Respiratory Periodicity and Electroencephalogram Arousals During Sleep in Older Adults

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The aim of this exploratory study was to examine the relationship of electroencephalogram (EEG) arousals to breathing patterns and the relationship of both arousals and breathing patterns to arterial oxygenation during sleep in older adults. Five older adults were monitored using standard polysomnography. Records were divided into 5-min segments and breathing patterns identified based on the level of respiratory periodicity and the variability in the frequency of breathing cycles. Standard criteria were used to determine sleep states and occurrence of EEG arousals. High respiratory periodicity was seen in 23% of the segments, whereas 24% had low respiratory periodicity with minimal variability in the frequency of breathing (Type A low respiratory periodicity) and 53% had low respiratory periodicity with high variability in the frequency of breathing (Type B low respiratory periodicity). Nearly all (97%) segments with high respiratory periodicity had EEG arousals, whereas fewer segments (33%) with low respiratory periodicity had arousals, regardless of the stage of sleep. Desaturations occurred more often in segments with high respiratory periodicity, $F_{(2,4)} = 57.3$, $p < .001$, but overall, the mean SaO$_2$ of segments with high respiratory periodicity did not differ from levels seen in segments with low respiratory periodicity, $F_{(2,4)} = 0.77$, ns. Our findings suggest that high respiratory periodicity is a common feature of EEG arousals and, in older adults, may be important for maintaining oxygen levels during desaturations during sleep.

**Key words**: older adults, oxygenation, breathing, respiratory periodicity, EEG arousals, methodology, desaturation

Respiratory periodicity, reflected in the variability in amplitude of breathing, is a centrally mediated

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process that modulates the neural drive to breathe during sleep (Ghazanshahi & Khoo, 1993; Gottschalk, Khoo, & Pack, 1995; Khoo, 2000). An extreme form of high respiratory periodicity associated with pathological states is Cheyne-Stokes breathing, which is characterized by cyclical clusters of breaths separated by intervals of either apnea or hypopnea (Cherniak, 1999). Other breathing patterns characterized by high levels of respiratory periodicity, however, can also be observed in healthy individuals, including infants (McNamara, Lijowska, & Thach, 2002), young adults (Trinder, Van Beveren, Smith, Kleiman, & Kay, 1997), and older adults (Pack, Cola, Goldsmith, Ogilvie, & Gottschalk, 1992; Pack et al., 1988; Shore, Millman, Silage, Chung, & Pack, 1985). Respiratory periodicity in older adults is the result of arousals that occur in response to decreases in blood oxygen during sleep (Pack et al., 1992; Shore et al., 1985); however, very little research has been done to systematically classify breathing patterns during sleep in older adults or to understand their relationship to electroencephalogram (EEG) arousals and arterial oxygenation.

The aim of this exploratory study was to examine the relationship of EEG arousals to breathing patterns as well as the relationship of both arousals and breathing patterns to arterial oxygenation during sleep in older adults. Breathing patterns were characterized primarily by their periodicity, defined primarily by variability in the amplitude of breathing cycles and secondarily by variability in the frequency of breathing cycles. Based on our findings, we discuss the implications of using respiratory periodicity as an indicator of risk for hypoxic injury during sleep in older adults.

**Background**

Investigations into breathing patterns that occur during EEG arousals and their effect on arterial oxygenation may help to identify mechanisms that lead to impaired ventilation and hypoxemia during sleep in older adults. Desaturations (4% and greater declines in oxyhemoglobin saturation) are commonly seen during sleep in older adults (Phillip, Dealberto, Dartigues, Guillemainault, & Bioulac, 1997; Redline et al., 2004). Frequent or prolonged desaturations generally result in reduced arterial oxygenation (Findley, Ries, Tisi, & Wagner, 1983; Gries & Brooks, 1996; Series, Cormier, & LaForge, 1990), but when the number of desaturations is controlled for, arterial oxygenation is reportedly lower in older adults than in younger individuals (Bixler, Vgontzas, Have, Tyson, & Kales, 1998; Gries & Brooks, 1996). One possible explanation for this difference is that the central mechanism that regulates ventilation in response to desaturations may weaken with age.

