Abstract—Objective: We aimed to investigate the differences in electroencephalogram (EEG) gamma power (30–40 Hz) of respiratory arousals between varying types and severities of respiratory events, and in different sleep stages. Methods: Power spectral densities of EEG signals from diagnostic Type I polysomnograms of 869 patients with clinically suspected obstructive sleep apnea were investigated. Arousal gamma powers were compared between sleep stages, and between the type (obstructive apnea and hypopnea) and duration (10–20 s, 20–30 s, and >30 s) of the related respiratory event. Moreover, we investigated whether the presence of a >3% blood oxygen desaturations influenced the arousal gamma power. Results: Gamma power of respiratory arousals was the lowest in Stage R sleep and increased from Stage N1 towards Stage N3. Gamma power was higher when the arousals were caused by obstructive apneas compared to hypopneas. Moreover, arousal gamma power increased when the duration of the related apnea increased, whereas an increase in the hypopnea duration did not have a similar effect. Furthermore, respiratory events associated with desaturations increased the arousal gamma power more than respiratory events not associated with desaturations. Conclusion: Gamma power of respiratory arousals increased towards deeper sleep and as the severity of the related respiratory event increased in terms of type and duration of obstruction, and presence of desaturation. Significance: As increased gamma power might indicate a greater shift towards wakefulness, the present findings demonstrate that the respiratory arousal intensity and the magnitude of sleep disruption may vary depending on the event type and severity.

Index Terms—Obstructive sleep apnea, respiratory arousal, electroencephalogram, spectral analysis, arousal intensity.

I. INTRODUCTION

SUFFICIENT, good quality sleep is essential for physical restoration, maintenance of physiological functions, and neurocognitive performance [1]. Inadequate sleep is recognized as a notable healthcare burden inflicting substantial costs on Western economies [1]. Obstructive sleep apnea (OSA) is a sleep disorder causing excessive daytime sleepiness and decreased daytime vigilance, affecting over 900 million individuals globally [2]. OSA is characterized by repetitive events of complete (apnea) or partial (hypopnea) obstructions of the upper airways, often leading to blood oxygen desaturations and arousals from sleep [3], [4]. Arousals constantly interrupt the normal sleep pattern, causing sleep fragmentation and impaired sleep efficiency, leading to adverse daytime symptoms and impairing the quality of life of OSA patients [3]–[6].

In normal sleep, the Stage R (rapid eye movement, REM) and non-REM (non-rapid eye movement, NREM) Stages N1, N2, and N3 alternate cyclically [4]. During the sleep cycle, the electroencephalogram (EEG) displays specific frequencies and patterns of electrical activity characterizing each stage of
sleep [7]. An arousal is defined by the American Academy of Sleep Medicine (AASM) as an abrupt shift in the EEG frequency containing theta (4–8 Hz), alpha (8–13 Hz), and/or frequencies >16 Hz, lasting at least 3 s [7]. The majority, approximately 64–97%, of respiratory event terminations are associated with arousals visible in the EEG [8]–[11]. Various studies have investigated the shift in the EEG frequency before and after respiratory event terminations [12]–[14]. However, some discrepancies remain in the findings between these studies.

Relative delta (1–4 Hz) power has been observed to decrease in the EEG spectral content after apnea and hypopnea termination by Xavier et al. [12]. This result is in opposition to the findings of Dingli et al. [13], who observed an increase in relative post-event delta power during NREM sleep; however, this increase was observed only when there was no visible EEG arousal at event termination. Relative theta (4–8 Hz) power has also been observed both to decrease [13], [14] and increase [12] after apnea and hypopnea termination. Relative alpha (8–12 Hz) and sigma (12–16 Hz) powers are known to increase after apnea and hypopnea termination in Stage R sleep [12], [14]. This increase has also been observed in NREM sleep when respiratory events were terminated by arousals [13].

Even though the investigated populations have been small (n = 13 [12], n = 15 [13], and n = 30 [14]), it is evident that the EEG spectral content is different before and after respiratory event termination. However, the amount of research comparing the post-event EEG spectral content between different respiratory events is limited. To the best of our knowledge, only Uddin et al. [14] have investigated the differences in post-event EEG spectral content between apneas with different durations. They found a significant reduction in relative theta (4–8 Hz), alpha (8–12 Hz), and sigma (12–14 Hz) powers after long (30–40 s) apneas compared to moderate (20–30 s) and short (10–20 s) apneas [14]. However, they did not find any significant differences in relative post-event delta (0.5–4 Hz) or beta (14–30 Hz) powers between any of the apnea duration groups [14].

