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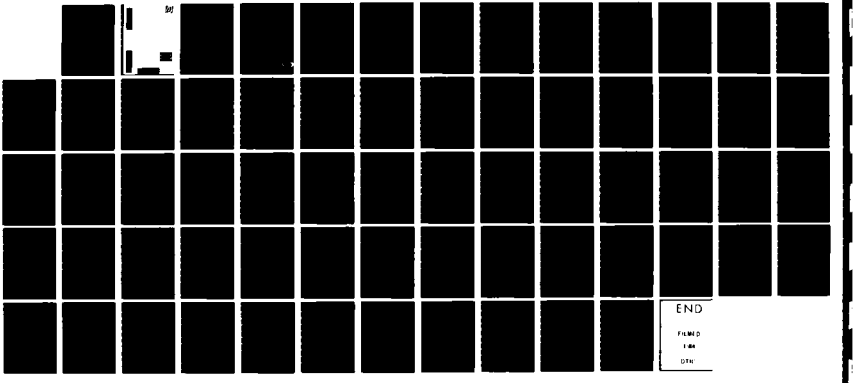

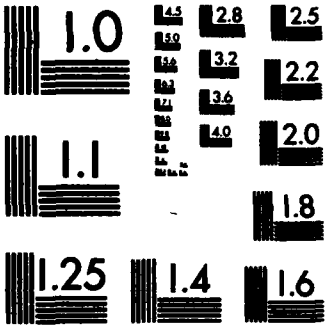

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REPORT DOCUMENTATION PAGE	READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER: AFIT/CI/NR 83-58T	2. GOVT ACCESSION NO.: A135380
	3. RECIPIENT'S CATALOG NUMBER:
4. TITLE (and Subtitle): Oxygen Desaturation and Arousal In Chronic Obstructive Pulmonary Disease Patients	5. TYPE OF REPORT & PERIOD COVERED: THESIS/DISSERTATION
	6. PERFORMING ORG. REPORT NUMBER:
7. AUTHOR(s): Juanita Sue Glick	8. CONTRACT OR GRANT NUMBER(s):
9. PERFORMING ORGANIZATION NAME AND ADDRESS: AFIT STUDENT AT:University of Washington	10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS:
11. CONTROLLING OFFICE NAME AND ADDRESS: AFIT/NR WPAFB OH 45433	12. REPORT DATE: 1983
	13. NUMBER OF PAGES: 57
14. MONITORING AGENCY NAME & ADDRESS(if different from Controlling Office):	15. SECURITY CLASS. (of this report): UNCLASS
	15a. DECLASSIFICATION DOWNGRADING SCHEDULE:

16. DISTRIBUTION STATEMENT (of this Report)

APPROVED FOR PUBLIC RELEASE; DISTRIBUTION UNLIMITED

17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)

18. SUPPLEMENTARY NOTES

APPROVED FOR PUBLIC RELEASE: IAW AFR 190-17

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Oxygen Desaturation and Arousal

In Chronic Obstructive Pulmonary Disease Patients

by

Juanita Sue Glick

A thesis submitted in partial
fulfillment of the requirements for the degree of

Master of Nursing

University of Washington

1983

Approved by _____
(Chairperson of Supervisory Committee)

Program Authorized
to Offer Degree _____

Date _____

ACKNOWLEDGEMENT

The author wishes to thank Dr. Elizabeth Giblin for the use of her data and for the many hours spent assisting with this project. Special thanks to Kathy Lee and Molly Tyler for the additional help needed to bring it all to completion.

Master's Thesis

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CHAPTER I

CONCEPTUAL FRAMEWORK

INTRODUCTION

Despite the fact that man has always been aware that sleep brings physiologic changes, no one has defined exactly how or why those changes occur. The introduction of the electroencephalogram (EEG) in the early 1930s, allowed measurement of brain electrical activity during sleep and stimulated much research. Initially, studies identified and defined sleep stages and states. Subsequent studies have investigated changes that sleep brings.

One of the major areas of interest has been respiration during sleep. In a now classic study conducted by Bulow, it was noted that artificially induced hypercarbia and hypoxia stimulate changes in ventilation in the sleeping subject. It was also noted that these same stimuli provoked arousal from sleep (Bulow, 4). Most of the subsequent research has focused on the ventilatory responses with little attention being given to the arousal response until recently.

In 1978 Phillipson wrote an editorial in the American Review of Respiratory Disease titled, "Arousal: The Forgotten Response to Respiratory Stimuli," suggesting that the arousal response to respiratory stimuli may be a life saving mechanism (Phillipson, 20). Respiratory stimuli include hypoxia, hypercarbia and mechanical loads. Using victims of sudden infant death syndrome and sleep apnea as examples, he points out that although these individuals may be viewed as possibly having a "failure of respiration" they might also be having a failure

to arouse. Phillipson's theory is that arousals are stimulated when blood gases reach unhealthy extremes. This response is necessary in order that the body might integrate behavioral, ventilatory, and cardiovascular activities directed at improving the blood gases and preventing tissue damage or possibly even death. The obstructive apnea syndrome is a good example of this situation. In obstructive apnea, relaxation of pharyngeal muscles during sleep causes obstruction of the airway which leads to apnea and in turn the development of hypoxia and hypercarbia. Apneas are generally terminated by arousal. The arousal restores muscle tone to the upper airway, thus removing the obstruction (Guilleminault, 12; Remmers, 26). Ventilation resumes and the blood gases return to their usual baseline levels. Some of these patients have prolonged apneas associated with severe oxygen desaturations. In order to prevent fatal apneic periods, treatment for these individuals is permanent tracheostomy (Guilleminault, 13; Sullivan, 29). Phillipson asks the questions: Why don't these people arouse in response to the life threatening changes in their arterial blood gases? Could it be that the apneas are prolonged in these patients because of a defect in the arousal response? These questions have opened the door to an entirely new area of research. Scientists, who have in the past been primarily interested in the ventilatory responses of sleeping subjects to respiratory stimuli, are now also considering the arousal responses to those same stimuli.

Problem Statement

In recent years as researchers have been investigating the alterations in respiration of chronic obstructive pulmonary disease

(COPD) victims, they have noted that these patients experience frequent arousals. Pierce, Leitch, Coccagna, Wynn and Koo all reported that their COPD subjects awakened often and spent a high proportion of their "in bed" time awake. Researchers have also noted that COPD patients experience episodes of severe oxygen desaturation during sleep (Table 1, page 4), and that there is wide variation in the duration of these episodes (Table 2, page 5). Douglas reported that seven of his twelve subjects had falls in oxygen saturation (SaO_2) below 50%, three fell below 30% and two dropped below 10% SaO_2 during sleep. Because recordings from the ear oximeter are not entirely reliable below 65%, Douglas also took periodic blood samples. The partial pressure of oxygen (PaO_2) noted was as low as 26 to 44 mmHg (Douglas, 5). The duration of desaturation ranged from a few seconds to over an hour. Obviously, if the most severe desaturations are also the longest in duration, the individual is in serious jeopardy of tissue damage due to hypoxia. Wynn noted that 68% of 83 episodes of desaturation were experienced by two of the seven subjects (Wynn, 32). This implies that some subjects are more prone to desaturate than others. Why is there such great variation in the degree, duration, and incidence of desaturation during sleep in these patients? And why don't the patients arouse before the desaturations become so severe?