It is well known that the sleep-wake cycle is tied to the neuronal networks that modulate the activity of different respiratory muscle groups (Cherniack, 1981), resulting in breathing patterns with varying degrees of respiratory periodicity (Shore et al., 1985). Whereas some of these patterns may resemble the cyclic periodicity of Cheyne-Stokes (Pack et al., 1988), others are characterized by a progressive decrease in the amplitude of breathing cycles followed by a brisk increase in amplitude (Bulow, 1963; Stradling, Chadwick, & Frew, 1985). It is these latter forms of respiratory periodicity that are more likely to be found in healthy samples (Shore et al., 1985; Trinder et al., 1997) and are thought to be the most efficient patterns for restoring oxygen levels to normal following desaturations (Ghazanshahi & Khoo, 1993; Gottschalk, Khoo, & Pack, 1995).

Studies have also shown that EEG arousals are an important mechanism for restoring ventilation following desaturations during sleep. Previous studies in middle-aged adults (30-50 years) report that when associated with apneas, EEG arousals evoke such large increases in the amplitude of breathing cycles that they shorten the duration of desaturations during sleep (Badr et al., 1997; Basner, Onal, Stepanski, & Lopata, 1995; D. M. Carlson, Carley, Onal, Lopata, & Basner, 1994). Similar studies in young adults indicate that it is the magnitude of the increase in the amplitude of breathing cycles that follow an apnea or hypopnea event that is predictive of the rate of return of the oxygen level to normal following the event (Bradley et al., 1985; Findley et al., 1983). Given that arousals are important for restoring ventilation after desaturations during sleep, prolonged desaturations might be a result of either failure to initiate an arousal or an inability to alter breathing patterns when an arousal occurs.

We previously examined the reliability and validity of three variables to identify breathing patterns associated with apneic events during sleep in older adults (B. W. Carlson & Neelon, 2002). Using an inductance plethysmograph to record abdominal movements, we defined breathing patterns in consecutive 5-min
segments in terms of variability in the amplitude (respiratory periodicity) and frequency of breathing cycles. The results showed that segments with apnea had greater variability in both the amplitude and frequency of breathing cycles. In that study, we did not measure EEG arousals, which may also explain the observed variability in breathing patterns, nor did we examine the influence of respiratory patterns on arterial oxygenation. Thus, the study reported here extends our previous work by exploring the relationship between EEG arousals and breathing patterns and the relationship of both of these to arterial oxygenation during sleep in community-dwelling older adults.

Method

Participant Procedure

Participants were 5 older adults (4 men; 1 African American participant, 4 White) between the ages of 70 and 86 years (M = 75.4 years) with no history or clinical evidence of a sleep disorder. The study took place in a university-affiliated general clinical research center. Each participant underwent a physical examination. Individuals were excluded who had known lung disorders, myocardial infarction, diabetes, seizures, substance abuse, or exposure to general anesthesia within the previous 6 months. Persons being treated for or with self-reported symptoms of sleep apnea (loud snoring, awakening gasping for air, nocturnal sweating), periodic limb movements (kicking in bed, aching muscles), nocturia (urinating more than three times per night), or excessive daytime sleepiness were also excluded. In addition, potential participants were excluded if they were currently using antidepressant medications, respiratory inhalers, narcotic analgesics, or sedative-hypnotic drugs.

All participants reported high levels of daytime function, as evidenced by a Mini-Mental State Examination (Folstein, Folstein, & McHugh, 1975) score of greater than 27, a Consortium to Establish A Registry for Alzheimer’s Disease (CERAD) version of the Boston Naming Test (Welsh et al., 1994) score of greater than 14, and an Older Americans Resources Study Independent Activity of Daily Living Scale (Fillenbaum, 1978) score of greater than 12. In addition, all had scores on the 30-item Geriatric Depression Scale (Yesavage et al., 1983) indicating few or no depressive symptoms. None had symptoms of allergy, cold, or fever in the 2 weeks preceding the study. Oral temperatures ranged from 36°C to 36.9°C. Body mass indices ranged from 20.8 to 26.4 kg/m². Examination of their overnight recordings showed that all participants had a respiratory disturbance index less than 10, which is significantly below the criterion for sleep apnea (American Academy of Sleep Medicine Task Force, 1999). The university’s Institutional Committee for the Protection of Human Subjects approved the study, and all participants gave informed consent.

Each participant was studied twice, for a total of 4 nights. The first pair of nights took place on 2 consecutive weekdays. The second pair of nights took place 2 weeks after the first, on the same weekdays as the first pair. Monitoring began at 11 p.m. and continued until 5 a.m. the following morning, for a total of 6 hrs. The participants slept in a typical hospital room, and data were collected in an adjoining room containing the monitoring equipment. The hospital room was maintained at a consistent temperature of 24°C and humidity of 19%. To minimize extraneous sounds, the rooms were located at the end of the hall, farthest from the nursing station. After the first night in each pair, participants left the unit after breakfast (8 a.m.) and returned in the evening for dinner (4 p.m.) and a second night of recording. They were asked to maintain their typical daytime routines between nights. All reported some form of moderate activity between the monitoring nights, usually equivalent to walking 1 mile.

Data Collection and Processing

The procedure for collecting and processing the physiological signals has been described elsewhere (B. W. Carlson & Neelon, 2002). Briefly, a standard polysomnogram (PSG), consisting of one central EEG channel, one occipital EEG channel, two (right and left) eye movement (EOG) channels, and one submental EMG channel, were used to record sleep and EEG arousals. The PSG signals were processed using standard bioelectric amplifiers (Gould TA11; Gould Instruments, Akron, OH). Arterial oxygen saturation (SaO₂) was continuously measured with a pulse oximeter (Nellcor N200; Mallinckrodt, Inc., St. Louis, MO), and the average SaO₂ was recorded every 3 s. By sampling every 3 s, we estimate that we achieved a lag between the change in arterial oxygen and detection by
the device of less than 8 s (Severinghaus & Naifeh, 1987), which is adequate for detecting brief increases and decreases in SaO$_2$ in adults.

Respiratory movements were monitored using inductance plethysmography (Respitrace, Ardsley, NY) with a band placed around the abdomen, just above the iliac crest. We elected to monitor abdome

nal movement rather than chest movement because previous work showed that the abdominal band was best tolerated by participants and more reliably kept its position than the chest band. In addition, the amplitude of the abdominal waveform increases 1 to 2 times more than the chest waveform during arousals (Badr et al., 1997; B. W. Carlson & Neelon, 2002; Masa et al., 2003).

The airflow and PSG signals as well as the pulse oximetry and inductance plethysmography signals were digitized using a 16-bit analog-to-digital converter (DI-200; Dataq Instruments, Akron, OH). The digitized data were stored to a computer at a rate of 250 samples per second using the Windaq Waveform Acquisition Program (Dataq Instruments).

The following procedures were performed to ensure the accuracy of measurements (Carskadon, 1996; Keenan, 1999). Sensor impedances were checked manually at the start and end of each session to ensure that impedances remained between 1.0 and 5.0 kΩ. Instrument calibrations, using known standards, were done at the start and end of each study to ensure the accuracy of the EEG, EMG, EOG, pulse oximetry, and inductance plethysmography measurements. A difference of no more than ± 2% from the standard was maintained across each night of study. Standard biological calibrations (blinking, close/open eyes, breath holding on inhalation/exhalation, a sigh and a cough) were also performed at the start and end of each study to ensure accurate detection of eye movements, alpha activity, body movements, and apneas.

**Variables and Their Measurement**

**Respiratory periodicity.** Respiratory periodicity was measured across each consecutive 5 min using the standard deviation in the amplitude of breathing cycles (sdAMP). The amplitude of breathing cycles (AMP), measured in volts, is derived from an inductance plethysmograph waveform and is a measure of the maximum expansion of the abdomen on inspiration; it has a range of 0.001 to 0.8 V, with higher values indicating greater expansion of the chest wall. The standard deviation of these voltage values (sdAMP) was computed for each segment to characterize differences in periodicity across segments. The procedure for processing the abdominal-band waveforms has been described elsewhere (B. W. Carlson & Neelon, 2002) and includes verification of the computer-generated marking of each respiratory cycle by two independent raters with experience in scoring respiratory records. Interrater agreement was quite high for marking the occurrence of each peak and valley (Pearson $r = .98$, absolute mean difference = 0.01 s) and the amplitude of each cycle (Pearson $r = .97$, absolute mean difference = 0.003 V).

**Variability in the frequency of breathing.** Because frequency often varies with the amplitude of breathing cycles, we used the standard deviation of interbreath frequency (sdIBF) as a second measure for characterizing patterns associated with low and high respiratory periodicity. Expressed in cycles per minute (cpm), the interbreath frequency is calculated by dividing 60 by the interval, in seconds, between maximum chest expansions; it is analogous to a breath-to-breath measure of respiratory rate and generally ranges between 0.01 and 4.5 cpm. The standard deviation of the interbreath frequencies was computed for each segment. Both sdAMP and sdIBF values were used to further classify segments into three different patterns of respiratory periodicity.

**Sleep states and EEG arousals.** The PSG was divided into 30-s epochs, and each epoch was assigned a score of Wake, Stage 1 and 2 NREM sleep, Stage 3 and 4 NREM sleep, or REM sleep using standard criteria for scoring sleep states for adults (Rechtschaffen & Kales, 1968). Consecutive 30-s epochs were aggregated into 5-min segments, and the percentage time spent in each sleep state was calculated for each segment. In 90% of the segments, one state composed greater than or equal to 60% of their length and thus became the state assigned to that segment. In the remaining 10%, the deepest stage of sleep (deepest to lightest: Stage 3 and 4 NREM, Stage 1 and 2 NREM, REM, and Wake) was assigned.

The criteria set by the American Sleep Disorders Association–Atlas Taskforce (1992) were used to identify EEG arousals within each 5-min segment. In epochs of NREM sleep, an EEG arousal was defined...
as an increase in EEG frequency (including theta, alpha, or frequencies greater than 16 Hz, but not spindles) of 3 s or greater. In epochs of REM sleep, an EEG arousal was defined by the same EEG frequency criteria along with a simultaneous increase in submental EMG amplitude.

Sleep states and arousals were independently scored by an investigator and by a certified technician who routinely scores sleep in a certified hospital–based sleep laboratory. An acceptable level of interrater agreement (states = 92%, arousals = 90%) was maintained across all the records. The scoring of the sleep recordings was done before the computer-derived variables were calculated to eliminate bias introduced by knowledge of the oxygen and breathing pattern measures.

Arterial oxygenation. The mean SaO₂ levels of all 5-min segments were used to compare the level of arterial oxygenation across segments. A change of ≥4% in SaO₂ is the standard clinical criterion for scoring desaturations during sleep (American Academy of Sleep Medicine, 2001; American Academy of Sleep Medicine Task Force, 1999) and was used to identify segments with desaturations. Because we were interested in desaturations that were likely to lead to hypoxia during sleep, we also required that segments with desaturations have a mean SaO₂ <92%.

Data Management and Analysis

Of the possible 1440 segments (72 segments × 5 participants × 4 nights), 72 segments (1 night’s worth of data) were lost because of technical failure (Night 4 from Participant 2) and another 67 segments were lost (from all participants) because of disconnection from the monitoring equipment. Because we were interested in studying breathing only during sleep, we excluded an additional 440 segments containing body movements and 176 segments in which the participant was awake for more than 50% of the segment. The remaining 785 segments were included in the analysis.

Scatterplots were used to devise cut points for characterizing breathing patterns within each of the two levels of periodicity. We first applied cut points established in a previous study (B. W. Carlson & Neelon, 2002) to classify segments into patterns of low respiratory periodicity (sdAMP <0.1 V) and high respiratory periodicity (sdAMP ≥0.1 V). The proportion of segments with high and low respiratory periodicity did not vary significantly across the nights (B. W. Carlson, Neelon, Carlson, Baker, & Dogra, 1999); therefore, the night of the study (1st to 4th night) was not included as a factor in this analysis.

Figure 1 shows all segments plotted by variability in amplitude (x-axis) and frequency (y-axis) of breathing cycles in segments with high (filled circles) and low (open circles) respiratory periodicity. Note that segments with low respiratory periodicity (standard deviation in the amplitude of breathing cycles [sdAMP] <0.1 V) can have low (Type A) as well as high variability (Type B) in the frequency of breathing cycles. sdIBF = standard deviation of interbreath frequency.
respiratory periodicity with low variability in the frequency of breathing.

Cross-tabulations on all 785 segments were next used to determine the frequency of sleep states and EEG arousals across each category of respiratory periodicity. Generalized estimating equations were used to assess the occurrence of EEG arousals among sleep states and patterns of respiratory periodicity. Analysis of variance was used to assess the effect of EEG arousal and respiratory periodicity classification on the range of SaO2 and mean SaO2 of segments. The multiple segments that each participant contributed to the analysis could not be assumed to be independent observations. To avoid inflating the level of Type I error, the probabilities of all tests were adjusted for the clustering of observations within participants by using generalized least squares estimators and Taylor expansion theory to estimate the sampling errors of the estimates (Liang & Zeger, 1986). Thus, the denominator degrees of freedom reflect the number of participants in the sample rather than the number of pooled segments.

Results

Breathing Patterns and Arousals

Of the 785 segments analyzed, 181 (23%) were classified as having high respiratory periodicity, whereas 186 (24%) were classified as having Type A low respiratory periodicity. More than half the segments, 418 (53%), were classified as having Type B low respiratory periodicity. Apneas, as defined by standard criteria (American Academy of Sleep Medicine Task Force, 1999), were observed in only 6.1% of the segments. Of the segments with apneas, 78% had high respiratory periodicity, and the remaining 22% had Type B low respiratory periodicity.

Respiratory Periodicity, Sleep State, and EEG Arousals

Stage 1 and 2 NREM sleep was found in 43% of segments, followed by Stage 3 and 4 NREM (35%) and REM (22%) sleep. Approximately half of the segments (49%) contained at least one EEG arousal. EEG arousals were less prevalent during Stage 3 and 4 NREM sleep than Stage 1 and 2 NREM sleep ($\chi^2 = 6.63, df = 4, p < .0001$) and REM sleep ($\chi^2 = 4.12, df = 4, p < .0001$) and at equal frequency during Stage 1 and 2 NREM and REM sleep ($\chi^2 = 0.63, df = 4, p = .43$).

Table 1 displays the presence and absence of EEG arousals by sleep state and pattern of respiratory periodicity. Each stage of sleep was observed in each pattern of respiratory periodicity. Stage 3 and 4 NREM sleep was more prevalent in segments with Type A low respiratory periodicity (64.5%), whereas Stage 1 and 2 NREM sleep (32.3%) and REM sleep (3%) were less prevalent in segments with Type A low respiratory periodicity ($\chi^2 = 23.15, df = 4, p < .0001$). Stage 1 and 2 NREM was most prevalent in segments with high respiratory periodicity (50.8%) and Type B low respiratory periodicity (44.7%), but the proportions of sleep states did not distinguish high respiratory periodicity from Type B low respiratory periodicity ($\chi^2 = 2.24, df = 4, p = .13$).

<table>
<thead>
<tr>
<th>Stage of Sleep</th>
<th>Pattern of Respiratory Periodicity</th>
<th>Total segments (n)</th>
<th>Arousals (%)</th>
<th>No arousals (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>High</td>
<td>Type A Low</td>
<td>Type B Low</td>
<td></td>
</tr>
<tr>
<td>Stage 1 and 2 NREM (n)</td>
<td>92</td>
<td>60</td>
<td>187</td>
<td>95.7</td>
</tr>
<tr>
<td>Stage 3 and 4 NREM (n)</td>
<td>35</td>
<td>120</td>
<td>122</td>
<td>97.1</td>
</tr>
<tr>
<td>REM (n)</td>
<td>54</td>
<td>6</td>
<td>109</td>
<td>90.8</td>
</tr>
<tr>
<td>Total segments (n)</td>
<td>181</td>
<td>186</td>
<td>418</td>
<td>23.1</td>
</tr>
</tbody>
</table>
There was a more consistent relationship between EEG arousals and respiratory periodicity. The prevalence of arousals was 90% or more in segments of high respiratory periodicity across all stages of sleep and least prevalent in segments with Type A low respiratory periodicity. This association between arousals and respiratory periodicity was seen across all segments of Stage 1 and 2 NREM ($\chi^2 = 21.9$, $df = 4$, $p < .0001$), Stage 3 and 4 NREM ($\chi^2 = 38.5$, $df = 4$, $p < .0001$), and REM sleep ($\chi^2 = 25.6$, $df = 4$, $p < .0001$).

Furthermore, the relationship between EEG arousals and respiratory periodicity held when we examined segments collected from each participant. Figure 2 shows the occurrence of segments with and without arousal within breathing patterns defined by respiratory periodicity and frequency of breathing. Each plot represents data collected from 1 participant. Segments with EEG arousals are indicated by closed circles and those with no EEG arousals by open circles. As in Figure 1, all the segments with high respiratory periodicity (sdAMP ≥ 0.1 V) are in the upper right quadrant, where the variability in frequency of breathing is also high (sdIBF ≥ 1.2 cpm). The bottom left quadrant contains segments with Type A low respiratory periodicity (sdAMP < 0.1 V and sdIBF < 1.2 cpm) and the upper left, Type B low respiratory periodicity (sdAMP < 0.1 V and sdIBF ≥ 1.2 cpm).

Figure 2. Distribution of segments with (closed circles) and without (open circles) electroencephalogram (EEG) arousals across breathing patterns in 5 older adults. sdIBF = standard deviation of interbreath frequency; sdAMP = standard deviation in the amplitude of breathing cycles.
Participants 4 and 5 had the highest percentage of segments with arousals, 55% and 72%, respectively. Arousals occurred in approximately one third of the segments from the remaining participants. In all 5 participants, the likelihood of observing a segment with an EEG arousal was greatest in segments with high respiratory periodicity. Almost all segments (94%) with high respiratory periodicity contained an EEG arousal, whereas only 43% of segments with Type B low respiratory periodicity contained an EEG arousal. Segments with Type A low respiratory periodicity had the fewest EEG arousals (8%).

**Relationship of Breathing Pattern and Arousals to Desaturations and Arterial Oxygenation**

Average changes in SaO2 values within a segment differed significantly among the three patterns of respiratory periodicity, $F_{(2,4)} = 57.3$, $p < .001$. Segments with high respiratory periodicity had desaturations with almost twice as great a change in SaO2 ($M \pm SD$: 7.1% ± 4.4%) as segments with low respiratory periodicity (Type A: 3.6% ± 2.4%; Type B: 3.0% ± 3.1%); the two types of low respiratory periodicity did not differ from each other. Average changes in SaO2 values within a segment also differed significantly by arousal classification, $F_{(1,4)} = 18.72$, $p < .04$. Segments with EEG arousals had greater changes in SaO2 (5.3 ± 3.7) than segments without EEG arousals (3.2 ± 2.9). Of the segments with desaturation, 72% contained EEG arousals. Nevertheless, the average level of SaO2 did not vary greatly between the high and low respiratory periodicity classifications, $F_{(2,4)} = 0.77$, nonsignificant (ns), nor did it differ significantly between segments with and without arousals, $F_{(2,4)} = 1.21$, ns.

**Breathing Patterns and EEG Arousals During Desaturations**

Although high respiratory periodicity and EEG arousals, but not interbreath frequency, were associated with greater variability in SaO2, the relationship between breathing patterns and EEG arousals also differed across participants. Suspecting that these individual differences may influence a participant’s ability to recover from desaturations, we examined how the relationship between patterns of respiratory periodicity and EEG arousals during desaturations differed across participants and how these differences related to arterial oxygenation in the 3 participants (Participants 3, 4, and 5) that contributed 207 of the 227 (91%) segments with desaturations.

Table 2 shows how the distribution of segments with desaturations varied across the 3 participants. Desaturations occurred in 37% to 43% of the segments collected from each participant. In general, the proportion of segments without EEG arousals did not differ among participants. Compared to Participant 3, Participants 4 and 5 had a significantly greater percentage of segments with desaturations containing both EEG arousals and high respiratory periodicity. Only Participant 3 showed a high percentage of segments with EEG arousals and low respiratory periodicity (47%). Participants 4 and 5 had mean SaO2 levels of 90% and 91%, respectively, and Participant 3 had the lowest mean SaO2 level, at 82%.

**Discussion**

Much of findings of this study correspond with early work of Bulow (1963) and Shore and colleagues (1985), who qualitatively classified breathing patterns by rating segments in terms of their regularity. Our definition of Type A low respiratory periodicity is consistent with the early descriptions of patterns of regular breathing. However, our findings suggest that irregular breathing can be further divided into two forms: high respiratory periodicity and Type B low respiratory periodicity. Our approach to characterizing breathing patterns seems to be sensitive for identifying patterns associated with EEG arousals during sleep and may assist in understanding...
mechanisms that are important for protecting sleepers from experiencing prolonged periods of hypoxemia during sleep.

Breathing Patterns and EEG Arousals During Sleep

Previous studies have reported that breathing patterns are very regular during Stages 3 and 4 NREM sleep, in which oxygen levels are most stable across the night (Pack et al., 1988; Shore et al., 1985) and EEG arousals are few (Shore et al., 1985). As with those previous studies, we also found that Stage 3 and 4 NREM sleep was most prevalent in segments of Type A respiratory periodicity. The observation that Type A low respiratory periodicity was also seldom associated with EEG arousals and desaturations may suggest that this pattern of breathing is likely to reflect a respiratory system that is not being challenged.

Type B low respiratory periodicity and high respiratory periodicity contained similar proportions of sleep states. Stage 1 and 2 NREM accounted for approximately half of the segments with these two patterns of irregular breathing, and REM sleep accounted for another 40% of the patterns. These findings are consistent with previous studies that report breathing as more irregular during REM and Stage 1 and 2 NREM sleep than Stage 3 and 4 NREM sleep (Bulow, 1963; Pack et al., 1988; Shore et al., 1985; Stradling et al., 1985; Tusiewicz, Moldofsky, Bryan, & Bryan, 1977). However, none of the earlier reports measured EEG arousals, which we found to be strongly associated with high respiratory periodicity.

The strong association between arousals and high respiratory periodicity has been noted in at least two previous studies (Pack et al., 1992; Trinder et al., 1997). Both the Pack et al. (1992) study in older adults and the Trinder et al. (1997) study in young adults found a significant correlation between the amplitude of oscillations in breathing cycles and the alpha content of the EEG during Stage 1 and 2 NREM sleep, a defining characteristic of EEG arousals. In addition, other studies have suggested that these oscillations in both breathing cycle amplitude and EEG frequency are important for maintaining arterial oxygenation during sleep (Busner et al., 1995; Levine, Cleave, & Dodds, 1995). In this study, we observed that segments with high respiratory periodicity not only contained a high proportion of EEG arousals but also contained a high proportion of desaturations. In addition, we observed that EEG arousals were found in 80% of segments with desaturations, but there were no simple effects of patterns or arousals on arterial oxygenation.

In contrast to patterns of high respiratory periodicity, Type B low respiratory periodicity is reminiscent of earlier descriptions of Tobin and colleagues (1983) in persons with restrictive airway disease. In such disorders, tidal volume generally falls during sleep, leading to desaturations. This decrease is often resolved by increases in the frequency of breathing (Tobin, 1992). However, studies also show that increasing the frequency of respiratory muscle contractions without any significant change in amplitude is a very inefficient way to increase ventilation (Peterson, Pack, Silage, & Fishman, 1981) and, over time, results in fatigue (Mador, 1991). In this study, EEG arousals were equally likely to be present or absent in segments with Type B low respiratory periodicity, suggesting that this pattern of breathing is not a typical response to EEG arousals during sleep. As discussed below, high and Type B low respiratory periodicity appears to have very different effects on arterial oxygenation during sleep.

Relationship of Respiratory Periodicity and EEG Arousals to Arterial Oxygenation

It is thought that as we age, the respiratory system loses some degree of adaptive response to challenges (Peng et al., 2002), and previous research has pointed to a number of age-associated changes that may contribute to ineffective breathing patterns in response to desaturations during sleep. Among these are the loss of muscle strength and endurance in the skeletal muscles and the muscles that hold open the upper airway (Crow & Ship, 1996; Fogel et al., 2003) as well as the muscles of the diaphragm (Frontera et al., 2000; Polkey et al., 1997). Such decline in muscle function results in the inability to generate adequate and sustained respiratory muscle tone to allow the amplitude of breathing cycles to vary and thus modulate ventilation during sleep. Using our method for classifying breathing patterns, we have shown that older adults can exhibit breathing patterns during sleep that do not involve apnea but can lead to states of low arterial oxygenation.

The most efficient way to increase ventilation is to slow the frequency of breathing, allowing the recruitment of respiratory muscles to further expand the
chest (Milic-Emili, 1982; Tobin, 1992) and thus increase the amplitude of breathing. In addition, episodic increases in the amplitude of breathing may result in some savings in muscular effort by giving the respiratory muscles sufficient time to rest between challenges (Gottschalk et al., 1995; Levine, Hathorn, & Cleave, 2000). In this respect, patterns similar to our definition of high respiratory periodicity are closely aligned with what is considered to be the most efficient means of increasing ventilation and may be particularly important for restoring oxygen to normal levels during desaturations.

The finding that changes in SaO₂ levels that meet our criteria for desaturations are greatest in segments with high respiratory periodicity and EEG arousals is consistent with a number of studies of young adults, which found that EEG arousals were often associated with a sudden rise in the amplitude of breathing cycles and the restoration of arterial oxygen levels to normal after relatively large drops in oxyhemoglobin saturation (Basner et al., 1995; Carley, Applebaum, Basner, Ona, & Lopata, 1996; D. M. Carlson et al., 1994; Masa et al., 2003). Although a decline in SaO₂ is the defining characteristic of desaturation, it is the rate of rise in SaO₂ that determines the effect of desaturations on the mean SaO₂ (Findley et al., 1983; Series et al., 1990). The finding that the mean SaO₂ in segments of high respiratory periodicity is essentially equivalent to that in segments with low respiratory periodicity suggests that high respiratory periodicity is important for increasing ventilation and restoring oxygen to normal levels during desaturations.

In a finding similar to that which has been described in persons with restrictive lung disease, we also observed that in the Type B breathing pattern, the increased variability in the frequency of breathing without any significant change in amplitude did not result in any significant change in SaO₂ (average changes in SaO₂ of <4%). In contrast, patterns with high respiratory periodicity is likely to be more efficient in restoring oxygen levels to normal between challenges. Of the 3 participants with desaturations, the participant with the most segments with arousals and low respiratory periodicity had the lowest mean SaO₂. Clearly, further study using more participants with this pattern of breathing is needed to fully understand the relationship between breathing patterns and recovery following desaturations during sleep.

**Implications for Further Study**

If it is true that as we age, the respiratory system loses some degree of adaptive response to challenges, it would be important to understand how these patterns of respiratory periodicity change over time and relate to diseases that are amendable to nursing intervention. It is important to study the interactive effects of apneas and arousals on our measures of breathing patterns and their effects on arterial oxygenation during sleep. By understanding these relationships, we can examine how the relationship between breathing patterns and arterial oxygenation in healthy older adults compares to that in young adults and older adults with chronic illnesses that are known to affect ventilation during sleep. Clearly, studies that include larger, more diverse samples, studied over years, will allow researchers to comprehensively examine individual differences in the relative frequency of these three patterns, possibly identify variants of the patterns, track the development of maladaptive patterns, and examine more complex relationships between respiratory periodicity, apneas, arousals, and oxygenation.

**References**