It remains unknown whether the spectral content of visible EEG arousals differs between sleep stages and varies types and severities of respiratory events. Moreover, even though elevated activity in the EEG gamma band (>30 Hz) has been associated with arousals and wakefulness [15]–[18], and the majority of respiratory events are known to be terminated by arousals [8]–[11], gamma power has not been investigated in the previous studies [12]–[14].

The present study tests the hypothesis that EEG gamma power of respiratory arousals is modulated by the type and severity of the preceding respiratory event (i.e., the event duration, the type of airway obstruction, and the presence of desaturation), as well as by the sleep stage preceding the arousal.

II. METHODS

A. Dataset

This was a retrospective study comprising 933 consecutive diagnostic Type I polysomnograms (PSGs) of patients with clinical suspicion of OSA. The PSGs were recorded at the Sleep Disorders Centre of Princess Alexandra Hospital (Brisbane, Australia) with the Compumedics Grael acquisition system (Compumedics, Abbotsford, Australia) in 2015–2017. The collection of the data was approved by the Institutional Research Ethics Committee of the Princess Alexandra Hospital (HREC/16/QPAH/021 and LNR/2019/QMS/54313). Out of the patients, 899 had successful recordings and were thus included in this study. Respiratory events, sleep stages, and arousals were manually scored at the Princess Alexandra Hospital in compliance with the AASM 2012 guidelines [7]. Sleep stages and arousals were scored based on the EEG (F4–M1, C4–M1, and O2–M1, sampled at 1024 Hz, with F3–M2, C3–M2, and O1–M2 as backup), left and right electrooculography (E1–E2 and M1–M2, sampled at 256 Hz), and chin electromyogram (mental/submental positioning, sampled at 256 Hz).

A total of 30 patients were discarded from the present analyses. This was due to lack of sleep stage scorings (n = 4), respiratory event information (n = 5), or demographic information (n = 6). Also, patients having no scored arousals related to obstructive apneas or hypopneas (n = 13) were excluded, as well as patients having only over 15-second respiratory arousals (n = 2). Thus, the final number of patients in the studied population was 869. Demographic information and sleep parameters of the patient cohort are presented in Table I.

B. Signal Preprocessing and Arousal Rules

Due to central EEG channels (C4 and C3) being most commonly used in previous similar studies [12]–[14], derivation C4–M1 was chosen for the present analyses. The EEG signals were filtered with a 3rd order Chebyshev Type I 10.3 Hz high-pass infinite impulse response (IIR) filter, and a 20th order Chebyshev Type I 128 Hz low-pass IIR filter, both having a passband ripple of 0.001 dB. After filtering, the EEG signals were downsampled to 256 Hz. No further preprocessing was applied to the signals.

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BMI, body mass index; TST, total sleep time; WASO, wake after sleep onset; AHI, apnea-hypopnea index; ArI, arousal index; ArRI, respiratory arousal index; Stage R, rapid eye movement (REM) sleep; NREM, non-REM sleep; Stage N1, NREM 1 sleep; Stage N2, NREM 2 sleep; Stage N3, NREM 3 sleep. Sleep stage percentages were calculated in relation to TST.
Based on the scored event information, 3–15 s respiratory arousals were located and separated from the EEG signals. Arousals were considered as respiratory arousals if they occurred ≥5 s after the termination of the related respiratory event. Moreover, only respiratory event terminating arousals were considered; that is, the related respiratory event had to terminate before the endpoint of the arousal.

As the arousal mechanism might be different between central and obstructive apneas [19], only obstructive apnea- and hypopnea-related arousals were included in the analyses, and central and mixed apnea-related arousals were excluded. Finally, if the standard deviation of C4–M1 during the arousal was below 1 µV or over 300 µV, the arousal was considered to contain too much artifact and was discarded (n = 419). Overall, a total of 56272 respiratory arousals were included in the subsequent analyses, of which 20725 occurred during Stage N1, 24184 during Stage N2, 1550 during Stage N3, and 9813 during Stage R.

C. Spectral Analysis

The power spectral densities PSD\{x(t)\} of the EEG signals x(t) during the arousals were computed as

\[
\text{PSD}_k \{x(t)\} = \begin{cases} \frac{\text{FFT}_k\{x(t)\}^2}{s}, & k = 1, N/2 + 1 \\ \frac{\text{FFT}_k\{x(t)\}^2}{s}, & k = 2, \ldots , N/2 \end{cases}, (1)
\]

where FFT\_k\{x(t)\} is the fast Fourier transform of signal x(t) at a frequency bin k, N is the number of data points in x(t), and f_s is the sampling frequency. As frequencies between zero frequency (at k = 1) and Nyquist frequency f_s/2 (at k = N/2 + 1) occur twice in the Fourier transform, the spectral power at those frequencies was multiplied by a factor of two to conserve the total power in the signal.

As the frequency resolution of the Fourier transform is dependent on the length of the signal and the arousal durations varied from 3 to 15 s, the resolutions of the PSDs ranged from 0.07 Hz to 0.33 Hz. To obtain an equal number of bins in the PSDs, the frequency resolutions of all PSDs were reduced to 0.33 Hz with linear interpolation.

Medians of the arousal PSDs were determined within groups according to the sleep stage preceding the arousal (Stage N1, Stage N2, Stage N3, and Stage R), the type of respiratory event inducing the arousal (obstructive apnea and hypopnea), and the duration of the respiratory event (short, 10–20 s; moderate, 20–30 s; and long, >30 s). Medians of the arousal PSDs were also determined within groups based on whether a ≥3% blood oxygen desaturation started between the onset of the respiratory event and the endpoint of the arousal.

To be able to compare the arousal PSDs with the PSD of stable sleep, 3-second EEG epochs of stable sleep were picked from derivation C4–M1. Epochs were picked only if they were not overlapping with any arousals (including respiratory, spontaneous, and limb movement-related arousals) or respiratory events (including obstructive, central, and mixed apneas, and hypopneas), and if the standard deviation of C4–M1 during the epoch was between 1 µV and 300 µV. These types of epochs were separated from all sleep stages (Stage N1, Stage N2, Stage N3, and Stage R) randomly from each patient in the studied population. The maximum number of epochs picked from each patient per sleep stage was set equal to the populations’ average number of arousals in that stage, rounded up to the nearest integer (24 in Stage N1, 28 in Stage N2, 2 in Stage N3, and 12 in Stage R). This was done to achieve approximately the same number of stable sleep epochs and arousals in all sleep stages, while simultaneously obtaining equal representation from all patients. The PSDs of the epochs were computed using (1), and PSD medians were determined within each sleep stage.

D. Statistical Analysis

Absolute spectral powers of the gamma bands (30–40 Hz) were computed from the PSDs via numerical integration using the trapezoidal method. Absolute power was computed instead of relative power due to the gamma band covering only a small fraction of the total EEG spectrum. Hence, relative gamma power might be strongly dominated by the changes in the rest of the spectrum. Statistical significances and effect sizes of the absolute gamma power differences were evaluated between arousals related to 1) obstructive apneas and hypopneas, 2) short (10–20 s), moderate (20–30 s), and long (>30 s) obstructive apneas, 3) short, moderate, and long hypopneas, 4) obstructive apneas with and without a ≥3% desaturation, and 5) hypopneas with and without a ≥3% desaturation.

As all arousals were from the same patient population, a physiological dependency was assumed between them. Therefore, statistical significances of the differences between the absolute powers were evaluated with the Wilcoxon signed-rank test. The test was computed for 5000 random permutations of the value pairs between the groups presented in categories 1)–5), such that in categories 2) and 3) two duration groups were compared at a time. The significance of the gamma power difference was estimated as the median of the 5000 obtained p-values. A p-value threshold of 0.01 was set for statistical significance. The effect sizes were evaluated as Cohen’s d.

All analyses in the present study were executed with MATLAB (R2019b; The MathWorks, Inc.; Natick, MA, USA).

III. RESULTS

A. Gamma Power of Stable Sleep and Arousals Between Sleep Stages

During stable NREM sleep, gamma power decreased as the sleep deepened from Stage N1 to Stage N3 (Fig. 1A). However, during respiratory arousals, gamma power was the highest during arousals occurring in Stage N3 and decreased towards lighter sleep (Fig. 1B). Gamma power was the lowest in Stage R compared to all NREM stages both during stable sleep and arousals.

B. Gamma Power of Arousals Between Respiratory Event Types and Severeities

Gamma power was significantly (p < 0.01) greater during arousals related to obstructive apneas compared to hypopneas.
Fig. 1. Median electroencephalography (C4–M1) power spectral densities during 3-second epochs of stable non-rapid eye movement (Stage N1, Stage N2, Stage N3) and rapid eye movement (Stage R) sleep (A) and during respiratory arousals (ArR) in the corresponding stages (B).

Fig. 2. Median electroencephalography (C4–M1) power spectral densities during respiratory arousals (ArR) related to obstructive apneas and hypopneas. (Fig. 2 and Table II). Moreover, arousal gamma power increased as obstructive apnea duration increased. This increase was significant ($p < 0.01$) between short and long, and between short and moderate events (Fig. 3A and Table II). An increase in hypopnea duration did not have a similar effect, as no significant change in arousal gamma power was observed between any of the hypopnea duration groups (Fig. 3B and Table II).

A significant ($p < 0.01$) increase in arousal gamma power was observed when the related respiratory event was accompanied by a desaturation compared to when a desaturation was not present. This observation was similar with obstructive apnea-related arousals (Fig. 3C and Table II) and hypopnea-related arousals (Fig. 3D and Table II). However, the effect size of the gamma power difference between arousals associated with and without a desaturation was considerably smaller in the case of obstructive apnea-related arousals compared to all other effect sizes in this study (Table II).

IV. DISCUSSION

In this study, we investigated EEG gamma band (30–40 Hz) power differences between respiratory arousals in a population of 869 patients with suspected OSA. The differences were studied between groups according to sleep stage, type and duration of the preceding respiratory event, and presence of an oxygen desaturation. Overall, the results indicate that the power in the arousal gamma band increases when the arousal occurs in deeper sleep, when the related respiratory event is accompanied by a blood oxygen desaturation, when the arousal is related to an obstructive apnea compared to a hypopnea, and when the duration of the related obstructive apnea increases.

Since increased EEG gamma band activity has been associated with wakefulness [15], [16], greater gamma power in the arousal could act as an indicator of a stronger arousal, i.e., a greater shift towards wakefulness.

Higher arousal gamma power was observed when the arousals occurred during a deeper stage of NREM sleep compared to lighter NREM sleep. Deeper stages of NREM sleep are known to increase the arousal threshold to inspiratory resistance and airway occlusion [19], [20]. Based on our results, this high arousal threshold might correlate with the arousal gamma power and, possibly, arousal intensity [15], [16]. Moreover, gamma power was observed to be the lowest during arousals occurring in Stage R sleep compared to all NREM stages. This finding is in line with the magnitude of the arousal threshold, as it is known to be the lowest during Stage R sleep [21].
The occurrence of respiratory events and arousals is known to be relatively low in Stage N3 compared to other sleep stages [22], [23], and the number of arousals was the lowest in Stage N3 in this study as well (Fig. 1B, Table II). Due to the high arousal threshold in deep sleep, most respiratory events might terminate without an arousal. Therefore, the arousals investigated in this study might only be related to the remaining, relatively low number of respiratory events, which have resulted in exceeding the arousal threshold. In turn, exceeding the high threshold might have resulted in high arousal intensity. This might partly explain the high gamma power during arousals from deeper sleep.

In this study, gamma power was greater during arousals caused by obstructive apneas compared to arousals caused by hypopneas. As the airway is completely blocked during an apnea, greater pharyngeal muscle response might be needed to open the airway compared to a hypopnea. As the magnitude of this muscle response is known to correlate with the arousal intensity [24], high arousal intensity might explain the greater arousal gamma power related to obstructive apneas compared to hypopneas. Furthermore, as blood oxygen desaturations are often more severe related to obstructive apneas compared to hypopneas [25], [26], the need for rapid restoration of blood oxygen saturation levels and dissipation of built-up carbon dioxide via hyperventilation might be elevated at obstructive apnea termination. As the ventilatory response to arousals is also known to increase with increasing arousal intensity [24], [27], this could provide further explanation on the higher gamma power during obstructive apnea-related arousals compared to hypopnea-related arousals.

Based on our results, arousal gamma band activity increases when the duration of the related obstructive apnea increases. As an increase in obstructive apnea duration is often associated with an increase in the depth of the related oxygen desaturation [25], a stronger ventilatory response might be needed to compensate for low blood oxygen and elevated carbon dioxide levels when the duration of the obstructive apnea increases. As the ventilatory response is known to correlate with the arousal intensity, it might in part explain the higher arousal gamma power following longer obstructive apneas [24], [27]. However, the gamma power increased significantly only up to the moderate event duration group. This observation could indicate a certain level of hypoxia and hypercapnia, beyond which the ventilatory response and the arousal intensity might not further increase.

An increase in hypopnea duration did not have a significant effect on the gamma power of the following arousal. Hypopneas are known to predominantly increase the duration, rather than the depth of the related desaturations [25]. Therefore, the present finding could imply, that should the arousal intensity correlate with the desaturation severity, this correlation might be primarily due to the depth of the desaturations, rather than their duration.

Arousal gamma power was greater related to respiratory events accompanied by ≥3% blood oxygen desaturations, compared to those events where desaturations were not present. Deeper blood oxygen desaturation and greater carbon dioxide retention might increase the ventilatory response at event termination, which is known to increase the arousal intensity [24], [27]. This observation might also be related to the present findings where arousal gamma power was higher following obstructive apneas compared to hypopneas, and following longer apneas compared to shorter ones. Desaturations are known to be more severe with obstructive apneas and they are likely to deepen with longer apneas [25], [26].

The effect size between obstructive apnea-related arousals with and without a desaturation compared to the other effect sizes. This might be due to the relatively low number of obstructive apnea-related arousals without a desaturation (Fig. 3C and Table II). Moreover, obstructive apnea-related arousals might be high in intensity regardless of the presence of a desaturation, due to the strong need for pharyngeal muscle responses at obstructive apnea termination in both cases [25].
Desaturation depth is also known to be correlated with daytime sleepiness and impaired vigilance [28], [29]. This correlation might in part be explained by the present findings, where arousal gamma power was higher when the related respiratory event was accompanied by a desaturation compared to when no desaturation was present. As increased activity in the gamma band might indicate a stronger arousal, these more intense interruptions of sleep might effectively prevent the sleep cycle from progressing to Stage N3 and Stage R, resulting in disrupted and insufficient sleep, leading to detrimental daytime symptoms.

This study has some limitations. Firstly, arousals related to central and mixed apneas were excluded from the present analyses, as the arousal mechanism of central apneas differ from that of obstructive apneas [19]. Secondly, as the gamma power is only a small fraction of the total power in the EEG spectrum, it is known to be prone to contamination by the electrical activity of muscles [30]. This can be a source of error, especially as respiratory arousals are often associated with pharyngeal muscle responses [11], [24]. However, these responses are not necessarily an unwanted characteristic in the analysis of respiratory arousals, as pharyngeal muscle responses are known to correlate with the arousal intensity [24]. Moreover, 50 Hz powerline noise appeared as a clear spike in the PSDs. To eliminate this artifact, the region of interest for the gamma band was set to 30–40 Hz. Finally, due to an incomplete record of the patients’ medications, the effect of sedatives and psychoactive medication was not considered in the present study. This is a weakness as, for example, central nervous system depressants...
are known to increase the arousal threshold related to airway occlusion [19].

V. Conclusion

We were able to detect noticeable differences in the EEG gamma band (30–40 Hz) power between respiratory arousals related to varying respiratory event types and their severities. In conclusion, the gamma band power was higher during arousals occurring in deeper sleep compared to lighter sleep, as well as related to obstructive apneas compared to hypopneas, related to longer obstructive apneas compared to shorter ones, and in the presence of a blood oxygen desaturation compared to when a desaturation was not present.

The observations in the present study support the hypothesis that the EEG gamma power of respiratory arousals is modulated by the type and severity of the preceding respiratory event, as well as by the sleep stage preceding the arousal. The present findings demonstrate that the intensity of respiratory arousals and, consequently, their ability to create sleep disruption may vary depending on the respiratory event type and severity. Our findings reinforce the importance of creating methods for more comprehensive assessment of OSA severity.

References