Thus far researchers have been looking at ventilatory responses to respiratory stimuli (hypercarbia and hypoxia) for the answers. They have determined the COPD causes changes in the steady state blood gases.

TABLE 1

Oxygen Desaturation During Sleep in Ten Studies

	Mean Minimum SaO_2 (%) (range)	Mean Minimum Decrease SaO_2 (%) (range)	Mean Minimum PaO_2 (mmHg) (range)	Mean Minimum Decrease PaO_2 (mmHg) (range)	Lowest PaO_2 (mmHg) in any one subject
Pierce, 19 17 Subjects	85.7 (63-96)	4.9		7.4+ 5.0 (a)	
Flick, 11 10 Subjects	68+ 12 (50-84)			20 (9-34)	28
Wynn, 33 10 Subjects		7.3 (4-16)			
Wynn, 32 7 Subjects		17 (3-36)			
Fleetham, 8 41 Subjects		16.9+ 1.9 (b)			
Littner, 17 6 Subjects		22+ 3.1 (b) (11-34)			
Koo, 15 15 Subjects			48.9+ 8.8 (a)		
Douglas, 5 10 Subjects	(81-38)	35 (10-77)			26-44
Flenley, 9 15 Subjects			37 (26-47)		

(a) SD

(b) SEM

TABLE 2

Reported Duration of Oxygen Desaturation Episodes
In Four Studies

Author and Year	Number of Subjects	Number of Nights	Number of Oxygen Desaturations	Desaturation Criteria	Duration of Desaturation (minutes)
Flick(8) 1977	10	1	100 per subject	not given	1 to 53
Douglas(3) 1979	10	15	36 for the group	fall of _10%	2 to 100
Wynn(28) 1979	7	1	83 (92 subjects had 68% of all desaturations)	fall of of _4%	1 to 30
Flenley(6) 1980	15	not given	not given	not given	20 to 60

Hypercarbia and hypoxia may develop either singly or in combination. The reason for these changes remains speculative Basically there are two theories. The first is that the disease proc creates an impedance to ventilation by increasing the mechanical resistance to respiration. Gradually this causes a decrease in alveolar ventilation and retention of carbon dioxide (CO_2) (Kepron, 14; Sorli, 28). Additionally, regional decreases in ventilation occur in areas where perfusion is maintained resulting in increased venous admixture and hypoxemia. The second is that acute or prolonged episodes of hypoxia or hypercarbia damage the respiratory center and reduce its sensitivity to further decreases in Oxygen (O_2) or increases in CO_2 (Fishman, 7; Kepron, 14).

Researchers have also found that after the steady state levels of the arterial blood gases have changed, there is a change in the sensitivity of the peripheral chemoreceptors to further changes in CO_2 and O_2. The responsiveness to CO_2 is particularly diminished in individuals who retain CO_2 (Fishman, 7; Flenley, 9; Kepron, 14). The ventilatory response to hypoxia does not seem to be affected by CO_2 retention and consequently hypoxia is generally accepted as a major contributor to ventilatory drive in CO_2 - retaining patients. Even hypoxic drive can be reduced, however. Kepron and Bradley both found that those COPD patients with both hypercarbia and hypoxia had the greatest suppression of the ventilatory response to further hypoxia (Bradley, 3; Kepron, 14). Acute episodes of hypoxia during sleep have also been linked to suppression of the ventilatory response to hypercarbia and hypoxia (Littner, 17).

Although these findings begin to explain why these patients have alterations in their blood gases and why the desaturations might be severe, they do not explain why the individuals do not arouse in response to the desaturation before it becomes so severe. Perhaps Phillipson's theory of the arousal response can provide an answer.

Phillipson points out that ventilation is controlled by two "anatomically separate but functionally integrated" systems (Phillipson, 18). They are the metabolic control system, and the behavioral control system. The metabolic system responds primarily to changes in arterial blood gases and is concerned with maintaining them in proper balance. The behavioral control system is responsible for using the respiratory apparatus for non-ventilatory functions such as speaking, singing, and other activities under voluntary control. This voluntary system commands from the cerebrum while the metabolic control system directs respiration from the brain stem. Phillipson theorizes that during sleep the voluntary or behavioral control system becomes inactive, leaving ventilatory regulation up to the metabolic control system. In situations where the ventilatory response to metabolic stimuli is too blunted to correct altered blood gases, it is necessary for the individual to recruit additional help. Arousal, stimulated by the altered blood gases, provides the needed help by activating the voluntary behavioral control system. Muscle tone increases, alertness increases, and the individual can respond to his need for oxygenation by moving or deliberately breathing more deeply. As a result, ventilation and blood gases improve (Phillipson, 17). As mentioned, Phillipson believes that suppression of the behavioral response may be a contributing factor

in the profound and prolonged episodes of O_2 desaturation seen in sleep apnea patients. Is it possible that arousal suppression may also play a part in the severe oxygen desaturation seen in COPD patients? If COPD patients, like sleep apnea patients, have a defect in arousal response mechanisms, they too might not awaken as readily to the stimulus of hypoxia as individuals who have no defect. As a result they could experience deeper and/or more prolonged oxygen desaturation.

The possiblity that oxygen desaturation may be potentiated by a failure in the arousal response mechanism has many implications for health care providers. Changes in the way these patients are monitored and treated may be indicated. For example, sleep studies of COPD patients may be indicated as a routine part of their diagnostic work-up. Nurses in particular would need to be alert to the fact that COPD patients may be subject to sudden death due to hypoxia during sleep and therefore would require special monitoring. It is, therefore, appropriate that we attempt to determine whether COPD patients are experiencing arousal problems.

Review of Literature

Before discussing further why the COPD patient may be at risk for arousal response problems, it will be helpful to review what is known thus far about the arousal response.

What is an arousal?

Rechtschaffen and Kales define an arousal as:

> "Any increase in EMG on any channel, which is accompanied by a change in the pattern on any additional channel. For EMG channels, the change in pattern may consist of either an increase in amplitude of the EMG signal or an

> amplifier blocking artifact. For EOG channels, the change of pattern may consist of either the occurence of EMG activity, amplifier blocking artifacts, or blink artifacts. For EEG channels, the change of pattern may consist of either a decrease in amplitude, an increase in alpha activity, a paroxysmal burst of high voltage activity, the presence of EMG activity or amplifier blocking artifacts."
> (Rechtschaffen and Kales, 25)

These changes represent a break in the continuity of sleep and precede a shift in sleep stage. The shift in sleep stage is from a deep stage such as stage 3 to a lighter stage such as stage 2. An arousal may also move the subject completely into the waking state.

What stimulates arousals?

Arousal from sleep may be stimulated by sound, light and movement. The physiological mechanism for arousals caused by these stimuli is probably related to catacholamine release. Ventilatory stimuli may also provoke arousal.

Bulow was one of the first researchers to note that arousals occurred in response to changes in arterial blood gases. Using a rebreathing technique on 13 normal subjects he found that the level of CO_2 at the point of arousal was consistently the same for a given sleep stage. As sleep deepened, the $PaCO_2$ that would stimulate arousal was progressively higher. In deep sleep the $PaCO_2$ occasionally exceeded 50 mmHg before an arousal occurred. Bulow felt that this phenomenon suggested a causal relationship between the increased $PaCO_2$ and the arousal event and called the CO_2 value at the time of arousal the "arousal threshold" (Bulow, 4).

This phenomenon was also described by Phillipson and his colleagues. Studying dogs, Phillipson found that dogs rebreathing CO_2 in an

hyperoxic gas mixture also demonstrated an "arousal threshold." The $PaCO_2$ at the point of arousal was "highly reproducible in each dog" (Phillipson, 23).

It appears that hypoxia will also stimulate arousals. Observing four tracheostomized dogs, Phillipson noted that when eucapnic hypoxia was induced, the dogs aroused consistently at the same SaO_2 (within subjects) (Phillipson, 24).

Sullivan studied five obstructive apnea patients and found that the O_2 desaturation-arousal relationship experienced by these patients was similar to arousals in Phillipson's dogs. The minimal SaO_2 levels reached prior to arousal were highly consistent within subjects. There was, however, a wide range between subjects. The mean minimum arousal SaO_2 reached for these subjects during non-rapid eye movement (NREM) sleep ranged from 66% to 87% SaO_2. During rapid eye movement (REM) sleep the range was 38% to 75% SaO_2 (Sullivan, 29).

Direct or indirect stimulation?

In the processes of observing the effects of hypoxia and hypercarbia on the ventilatory and arousal responses of dogs, Phillipson made an interesting observation, "In the two dogs studied during both hypercapnia ... and hypoxia ... arousal from slow wave sleep (SWS) due to either stimulus occurred at a relatively constant volume of inspired air ($\dot{V}_I$). Similarly, arousal due to varying combinations of hypercapnia and hypoxia also occurred at a relatively constant $\dot{V}_I$ during SWS" (Phillipson, 23:517). In the hypoxia study the arousal was usually associated with a "large breath." These observations suggest that the large breath, ie., the increase in tidal volume, might be the direct

simulus for the arousal response rather than the blood gas alterations. This would mean that hypercarbia and hypoxia stimulate arousals indirectly by prompting increased ventilation which in turn stimulates the actual arousal. More research is needed to determine if the blood gas changes are direct or indirect stimuli for arousal.

Which stimulus is the major stimulus?

Although the question of which of the respiratory stimuli is the major stimulus for arousal has not yet been answered conclusively, there is some evidence that hypoxia may be the major stimulus. Indirect evidence that hypoxia is the major stimulus for arousal, particularly during REM sleep, comes from Phillipson's study of the combined effects of hypoxia and hypercapnia on the arousal response in dogs. Phillipson found that:

> "During SWS there was a clear interaction between the $PaCO_2$ during hypoxia and the waking SaO_2. Thus, the higher the $PaCO_2$ the higher was the SaO_2 that produced arousal. In contrast, during REM sleep this interaction between CO_2 and hypoxia appeared to be absent, with the $PaCO_2$ held during rebreathing having little influence on the waking SaO_2." (Phillipson, 23:514)

It appears that during NREM sleep the two stimuli potentiate each other, while during REM sleep the declining SaO_2 alone is responsible for arousal.

Guilleminault provided more direct evidence that hypoxia is the major stimulus. He administered 100% oxygen to subjects with sleep apnea for five minute periods which included apneic episodes. The oxygen prolonged the apneas. That is, the usual arousal response to apnea was delayed. The administration of 5 to 7% CO_2, on the other hand, had little effect on arousals. He was unable to detect any

change in the duration of apnea as a result of increased CO_2 (Guilleminault, 12). How might this be explained? Administration of 100% oxygen would increase the blood SaO_2. Blood at a higher O_2 saturation would require more time to desaturate prior to reaching the O_2 arousal threshold. This increase in time needed to reach the arousal threshold would delay the arousal and prolong the apnea. Increases in CO_2 during apnea should cause the individual to reach the CO_2 arousal threshold sooner and, therefore, to arouse earlier. Because the apneas were prolonged by the oxygen, but not shortened by the CO_2, it appears that hypoxia is a more effective stimulus for arousal in these subjects then hypercarbia. Sullivan has suggested that hypoxia is the major stimulus in obstructive apnea patients. (Sullivan, 29).

Does the arousal response vary?

Throughout his studies Phillipson has noted the differences between REM and N-REM arousals. In the study of CO_2 as an arousal stimulus he found that the mean $PaCO_2$ at the point of arousal was 54.2$\pm$ 3.4 mmHg (SE) during N-REM compared to a mean of 60.3$\pm$ 4.2 mmHg during REM. The arousal response to hypercapnia was significantly different for the two sleep states ($p < 0.05$) (Phillipson, 23). In the study of hypoxia as an arousal stimulus, he noted that arousal from N-REM sleep occurred at an average SaO_2 of 87.5% and after only 0.53$\pm$ 0.07 (SE) minutes of rebreathing. Arousal from REM occurred at a mean SaO_2 of 70.5% after a mean 1.5$\pm$ 0.16 minutes of rebreathing ($p< 0.005$) (Phillipson, 24). The arousal response to both hypercapnia and hypoxia seem to be supressed during REM sleep compared to N-REM sleep. Even in his

discussion of inspired volume ($\dot{V}_I$) as an arousal stimulus, Phillipson mentions that the levels of $\dot{V}_I$ achieved prior to arousal from REM were "considerably greater" than those associated with N-REM arousals (Phillipson, 24). The conclusion drawn from these reports is that whatever the stimulus, the arousal threshold is higher during REM sleep than it is during N-REM sleep (Phillipson, 24). It could be expected then, that individuals with a suppressed arousal response would be most vulnerable to severe changes in arterial blood gases during REM sleep.

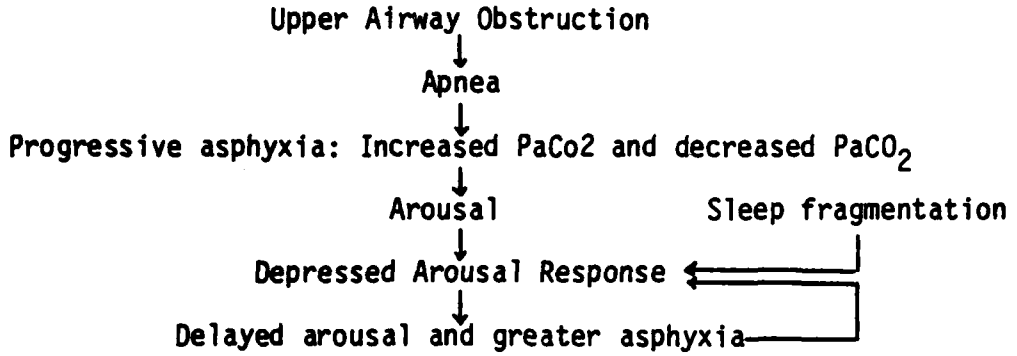
Does the arousal threshold ever change?

The arousal threshold to hypoxia may increase in some situations. Patients who have chronic prolonged episodes of hypoxia may eventually experience a depressed hypoxic arousal response. Sullivan demonstrated this in his study of sleep apnea patients. Sleep studies were made of two obstructive apnea patients several weeks after permanent tracheostomies were performed. During the study the tracheal fistulas were occluded so that the subjects were required to breath via their natural airways. In both subjects there was a marked reduction in the total number of sleep apnea episodes compared to tests prior to surgery. There were no apnea episodes during N-REM in either subject during the post surgery tests. As a result, comparisons were made of REM arousals only. In both patients, arousals occurred at higher levels of oxygen saturation in the post surgery tests than in the pre-surgery tests. In one subject the threshold changed from 50% SaO_2 to 70% SaO_2 after surgery. The other subject's change was from 60% to 85% (Sullivan, 29). It is theorized that the chronic, prolonged hypoxia may alter the responsiveness of the CNS arousal center to further declines in oxygen

saturation. After tracheostomy provided a patent airway, the episodes of hypoxia were eliminated and the arousal control center became resensitized to acute falls.

Another problem can alter the arousal threshold: sleep fragmentation. Bowes compared arousal responses of dogs before and after 2 to 3 nights of sleep fragmentation. Sleep fragmentation was accomplished by waking the dogs repeatedly with 30 seconds of noise every 150 seconds. This process resulted in sleep fragmentation via brief recurrent arousals rather than prolonged sleep deprivation. Following the sleep fragmentation the arousal responses to both hyperoxic hypercarbia and isocapnic hypoxia were significantly impaired, (p 0.05). In the hypercarbia tests the arousal $PaCO_2$ increased a mean 3.4 mmHg in both REM and N-REM sleep. In the hypoxia tests the mean SaO_2 of arousal decreased 10% during SWS (N-REM) and 12% during REM sleep (Phillipson, 22). Apparently, the fragmentation of sleep impairs the arousal response to these respiratory stimuli. How and why this occurs is not known.

Theoretically, if these two events (hypoxia and sleep fragmentation) occur repeatedly over an extended period of time, the individual could experience a progressive suppression of the arousal response. Sullivan outlined a possible sequence of events for the obstructive apnea patient this way:



(Sullivan, 29.241)

Using this theory, it is possible to speculate that any patient whose disease process causes episodes of asphyxia and/or sleep fragmentation is in jeopardy of eventually having a suppressed arousal response.

Summary

In summary then, arousal response research is just beginning. Arousals may be stimulated by respiratory stimuli, i.e., hypoxia and hypercarbia. There is some evidence that hypoxia may be the major stimulus in at least one pathologic condition: sleep apnea. There is also evidence that respiratory stimuli may provoke arousal indirectly via an increase in tidal volume. And, it is theorized that prolonged hypoxia and sleep fragmentation may suppress the arousal response to changes in respiratory stimuli.

Why then, should we suspect that COPD patients might be at risk for arousal problems? As previously mentioned, COPD patients experience both sleep fragmentation and episodes of oxygen desaturation. Recalling that sleep fragmentation and acute or chronic hypoxia are the factors theorized to cause arousal suppression, one may suspect that the COPD patient is, therefore, vulnerable to arousal suppression.

Before it can be determined that the arousal response is suppressed, however, it must first be determined if there is a correlation between the incidence of desaturation episodes and the incidence of arousal in these patients.

Purpose Statement

The purpose of this study, therefore, was to determine if a temporal relationship exists between episodes of oxygen desaturation and episodes of arousal in COPD patients.

Study Questions

1. Is there an association between falls in SaO_2 of $\geq$4% below the pre-sleep mean minimum value and arousals in COPD patients?
2. Is the level of SaO_2 associated with arousals consistent over 2 nights within individual COPD patients for REM and N-REM sleep?
3. Is the actual drop in percentage SaO_2 associated with arousal consistent within individual COPD patients during REM and N-REM sleep?

CHAPTER II

METHODOLOGY

Design

The purpose of this study was to describe the relationship between the occurrence of arousal and episodes of oxygen desaturation in COPD patients. A descriptive design was used in which the variables of interest, i.e., arousals and episodes of desaturation were measured simultaneously during sleep. The odds of these two events occurring at the same time, i.e., within the same 15 seconds epoch was then calculated using the odds ratio.

Selection of Subjects

During a study of sleep and breathing patterns in COPD subjects performed at the University of Washington School of Nursing, it was noted that several subjects had falls in oxygen saturation during sleep of greater than 4% below their pre-sleep SaO_2 values. Using a table of random numbers the data (polysomographic recordings and computer printouts) from 5 of these subjects was selected for evaluation in this study.

The original study was approved by the Human Subjects Review Committee and informed consent was obtained from each subject prior to data collection. Specific identies of the five subjects whose data was used in this study remained unknown to this researcher.

Criteria for admission to the original study were male between the ages of 50 and 70 with chronic bronchitis and/or emphysema. Pulmonary function parameters were an $FEV_1 \leq 1.5$ L, and $FEV_1/VC \leq 60$ percent, with an increase in residual volume (RV) compared to normal, and

arterial blood gases showing an SaO_2 of less than 95% and a PaO_2 of less than 75 mmHg with or without hypercapnia (Pa CO_2 of >40 mmHg).

Additional criteria included a bilirubin of 10 to insure accuracy of the ear oximeter, measurement and a weight limit of no more than 15% over the standard based on height/age, to avoid admission of possible pickwickian syndrome subjects to study.

Patients with known cardiac or neurological disease, polycythemia, thyroid disease, or alcoholism were excluded, as well as those taking either prescribed or over-the-counter medications which could interfere with sleep.

Setting

Recordings were made during sleep on three consecutive nights in a sleep laboratory. The subject came to the laboratory one and a half hours prior to his usual sleep time and was fitted with the necessary instrumentation. The recording equipment was maintained and monitored by a technician in an adjoining soundproof room.

Instrumentation

Sleep Parameters

An eight-channel Beckman Accutrace was used to record the electroencephalogram (EEG), electromylogram (EMG), and electrooculogram (EOG) according to the standardized procedure of Rechtschaffen and Kales (Rechtschaffen, 25). The machine was stndadrdized with a calibration voltage of 50 microvolts (μv), master sensitivity of 7.5 microvolts per millimeter (μv/mm.), and a time constant of 0.3 seconds (sec.). The filters were set with the high frequency at 50 Hertz (Hz) and the low

frequency at 0.5 Hz in order to display the low voltage output from the brain. Two channels were used for EEG, one channel for EOG, and one channel for EMG. To provide for an improved EMG signal a sensitivity of 0.25 Hz and a time constant of 0.03 seconds was utilized.

Respiratory Parameters

Two carbonized rubber strain gauges were utilized for chest and abdominal excursions. The changes in strain gauge measurement were converted into electrical signals, amplified, and displayed on two separate channels of the accutrace into inspiration and expiration curves The sensitivity of the machine was adjusted to form a sine wave on the graph paper for each respiratory cycle. Thus, increases or decreases in ventilation would be graphed as either squared or diminished sine waves respectively.

Nasal and buccal thermistors were utilized to measure air flow. These were recorded on separate channels of the Accutrace. The recordings for the Accutrace were run at a paper speed of 10mm/sec; to produce the standard 30 second sleep scoring epoch.

Procedure

The subjects were asked to refrain from drinking alcoholic beverages, tea, cola, or coffee and to refrain from napping on the afternoon or evening of each night's recording. No other changes in the subject's daily activity were recommended.

Upon the subject's arrival at the sleep laboratory, EEG, EOG and EMG electrodes were placed and secured. The chest and abdominal strain gauges, the nasal thermistor, and oral thermistor were positioned and

secured. After the ear oximeter was positioned, a final check of the instrumentation was performed. The subject was then permitted to sleep.

Data Analysis

Data for this study was obtained from polysomnographic recordings and computer printouts of oxygen saturation data. A time signal had been simultaneously recorded on the oxygen saturation analogue tape and the polygraph record to enable identification of time related events in 30 second intervals. This made it possible to associate a specific oxygen saturation to a specific epoch and the events that occurred within that epoch.

Sleep stages had been identified previously from polysomnographic recordings using the criteria defined by Rechtschaffen and Kales. A random rescoring of 10 per cent of these epochs was done by a second scorer for reliability.

Identification of arousals was also accomplished using criteria defined by Rechtschaffen and Kales. (See definitions) Arousals were rescored by the primary investigator as well as a secondary scorer for reliability. Arousal frequencies were counted and converted to arousal indexes. This made comparison within and across subjects possible.

The oxygen desaturation data was processed by computer to provide mean and minimum levels for each epoch. Arousal and SaO_2 data from sleep stages 1-4 were combined to allow comparison of the two sleep states, N-REM and REM. Mean and minimum SaO_2 values for the night and for arousal epochs were then tabled for comparison.

Contingency tables and the odds ratio were used to determine relationships between epochs of desaturation and arousal. A sample

contingency table is included here for clarification.

		Desaturation	
		Yes	No
Arousal	Yes	a	b
	No	c	d

The odds ratio was then determined using the following formula: $\frac{ad}{cb}$

A ratio of 1 indicates no relationship between the variables. A ratio of 1 indicates that the two variables are more likely to occur together while a ratio of 1 indicates that the two variables are more likely not to occur together. The power of the relationship is indicated by the magnitude of the ratio above or below 1.

The two tailed student T test was used to determine if the variance from the mean SaO_2 values for the two nights was significant. Data are reported as mean $\pm$ SD and $p < .05$ level of significance was used throughout the study.

Arousal frequencies were converted to percentage of total arousals to determine what proportion of arousals occurred at levels $\geq$4% below the pre sleep mean minimum.

Definitions

The following definitions apply to this study:

Arousal: As defined by Rechtschaffen and Kales an arousal is "any increase in EMG on any channel, which is accompanied by a change in the pattern on any additional channel. For EMG channels, the change in pattern may consist of either an increase in amplitude of the EMG

signal or an amplifier blocking artifact. For EOG channels, the change of pattern may consist of either the occurrence of EMG activity, amplifier blocking artifacts, or blink artifacts. For EEG channels, the change of pattern may consist of either a decrease in amplitude, an increase in alpha activity, a paroxysmal burst of high voltage activity, the presence of EMG activity or amplifier blocking artifacts." (Rechtschaffen and Kales, 25:4)

The duration of these changes was from 3-15 seconds.

Alpha Arousal: An arousal which contains 3-15 seconds of alpha wave activity.

Movement Arousal: An arousal which lasts from 3-15 seconds but contains less than 3 seconds of alpha wave activity.

Arousal Index: The frequency of arousals divided by the amount of sleep in hours.

Epoch: A 30 second interval of time.

Pre-sleep Mean Minimum SaO_2: An average value of the minimum SaO_2 values for 30 second intervals from the beginning of the recording until the onset of sleep.

CHAPTER III

RESULTS

The purpose of this study was to determine if the occurrence of arousal is related to the occurrence of a fall in O_2 saturation of _4% below the pre-sleep mean minimum value. Two additional questions were also considered. Is the level of SaO_2 associated with arousals consistent within individual COPD patients for REM and N-REM sleep? And, is the actual drop in percentage SaO_2 associated with arousal consistent within individual COPD patients during REM and N-REM?

Description of Subjects

The five subjects had a mean age of 64 years, ranging from 59 to 69, and ranged in weight from 122-198 lbs. (See Appendix I) Pulmonary function data indicated all had COPD. (See Appendices II & III) The mean and (range) for forced expiratory volume (FEV_1) for the group was 25.6% (22-30) of the predicted. Vital capacity (VC) was also greatly diminished ranging from 52-75% of the predicted with a mean of 62.8% for the group. The FEV^1/VC ratio was from 27-35 with a mean of 32.4, well below the criterion for normals of 60. The mean residual volume was 222.75% of the predicted volume. Three of the subjects chronically retained CO_2 (see Appendix II) with $PaCO_2$ levels of 47-51 mmHg and normal pH values. The SaO_2 mean was 90.36%, range from 87-93% and the PaO_2 mean was 58 mmHg, range from 53-65 mmHg.

Characteristics of Sleep

The mean total sleep time (TST) for these subjects was 5.9± .62 (SD) hrs. per night (see Table 3) Within subjects sleep onset latency

(SOL) was fairly constant for the two nights. For the group, however, there was wide variance with SOL ranging from .5 to 22 minutes. REM onset latency (ROL) also varied widely for the group. The range was 2-139 minutes with a mean of 48.5 minutes. The mean time spent awake after the initial onset of sleep was 38.8 minutes $\pm$ 21.04. Sleep stage changes ranged from 91 to 204 with a mean of 138.4 per night. The majority of sleep time was spent in stage 2, 57.6% (see Table 4). Only 16.7% of the TST was spent in stage 3 sleep and virtually none was spent in stage 4. (Subject 33 had only 1 minute of stage 4 on night 2.) REM sleep comprised 17.8% of the TST.

TABLE 3

SUBJECT	NIGHT	SPT (Hrs)	TST (Hrs)	SOL (Mins)	ROL (Mins)	0 (Mins)	SSCH #
28	2	6.61	6.05	1.0	10	34.0	91
	3	6.22	5.69	4.0	2	31.5	97
31	2	7.34	6.26	6.5	67	65.0	122
		5.64	4.98	8.0	139	42.5	184
33	2	6.94	5.67	11.0	62.5	76.5	159
	3	7.42	7.18	8.5	12.5	14.0	204
58	2	6.78	6.13	19.0	62.5	39.5	114
	3	7.15	6.33	22.0	77.5	49.0	148
63	2	5.75	5.28	0.0	11.0	28.0	123
	3	5.70	5.57	0.5	40.5	8.0	142
Mean		6.56	5.91	8.05	48.5	38.8	138.4
SD		.68	.62	7.56	42.0	21.04	36.48

Sleep Characteristics
for 5 COPD Subjects

KEY:

SPT = Sleep Period Time
TST = Total Sleep Time
SOL = Sleep Onset Latency
ROL = REM Onset Latency
0 = Time Awake After Sleep Onset
SSCH = Sleep Stage Changes

TABLE 4

SUBJECT	NIGHT	SLEEP STAGES (% OF TST)					
		1	2	3	4	REM	MOVEMENT TIME
28	2	21	51	01	--	27	--
	3	20	58	01	--	21	--
31	2	10	61	10	--	17	02
	3	6	62	14	--	16	02
33	2	17	62	8	1	11	01
	3	17	53	12	--	17	01
58	2	17	63	2	--	17	01
	3	36	44	1	--	15	4
63	2	7	68	6	--	17	2
	3	16	54	8	--	20	2
Mean		16.7	57.6	6.3	--	17.8	1.5
SD		8.54	7.07	4.88	--	4.21	1.18

Percent of Total Sleep Time
Spent in Various Sleep Stages
for 5 COPD Subjects

Incidence of Arousal

All of the five subjects had movement arousals during both N-REM and REM sleep and alpha arousals during N-REM sleep but only two had alpha arousals during REM sleep both nights. Two had alpha arousals on one night each and one subject had no alpha arousals during REM sleep either night.

All of the subjects had a high number of arousals per hour of sleep. The mean number of total arousals for the group was 22± 9.84/hr. (See Table 5) In general, arousals during N-REM, with a mean rate of 14.2 ± 6.3/hr. were more frequent than arousals from REM with a mean rate of 8.7± .4.85/hr. Movement arousals, occurring at a mean rate of 15.84± 6.90/hr. were more frequent than alpha arousals, mean rate 7.07± 6.95/hr. (See Appendice IV and V) Movement arousals occurred most often during N-REM, mean rate 10.85± 5.97/hr. compared to 4.99± 2.99/hr. during REM. Alpha arousal indexes were nearly the same for N-REM and REM but the variance was wider for the REM index, 3.55± 2.45/hr. for N-REM and 3.72± 5.07/hr. for REM.

TABLE 5

SUBJECT	NIGHT	AROUSAL INDEX (Number/Hour) N-REM	REM	TOTAL
28	2	11.57	6.70	18.27
	3	8.18	12.76	20.94
31	2	12.07	3.81	15.88
	3	6.86	6.10	12.96
33	2	22.20	18.46	40.66
	3	23.40	11.86	35.26
58	2	14.88	6.80	21.68
	3	22.70	10.00	32.70
63	2	9.32	8.88	18.20
	3	10.85	1.77	12.62
Mean		14.20	8.70	22.92
SD		6.30	4.85	9.81

Frequency of All Arousals per
Hour of N-REM and REM
Sleep in 5 COPD Subjects

Characteristics of Oxygen Saturation

Oxygen desaturation during sleep was a frequent occurrence in these subjects. The mean time spent at SaO_2 levels $\geq$4% below the pre-sleep mean minimum SaO_2 was 1.83 hrs./night, ranging from 0.6 to 5.5 hrs. Generally, the percent of total sleep time spent at SaO_2 levels $\geq$4% below the pre-sleep mean minimum was 20%. However, the mean value for the group was 31.8% of TST because two subjects spent 70% of TST at SaO_2 levels $\geq$4% below their pre-sleep SaO_2 value. (See Table 6) (Pre-sleep mean minimum values can be found on Table 7.)

During sleep the group mean minimum SaO_2 for N-REM sleep was 86.4$\pm$ 2.8 percent. (See Table 7) The REM mean minimum was 81.8$\pm$ 3.9 percent, 7 percent below the pre-sleep mean minimum. The lowest SaO_2 values observed irregardless of sleep state for both nights ranged from 61.2 to 80.6 with a mean of 73.1 percent, nearly 16 percent below the mean pre-sleep value. The lowest SaO_2 values occurred during REM sleep in all but one subject. The one exception, subject 31, (night 2) was in transition from REM sleep to stage 1 sleep when the low value was observed. This indicates that the desaturation probably occurred during REM in that case also, but was registered in stage 1 due to the lag time in recording. Generally, the duration of the minimal SaO_2 levels was 30 seconds to one minute.

TABLE 6

Subject	Night	Freq. of Desat. Epochs ≥4% below the psmm* SaO_2	Sleep Time (hrs) Spent at ≥4% below psmm SaO_2	% of Total Sleep Time Spent at ≥4% below psmm SaO_2
28	2	141	1.2 Hrs	22%
	3	77	0.6	11%
31	2	658	5.5	88%
	3	227	1.9	38%
33	2	73	0.6	11%
	3	124	1.0	14%
58	2	81	0.7	11%
	3	112	0.9	15%
63	2	456	3.8	72%
	3	256	2.1	38%
Mean			1.8	31.8

Sleep Time Spent at SaO_2
Levels ≥4% Below the Pre-sleep
Mean Minimum in 5 COPD Subjects

*psmm = presleep mean minimum

TABLE 7

SUBJECT	NIGHT	PRESLEEP MEAN MIN SaO2 (%)	N-REM MEAN MIN SaO2(%)	SD	REM MEAN MIN SaO2(%)	SD	Minimum SaO_2 FOR NIGHT (%)
28	2	88.3	86.4	1.19	82.9	2.96	72.1
	3	89.8	88.0	1.18	85.7	1.97	80.6
31	2	89.8	84.2	1.51	81.2	1.76	76.8
	3	87.9	84.4	1.27	80.3	2.02	74.9
33	2	88.9	87.9	1.60	82.4	2.94	76.5
	3	89.1	88.6	1.68	82.7	3.25	69.0
58	2	89.8	88.6	1.10	84.8	3.25	73.8
	3	93.2	91.1	1.07	87.1	2.85	78.7
63	2	86.8	81.8	2.23	74.2	6.72	61.2
	3	86.0	82.8	2.73	77.0	5.55	67.4
Mean		88.9	86.4		81.8		73.1
SD		1.9	2.8		3.9		5.8

The Pre-sleep Mean Minimum SaO_2 Values,
Mean Minimum SaO_2 Values for NREM & REM Epochs
and the Minimum SaO_2 Value for the Night
in 5 COPD Subjects

Oxygen Saturation and Arousal

Minimum oxygen saturation levels of arousal epochs varied widely. (see Table 8) Group means for movement arousals were 80.7± 4.6 in N-REM and 77.4± 5.4 in REM. For alpha arousals group means were 83.4± 3.6 for N-REM and 75.6± 5.4 for REM. The lowest SaO_2 levels associated with arousal were seen in subject 63 on night 2 during REM sleep, 66.2 for movement arousals and 65.5 for alpha arousals.

Using contingency tables and odds ratios the relationship between arousal epochs and epochs of desaturation ≥4% below the pre-sleep mean, minimum was determined. (See Table 9) Two subjects had relationships of 1 both nights. Two subjects had a 1 ratio one night, but 1 ratio the other. Only one subject had a ratio of 1 on both nights. Of the four odds ratios which were 1, only one indicated a strong association (Subject 63, night 2) between arousal and desaturation of ≥4% below the pre-sleep value.

TABLE 8

		MINIMUM SaO2 VALUES			
		MOVEMENT AROUSAL EPOCHS		ALPHA AROUSAL EPOCHS	
SUBJECT	NIGHT	N-REM	REM	N-REM	REM
28	2	80.9	82.1	81.8	72.1
	3	86.2	84.1	85.4	83.5
31	2	79.4	77.5	82.3	-
	3	81.2	76.9	84.2	82.2
33	2	84.6	78.8	84.7	76.5
	3	78.3	74.6	82.1	80.5
58	2	85.1	82.3	86.7	-
	3	84.3	79.8	89.5	-
63	2	72.0	66.2	76.2	65.5
	3	74.8	71.7	81.4	-
Mean		80.7	77.4	83.4	75.6
SD		4.6	5.4	3.6	5.4

Minimum SaO_2 Values reached in
Movement and Alpha Arousal
Epochs in N-REM and REM
Sleep for 5 COPD Subjects

TABLE 9

SUBJECT	NIGHT	ODDS RATIO
28	2	.78
	3	1.48
31	2	.30
	3	.78
33	2	1.18
	3	.86
58	2	.60
	3	.54
63	2	4.35
	3	1.55

Odds Ratios of
Arousal and Desaturation $\geq$4% Below
The Pre-sleep Mean Mininum
Occurring in the Same Epoch

There was no single SaO_2 value at which arousal would occur within subjects for any given arousal/sleep state combination. The two tailed student T test was applied to determine if variance from mean SaO_2 values for the two nights was significant. Alpha was set at the $p<.05$ level. (See Tables 10-13)

The statistical results of this study suggest that the same level of SaO_2 was not associated with arousal on both nights studied. All five subjects had $p<.05$ for the SaO_2 values of movement arousals from REM. There also was no statistical difference seen between the SaO_2 values of movement arousals during N-REM on the two nights studied.

Alpha arousals had inconsistent SaO_2 levels as well. Three of the five had $p<.05$ from N-REM. Only two subjects had alpha arousals from REM both nights. Of those two subjects the SaO_2 levels were significantly different for one and not significantly different for the other. Despite these statistical conclusions, further inspection of the tables shows that the SaO_2 values on the two nights were very similar and always within the error of the ear oximeter ($\pm 2\%$). This implies that clinically significant differences in the SaO_2 level associated with arousal did not occur in these patients from night to night.

TABLE 10

SUBJECT	NIGHT	MOVEMENT AROUSAL EPOCHS IN N-REM		
		Mean Min SaO_2	SD	P
28	2	86.0	1.6	.005
	3	87.8	1.2	
31	2	83.9	2.0	.5
	3	83.9	1.3	
33	2	87.6	1.6	.01
	3	88.4	2.1	
58	2	88.5	1.0	.001
	3	91.2	1.8	
63	2	80.6	2.1	.02
	3	82.0	1.8	

Statistical Comparison of
the Mean Minimum SaO2
Values of Movement Arousals
from N-REM Sleep for
5 COPD Subjects

TABLE 11

SUBJECT	NIGHT	MOVEMENT AROUSAL EPOCHS IN REM		
		Mean Min SaO_2	SD	P
28	2	83.4	1.3	.5
	3	85.3	1.7	
31	2	80.6	2.1	.5
	3	79.7	2.4	
33	2	83.6	-	.5
	3	81.3	3.3	
58	2	85.0	1.7	.2
	3	87.2	3.2	
63	2	75.1	7.4	.5
	3	73.0	-	

Statistical Comparison
of the Mean Minimum
SaO_2 values of Movement Arousals
from REM Sleep for
5 COPD Subjects

TABLE 12

SUBJECT	NIGHT	ALPHA AROUSAL EPOCHS IN N-REM		
		MEAN MIN SaO_2	SD	P
28	2	85.9	1.3	.001
	3	88.0	1.3	
31	2	85.3	1.5	.10
	3	84.5	-	
33	2	88.6	1.5	.10
	3	87.8	1.8	
58	2	88.5	1.4	.001
	3	91.4	.9	
63	2	78.4	1.6	.005
	3	82.1	.4	

Statistical Comparison
of the Mean Minimum SaO_2 Values of
Alpha Arousals from N-REM Sleep for
5 COPD Subjects

TABLE 13

SUBJECT	NIGHT	ALPHA AROUSAL EPOCHS IN REM		
		Mean Min SaO_2	SD	P
28	2	86.1	4.8	.05
	3	86.4	1.9	
31	2	-	-	-
	3	82.2	-	
33	2	81.7	3.0	.5
	3	82.0	1.4	
58	2	-	-	-
	3	-	-	
63	2	70.9	4.4	-
	3	-	-	

Statistical Comparison of the
Mean Minimum SaO_2 Values of
Alpha Arousals from REM Sleep
for 5 COPD Subjects

The actual drop in SaO_2 from the pre-sleep minimum associated with arousal was not consistent in these subjects either. In general, N-REM arousals were associated with higher SaO_2 levels than were REM arousals. (See Table 14) During N-REM sleep three of the five subjects had 94-100% of their alpha arousals occur at SaO_2 levels $\geq$4% below the pre-sleep mean minimum SaO_2 level. During REM four subjects had 75-100% of their movement arousals and three had 95-100% of their alpha arousals at $\geq$4% below the pre-sleep mean minimum. This study did not tabulate specifically the frequency of arousal at SaO_2 levels below the $\geq$4% level. However, upon inspection it was apparent that there was no one consistent level below the pre-sleep mean minimum at which arousal would occur.

TABLE 14

SUBJECT	N-REM		REM	
	Movement Arousal %	Alpha Arousal %	Movement Arousal %	Alpha Arousal %
28	2.5	6.5	75	39.5
31	58	27	100	100
33	5.5	4.5	66	95
58	2.5	0	75.5	0
63	69	75	87.5	100

The Mean Percentage of Movement and Alpha Arousals from N-REM and REM Occurring at $\geq$4% Below the Pre-Sleep Mean Minimum SaO_2 in 5 COPD Subjects

Summary of Findings

All 5 of these COPD subjects experienced frequent arousals and episodes of desaturation during sleep. Only in one subject was there an association between arousal and oxygen falls of _4% and that association occurred on one night only.

By statistical test, there was no common SaO_2 at which arousal occurred within subjects. Although this suggests that the SaO_2 level of arousal epochs was statistically different, clinically this difference was not significant.

There was no specific percentage fall below the pre-sleep SaO_2 which was consistently associated with arousal in any of these subjects. However, it was noted that N-REM arousals generally were associated with higher SaO_2 levels than were REM arousals.

Discussion

As expected these five COPD subjects were similar to other COPD subjects in that they had multiple arousals and frequent episodes of desaturation. This study attempted to determine if the two events were related. It appears from the results that they are not. Only one subject had a strong association between arousal and episodes of desaturation, and that was for one night only. All others showed no relationship between the two events.

One explanation for the low association between arousal and oxygen desaturation is that the arousal response to hypoxia may have been reduced due to sleep fragmentation. Studies have shown that sleep fragmentation will elevate the arousal threshold to hypoxia. (Phillipson, 22) Conceptually then, it is possible that the association between

episodes of desaturation and arousal in COPD subjects who experience sleep fragmentation might be low.

All five subjects in this study had evidence of sleep fagmentation, i.e, high arousal indexes, frequent stage changes, and large amounts of awake time. On night 2 subject 33's total arousal index was 40.66/hr. TST was 5.67 hrs and time awake was 76.5 mins. On night 3 his total arousal index dropped to 35.26/hr. TST increased to 7.18 hrs. and time awake decreased to 14 min. Clearly sleep was much more fragmented on night 2 than on night 3 and clearly there were fewer arousals on night 3 than on night 2. This pattern of decreased arousal index, increased TST and decreased awake time was not seen in the other subjects. Subject 31 on night 2, aroused 15.88 times per hour, was asleep 6.26 hrs and awake 65 minutes. On night 3 his arousal index dropped slightly to 12.96/hr., however, his TST rather than increasing, decreased to 4.98 hrs. Time awake also decreased. Subject 28 on night 2, aroused 18.27 times per hour slept 6.05 hrs. and was awake 34 minutes. On night 3 his arousal index was nearly the same at 20.94/hr, TST was also nearly the same at 5.69 hrs and time awake was constistent at 31.5 minutes. Subject 58 slept 6.13 hrs. aroused 21.68 times per hour and was awake 39.5 minutes on night 2. On night 3 his TST was nearly the same, 6.33 hrs but the total arousal index increased to 32.7/hr. Time awake also increased slightly to 49 minutes. Obviously, these subjects were experiencing sleep fragmentation but arousal indexes and sleep patterns for the two nights were so similar that it is difficult to claim that these subjects experienced arousal suppression. If the pattern seen in subject 33 had occurred in the other subjects it could be argued that

the poor association between arousal and oxygen desaturation was the result of an increased arousal threshold to hypoxia. Because it was not seen consistently however, it is doubtful that the arousal threshold to hypoxia was involved in the sleep changes seen in these subjects.

In a recent editorial Anthonisen and Krygen suggested that hypoxia may stimulate arousals but it may be only when the SaO_2 level falls to 50% or less. Berthon-Jones and Sullivan studying normal subjects found that when eucapnic hypoxia was induced normal humans failed to arouse to SaO_2 levels of 70% from either REM or N-REM sleep. (Further desaturation was not attempted due to the high potential for tissue damage.) (Berthon-Jones, 2) This theory could explain why the COPD subjects in this study had no association between hypoxia and arousal. Of the five, only one subject, 63, desaturated consistently to levels near 70% SaO2. His mean minimum SaO_2 values ranged from 70 to 80% while the mean minimum values for the other subjects ranged from 80 to 90%. Minimum SaO_2 values for subject 63 were well below 70% SaO2. His minimum SaO_2 on night 2 was 61.2% and on night 3 was 67.4%. His lowest SaO_2 value associated with an arousal was 65.5% on night 2. Subject 63 further supports Anthonism's theory in that he was the only subject who showed a strong relationship between episodes of arousal and oxygen desaturation. (Night 2) He had evidence of sleep fragmentation as did the other subjects but rather than demonstrating a suppressed arousal response to hypoxia he had a high response, higher than any other subject. It is possible that arousal in the other subjects was generally stimulated by other factors such as coughing, movement, discomfort and/or changes in breathing. While in subject 63 oxygen levels

were falling to levels that were not only endangering tissues but were actually life threatening. Arousal was imperative for survival. Arousals for any other reason could be suppressed in an effort to increase sleep time. Ultimately, however, as desaturation progressed arousal triggered by hypoxia had to occur to preserve life. If the other subjects had desaturated to levels as low as subject 63 would they too have had higher associations between arousal and oxygen desaturation?

Conclusion

This study was unsuccessful in demonstrating an association between episodes of arousal and desaturation in all of the COPD subjects tested. Nevertheless, it does appear that there may be a relationship when saturation levels fall to levels near or below 70% SaO_2. This arousal mechanism may be a life saving measure in these individuals reserved for times when the threat of tissue damage or death is high.

COPD subjects may be experiencing some arousal suppression as a result of sleep fragmentation but it is likely that the stimuli involved are things less life threatening than severe oxygen desaturation, i.e., pain, noise, movement. Obviously much more research is needed to answer the questions posed by this study.

Study Limitations

1. Small sample size
2. Focus on one arousal stimulus
3. Absense of comparative data from normals.

Recommendations for Further Studies

1. