The signals analysed appeared to be of good quality. Given the high complexity of EEG recordings, the recognition of artifacts requires a lot of expertise in the topic. We performed an Independent Component Analysis (using FasICA algorithm) of a subset of EEG signals, along with the ECG and chin EMG recordings. We did not have EOG data, which would have been important to extract possible ocular artifacts. With the channels provided, ICA was not able to isolate evident sources of artifacts. Thus, considering the apparently good quality of the data and in order to preserve as many characteristics of the signal as possible, we decided not to apply any additional method to remove artifacts.

Then, in order to reduce inter-subject variability, the EEG-channels of interest were normalized in the time-domain to have zero-mean and amplitude within the interval [-1,1].

The last step of the pre-processing phase was the use of a set of five IIR Butterworth bandpass filters in order to separate the C3 and C4 signals into the 5 EEG bands of interest: delta (δ, 0.5-4 Hz), theta (θ, 4-8 Hz), alpha (α, 8-12 Hz), sigma (σ, 12-16 Hz) and beta (β, 16–30 Hz).

4.3 Proposed Solution - Feature Extraction

After pre-processing, we tested and extracted several EEG features in the 3 periods considered in this study (before, during, and after each respiratory event) to evaluate the most relevant ones. We also extracted the minimum, mean, and standard deviation of the oxygen saturation in those periods, as well as the respective sleep stages. For both signals C3 and C4, we computed the absolute and relative powers, the variance, and the entropy for the 5 bands of interest. The definitions used for each EEG feature are described below.

A. Power

The power of a signal is the sum of the absolute squares of its time-domain samples (energy) divided by the signal length.

$$P = \frac{1}{N}\sum_{n=1}^{N}|x(n)|^2$$

For relative power, we simply divided the power of each band by the total power of the bands.

B. Variance

Variance measures the deviation of each value in the signal from the mean.

$$\sigma^2 = \frac{1}{N-1}\sum_{n=1}^{n}|x(n)-\mu|^2$$

where μ is the mean of the signal.

C. Entropy

The entropy of a signal is a statistical measure of its randomness or uncertainty. Here, we used the definition of the Shannon entropy, where the probabilities of each sample-value were obtained from the normalized histogram counts of the signal.

$$E(n) = -\sum_{n=1}^{N}P(x_n)\log_2(P(x_n))$$

The structure of the final feature matrix is presented below. For each respiratory event (row), there are 132 columns in the feature matrix. It should be noted that each "C3" and "C4" in the EEG features is composed of 5 columns, one for each EEG band of the corresponding channel.

Table 1 - Simplified structure of feature matrix

Before			During			After			Single Event Features
Features SAO2 (if available)	**Features EEG**		**Features SAO2** (if available)	**Features EEG**		**Features SAO2** (if available)	**Features EEG**		
	C3	C4		C3	C4		C3	C4	

From the initial set of features, a subset was selection via Neighborhood Component Analysis (NCA), and classification of types of AH events and AH events occurrence was tested for a number of different classification algorithms, with K-Nearest Neighbor (KNN), Linear Discriminant Analysis (LDA), and Support Vector Machine (SVM) classifiers.

KNN is a non-linear classification method, based on computing distances among several feature values between the test data and the training set, in order to determine the most similar top k data within the training set. Euclidean or cosine distance are generally used as distance metrics [9]. Herein, we used euclidean distance, which yielded the best overall performance. SVM classifies data by finding an optimal hyperplane that best separates the data according to their classification. It was originally designed for binary classification, but it can also be used for multiclass classification, by dividing the original problem into multiple binary classification problems [9]. In this study we used a one-vs-one approach, which splits the dataset into one binary classification dataset for each pair of classes, and chose a linear kernel as the kernel function to design the hyperplanes, given it yielded the best results. Finally, LDA assumes each class generates data based on different gaussian distributions to find a linear combination of features such that the projection maximizes the distance between the means of two classes while minimizing the variance within each class.

5. RESULTS AND CONTRIBUTIONS

5.1 Features Analysis

A. Oxygen Saturation (SAO_2)

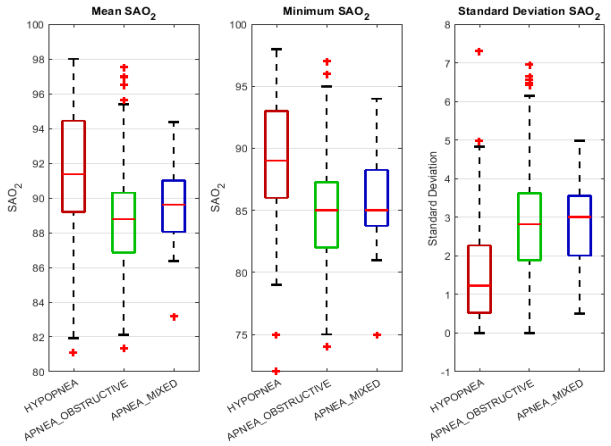


Figure 1: Boxplots of mean, minimum, and standard deviation of O_2 saturation during each type of event.

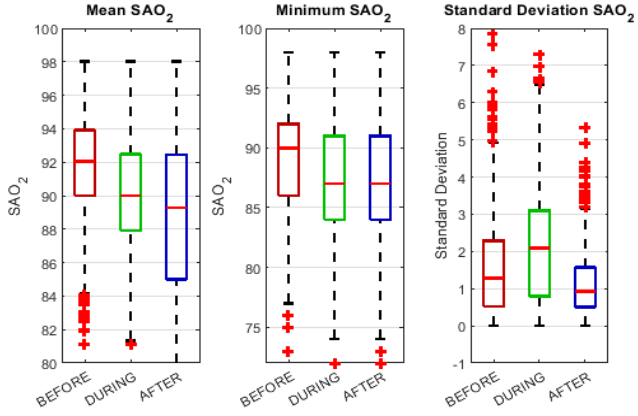


Figure 2: Boxplots of mean, minimum, and standard deviation of O_2 saturation, for the periods before, during, and after the event, for any type of respiratory event.

First, in Figure1, we present some statistics on the oxygen saturation levels (SAO_2) measured during the intervals scored as hypopnea, obstructive apnea and mixed apnea, respectively. The mean and minimum SAO_2 values were typically lower for both types of apneas than for hypopneas, while the standard deviation was higher. This is consistent with the definitions for classification of apneas and hypopneas described before (reduction of airflow greater than 90% of baseline for apneas and greater than 50% for hypopneas).

When considering the periods before, during and after any respiratory event, we noticed a decrease in the mean and minimum of the SAO_2 during the event in comparison with the 10-second period immediately before, as shown in Figure 2. Once again, the results are in line with the expected consequences of these respiratory events. Moreover, such low SAO_2 levels tend to persist in the 10-second period after the event, but the minimum values did not further decrease, in general. This suggests that some physiological responses were triggered to avoid the perpetuation of the respiratory event. However, it seems that it takes some time (more than the 10 s considered) for the person to restore the normal SAO_2 levels after an AH event. The standard deviation was clearly higher during the event, given the drop in the SAO_2 observed.

B. Sleep states

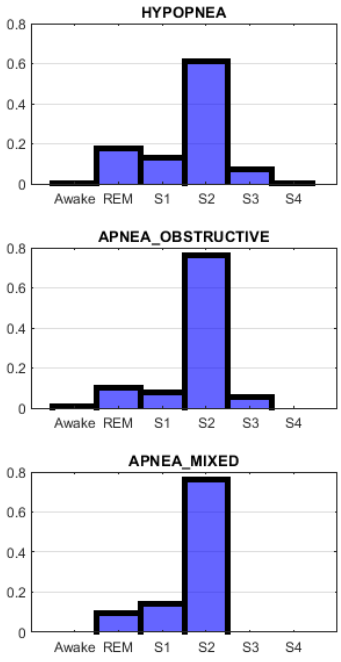


Figure 3: Percentage of events that occur in each sleep stage, for each type of event.

In regards to the sleep stage, it is clear that most respiratory events occurred during stage 2, which is normal since about 50% of an adult's sleep is spent in that stage [13]. Apnea events occur more often in stage 2 than hypopneas (~80% vs 60%), and less in Rapid Eye Movement sleep (REM).

A sleep episode normally begins with a short period of NREM (non-rapid eye movement) stage 1 progressing through stage 2, followed by stage 3 and finally to REM. In OSA, sleep is fragmented by frequent arousals with increase in the lighter stages of sleep and decrease in stage N3 sleep and REM sleep [14]. Thus, an hypothesis is that the apneas occur more often in NREM stage 2 than the hypopneas because they are more severe, and thus the person exhibits more sleep fragmentation and is more deprived of deep sleep.

C. Entropy of EEG bands

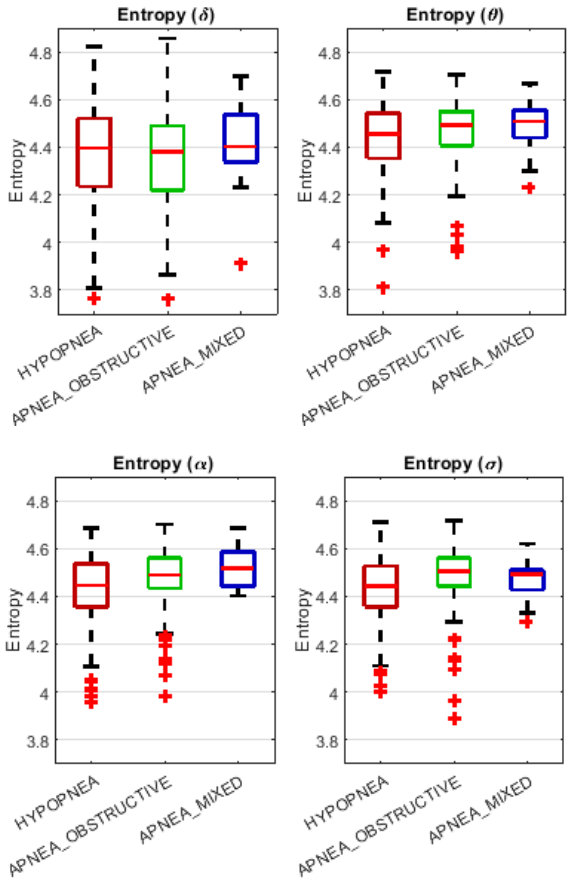


Figure 4: Boxplots of entropy of α, δ, θ, and σ bands during each type of event, for the C3 channel.

In regards to entropy, there appears to be a slight increase in the α, θ, and σ bands in apneas relative to hypopneas. Nevertheless, given the small difference and the high number of outliers with lower entropies in the obstructive apneas subset, it is very likely that these differences are not significant. There were also no significant differences in the periods before, during, and after the events.

D. Power of EEG bands

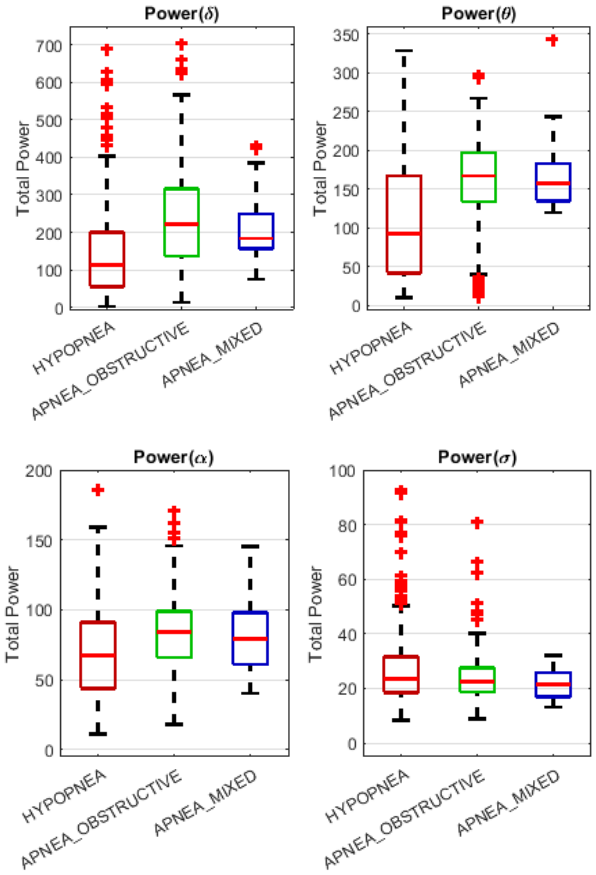


Figure 5: Boxplots of absolute power of α, δ, θ, and σ bands during each type of event, for the C3 channel.

The boxplots in Figure 5 clearly show that the absolute power of the α and, more markedly, the θ bands is higher in the apneas than in hypopneas. This may be a hint to the severity of the respiratory disturbance (i.e., of the oxygen depletion): in healthy adults, α rhythms are mostly associated with an awake state; θ waves are mostly present in light sleep. Thus, the higher intensity of these rhythms during apnea events might suggest a stronger attempt to promote lighter sleep stages or even awakening so that the person starts breathing again. In hypopneas, these mechanisms may be less significant, as the hipoxia is usually less severe (as suggested by Figure 1).

On the contrary, no significant difference between respiratory events is observed in terms of the absolute power of the σ band. Indeed, the σ band overlaps with the frequency range of sleep spindles, which is not an EEG manifestation of an arousal, according to ASDA's definition. Thus, it seems that the σ rhythm does not play a decisive role in the response to these events, thereby not differing significantly between apneas and hypopneas.

Another interesting result shown in Figure 5 was the higher power of the δ band in the apnea events. This rhythm is a marker of deep sleep and so, at first sight, this might seem to contradict the reasoning made above for the α and θ bands. However, this may be a mechanism of counteracting the tendency for arousal, thus trying to keep the person asleep. Arousal-associated increases of slow EEG rhythms have been associated with protecting sleep stability [10].

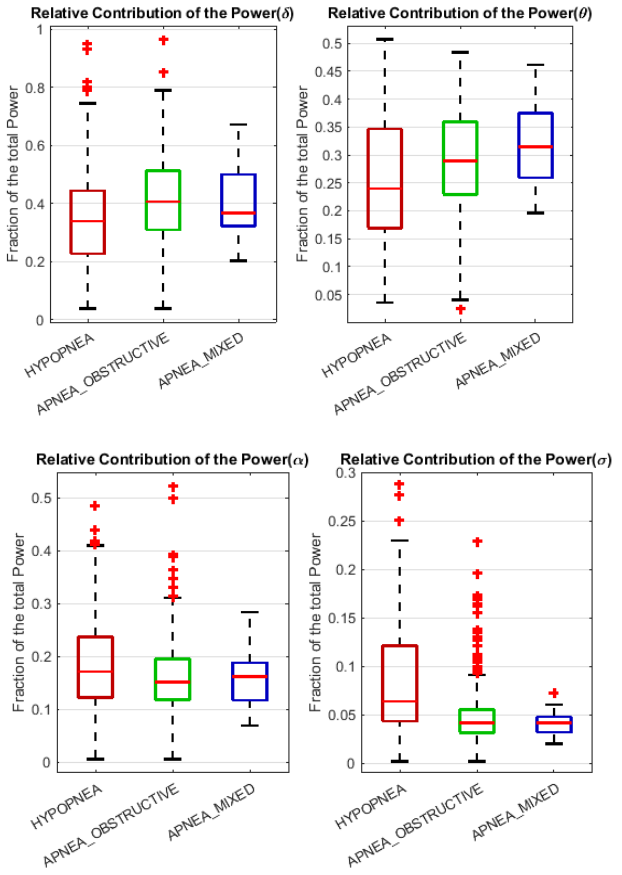


Figure 6: Boxplots of relative power of α, δ, θ, and σ bands during each type of event, for the C3 channel.

In the plots of relative power in Figure 6, higher values are observed in the δ and θ bands in apneas relative to hypopneas, but not in the α band. This may be a consequence of the "competition" described above between the medium and low frequencies of the brain: even though the absolute α power is higher during apneas, it can easily be masked by the higher powers of the δ and θ bands, since slower EEG waves have higher amplitudes. Thus, the overall contribution of the α to the total power may actually be lower. Arousal-associated power changes in low and medium frequency are implicated for protecting sleep stability, so taking into account these relative changes in EEG power across the different bands is important to gain a complete qualitative characterization of the EEG response during respiratory events [10].

In summary, these differences in EEG band power could mean that different respiratory events have different arousal probability or patterns based on their severity. We also note that both the absolute and relative powers of the δ band are much higher than in the other bands, which is normal in polysomnographic records.

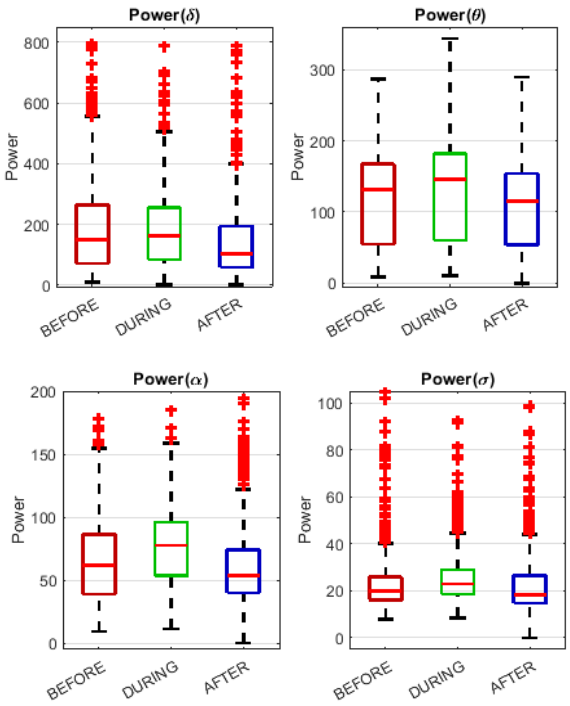
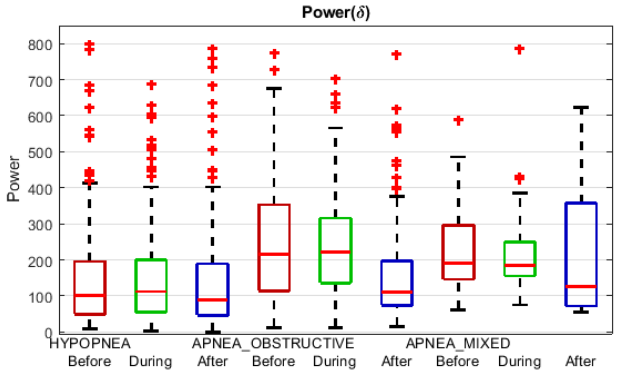


Figure 7: Boxplots of absolute power of α, δ, θ, and σ bands for periods before, during, and after all events, for the C3 channel.

In regards to the periods before and after the AH events, the pattern in Figure 7 was observed for both types of apneas and for the hypopneas. Overall, there is a slight increase of the power of each band during each respiratory event, when compared to the time windows before and after. It is also clear that this increase is much more pronounced for the α band, probably for the reasons discussed before.

To gain a better understanding of the differences in band power for different types of AH events, we analyzed the absolute power of the α, δ, and θ bands for the three time windows discriminated by type of event.



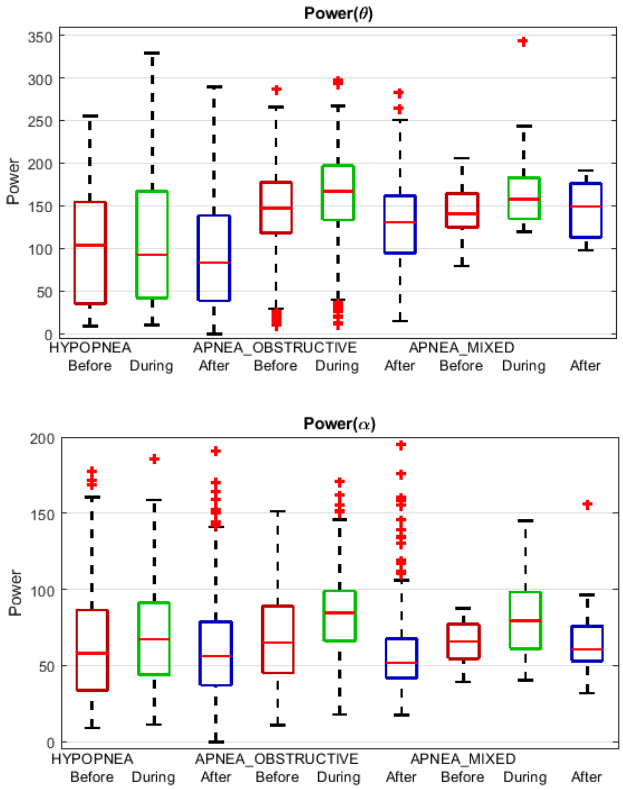
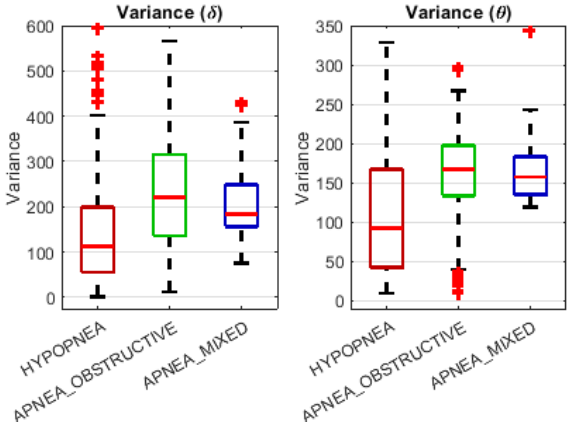


Figure 8: Boxplots of absolute power of α, δ, and θ bands for periods before, during, and after discriminated by type of event, for the C3 channel.

There are differences in the EEG characteristics depending on the severity of the respiratory event: apneas show slightly higher α power during the event (and lower in the periods before and after), higher δ power before and during the event, and higher θ power in the 3 time periods, when compared to hypopneas.

E. Variance of EEG bands



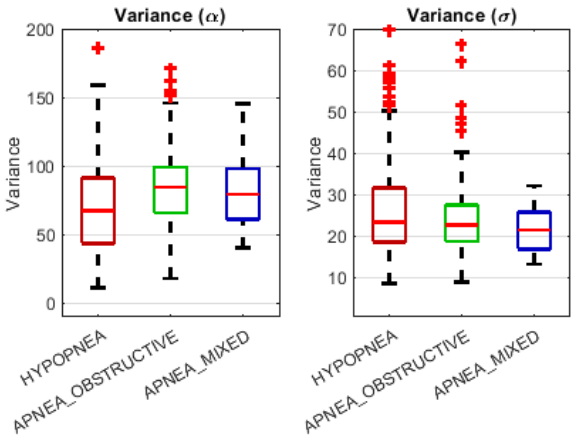


Figure 9: Boxplots of variance of α, δ, θ, and σ bands during each type of event, for the C3 channel.

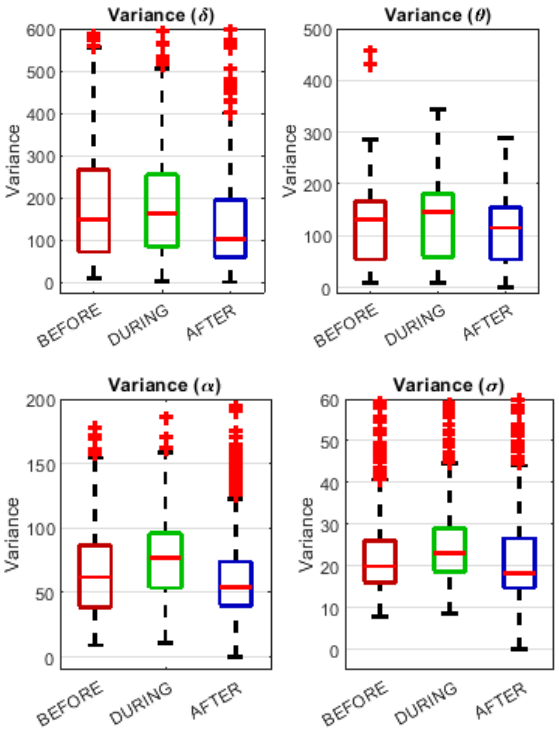


Figure 10: Boxplots of variance of α, δ, θ, and σ bands for periods before, during, and after all events, for the C3 channel.

In regards to the variance, in Figure 9, the pattern was similar to the ones observed for the absolute and relative powers: higher variance in the δ, θ, and α bands (much more pronounced in the θ band) in apneas when compared to hypopneas, but not in the σ band; and an increase in the variance of each band during each respiratory event when compared to the time windows before and after (more pronounced for the α band).

5.2 Feature Selection and Classification

From this statistical analysis, we can make some initial extrapolations regarding the EEG features.

First, that the time windows that correspond to the periods of the annotated events ("During") consistently show elevated α band power and variance when compared to the time windows immediately before and immediately after, which is consistent with the association of arousals with respiratory events.

Second, that the EEG response caused by apneas and hypopneas are not similar, with the ones caused by apneas showing significantly larger changes in the variance and power of the δ, θ, and α bands. There appears to be a correlation between the severity of the respiratory event and the changes in the EEG.

These differences show that the extracted features could be useful for classification of types of AH events and identification of events based on EEG response.

A. AH event type classification

From the previous analysis, we hypothesized that the most significant features to distinguish between AH event types were the mean, minimum, and standard deviation of oxygen saturation, the variance of the δ, θ, and α bands, and the power and relative power of the δ, θ, and α bands. To strengthen this intuition, we used Neighborhood Component Analysis (NCA) to select the features that maximize prediction accuracy of classification algorithms.

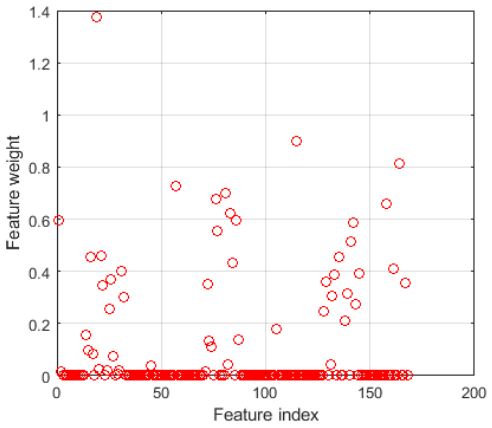


Figure 11: Feature weights after applying neighborhood component analysis.

It is clear that there are a lot of features with close to 0 weight that aren't relevant for prediction accuracy. With an overview of the feature indexes, we verified that the sleep states, and the entropy and relative power features of all EEG bands had been eliminated in all time windows. The "during event" window had the most relevant features, as expected. Most of the high weight features were from the variance or absolute band power, showing that the EEG characteristics are good predictors. Most oxygen saturation features were also eliminated, contrary to our predictions.

Then, using the remaining features, we tested different classifiers: Linear Discriminant Analysis, Support Vector Machine, and K-Nearest Neighbor. We obtained a validation accuracy of 64.5%

for LDA, 66.7% for SVM, and 68.2% for KNN. We present the confusion matrices for the three classifiers in Figure 12.

They all had high sensitivity for OSAs and hypopneas (true positive rates close to 70%), but very low sensitivity for mixed apneas. This is probably because of the relatively low number of mixed apnea events in our data (only 21 events in a total of 510), which could lead to a skewed classifier.

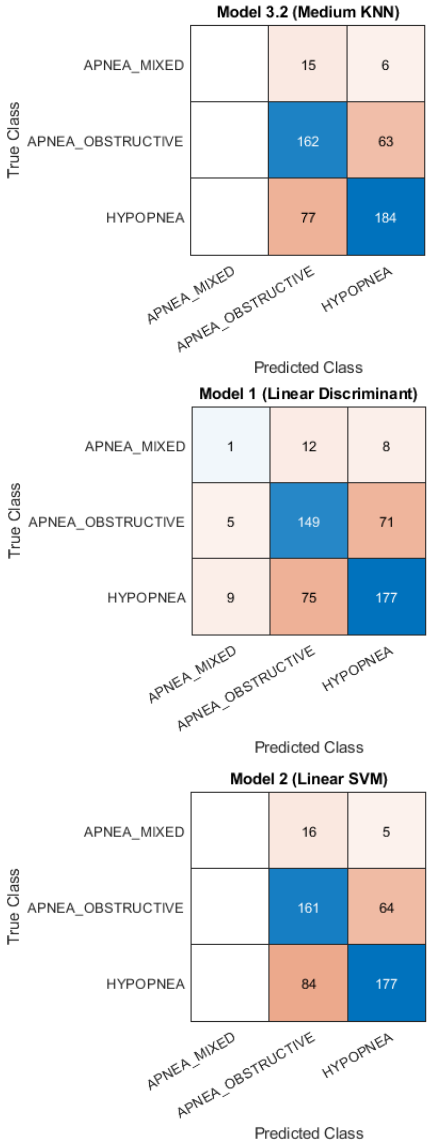


Figure 12: Confusion matrices for K-Nearest Neighbor, Linear Discriminant Analysis, and Support Vector Machine classifiers in apnea classification.

Despite this, and considering the small amount of events in our study, we believe the classifiers performed well in the distinction between apneas and hypopneas. Since most of the high weight predictors were EEG features, it also confirms that the EEG response pattern varies with the type of respiratory event. The role that each event has on the probability of occurrence of an arousal is still uncertain, though it has been shown that there is a strong correlation between the duration of apneas and the duration of arousals, and that arousals caused by apneas and hypopneas are not similar, with the arousals caused by apneas being more severe [15] (which is concordant with our results). Further tests with more data from CSAs and mixed apneas are needed to gain a full scope of the relationship between these features and apnea characteristics and severity.

B. AH event prediction based on EEG characteristics

Finally, we tested our feature set in the classification of AH events when compared to a baseline, to evaluate how well the EEG characteristics can predict the occurrence of respiratory events. Taking into account our previous analysis of the features in section 5.1, we considered the "Before" time windows to be a good approximation of the baseline of a normal sleep period, and used two classes for classification: "Before" (the non-event), and "AH event" (any respiratory event). All the features that weren't extracted from the EEG were excluded prior to NCA. After NCA, only 2 additional features were excluded, and then we tested this data with the Linear Discriminant Analysis, Support Vector Machine, and K-Nearest Neighbor classifiers once again.

SVM and KNN yielded poor results, with less than 60% accuracy, but the LDA classifier had an accuracy of 81.7%. We present the respective confusion matrix below.

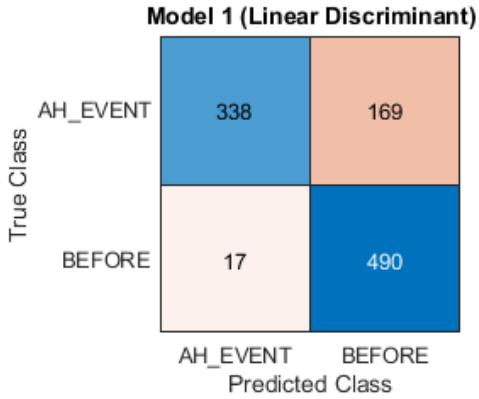


Figure 13: Confusion matrix for Linear Discriminant Analysis classifier in event classification.

The sensitivity for "Before" was 96.6%, and the sensitivity for AH events was 66.7%. This shows that, by using only EEG features, our model was able to identify two thirds of the respiratory events. We should however note that the "Before" time windows may not be the most accurate baseline for a normal sleep period. We chose not to consider sleep periods outside of the annotated events as normal sleep because the patients could have other respiratory events that cause arousals or changes in the EEG during the night, which don't fit the definitions of apnea or hypopnea (RERAs) and that weren't annotated in this dataset. It would be interesting to evaluate this model with data that had annotations of all respiratory events, to see how well the EEG characteristics can identify periods of sleep fragmentation caused by changes in airflow.

We consider this a good preliminary result, once again limited by the small amount of events and the lack of annotations on RERAs.

DISCUSSIONS AND CONCLUSIONS

In this study, the EEG characteristics during AH events were analyzed in depth in order to gain a better understanding of the responses of the brain to respiratory disturbances. Our preliminary results were consistent with the ones in the literature and with the ASDA definitions for the frequency content of arousals. In general, during the respiratory events, the α band had higher power and variance when compared to time windows immediately before and immediately after.

There were also differences in the EEG characteristics depending on the severity of the respiratory event: apneas showed slightly higher α power and variance, and significantly higher δ and θ power and variance when compared to hypopneas, with no differences in the σ band (associated with sleep spindles). Even though there is a correlation between respiratory event and arousal severity [15], we found no studies in the literature that evaluated the differential EEG band characteristics in hypopneas vs apneas. Further research is needed to gauge whether these differences in δ and θ power are significant, since we worked with a small number of events.

Most of our apnea events were also from OSA, that is an heterogeneous disease, and several factors can affect its severity and the mechanisms that cause it [15]. For that reason, we cannot exclude that inter-subject variations may be a factor at play in some of these differences. In fact, some authors [16] believe that the arousals in OSA may have patient-specific features (i.e., that each patient's reaction to an obstructive respiratory event may have its own signature). Future studies considering patient-specific EEG features are also warranted, and could provide insight on the relationship between EEG characteristics and clinical observations.

These differences could be useful for apnea and respiratory events classification that isn't based on manual scoring, so we also tested the two classifiers. They yielded acceptable preliminary results, but once again, future testing with more data with a significant amount of respiratory events of all types (OSA, CSA, mixed apnea, hypopnea, and RERA) would be interesting to fully understand the relationship of EEG characteristics with AH events.

In conclusion, our main observation was that EEG responses triggered by the respiratory events show differences in frequency content depending on the severity and type of event. This demonstrates that using a strict definition for arousal scoring and counting such events may not be enough to fully capture the complexity of the mechanisms of arousal and sleep fragmentation in patients with sleep apnea. Thus, we believe that more research in this subject is warranted and could lead to the development of clinically significant indices that improve diagnostic and prognostic accuracy in sleep apnea patients.

6. REFERENCES

[1] American Sleep Disorders Association and Sleep Research Society, *EEG arousals: scoring rules and examples*, Sleep 15 (2) (1992) 173–184.

[2] Álvarez-Estévez, D., & Moret-Bonillo, V.. *Identification of Electroencephalographic Arousals in Multichannel Sleep Recordings.* IEEE Transactions on Biomedical Engineering, 58(1) (2011) 54–63.

[3] Saha, S., Bhattacharjee, A., & Fattah, S. A. *Automatic detection of sleep apnea events based on inter-band energy ratio obtained from multi-band EEG signal.* Healthcare Technology Letters, 6(3) (2019), 82-86

[4] Vimala, V., Ramar, K., & Ettappan, M. *An Intelligent Sleep Apnea Classification System Based on EEG Signals*. Journal of Medical Systems, 43(2) (2019).

[5] Tsara V, Amfilochiou A, Papagrigorakis MJ, Georgopoulos D, Liolios E *Guidelines for Diagnosis and Treatment of Sleep-related Breathing Disorders in Adults and Children*. HIPPOKRATIA 13(3) (2009) 187-181.

[6] Davies, R. J. O., Bennett, L. S., & Stradling, J. R. *What is an arousal and how should it be quantified?* Sleep Medicine Reviews, 1(2) (1997), 87–95.

[7] Cho, S. P., Lee, J., Park, H. D., & Lee, K. J. *Detection of Arousals in Patients with Respiratory Sleep Disorders Using a Single Channel EEG*. IEEE Engineering in Medicine and Biology 27th Annual Conference 2005.

[8] Álvarez-Estévez, D., & Moret-Bonillo, V. *Identification of Electroencephalographic Arousals in Multichannel Sleep Recordings*. IEEE Transactions on Biomedical Engineering, 58(1) (2011), 54–63.

[9] Zhao, Xiaoyun & Wang, Xiaohong & Yang, Tianshun & Ji, Siyu & Wang, Huiquan & Wang, Jinhai & Wang, Yao &Wu, Qi. *Classification of sleep apnea based on EEG sub-band signal characteristics*. Scientific Reports. 11 (2021)

[10] Liu, J. V., & Yaggi, H. K. *Characterization of Arousals in Polysomnography Using the Statistical Significance of Power Change*. 2018 IEEE Signal Processing in Medicine and Biology Symposium (SPMB). (2018).

[11] Prucnal, M. A., & Polak, A. G. *Analysis of Features Extracted from EEG Epochs by Discrete Wavelet Decomposition and Hilbert Transform for Sleep Apnea Detection.* 2018 40th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC). (2018).

[12] The McGill Physiology Virtual Lab, *Biomedical Signals Acquisition, EEG Introduction.* https://www.medicine.mcgill.ca/physio/vlab/biomed_signals/eeg_n.htm

[13] Shrivastava, D., Jung, S., Saadat, M., Sirohi, R., & Crewson, K. *How to interpret the results of a sleep study.* Journal of community hospital internal medicine perspectives, 4(5), (2014).

[14] Basunia, M., Fahmy, S. A., Schmidt, F., Agu, C., Bhattarai, B., Oke, V., Quist, J. *Relationship of symptoms with*

sleep-stage abnormalities in obstructive sleep apnea-hypopnea syndrome. Journal of Community Hospital Internal Medicine Perspectives*, 6*(4) (2016).

[15] Leppänen, T., Kulkas, A., Oksenberg, A., Duce, B., Mervaala, E., & Töyräs, J. *Differences in arousal probability and duration after apnea and hypopnea events in adult OSA patients.* Physiological Measurement. (2018).

[16] K. Bahr, V. Geisler, T. Huppertz, S. Groppa, C. Matthias, H. Gouveris, and M. Muthuraman, *Intensity of Respiratory Cortical Arousals Is a Distinct Pathophysiologic Feature and Is Associated with Disease Severity in Obstructive Sleep Apnea Patients*, Brain Sciences, vol. 11, no. 3, p. 282, Feb. 2021.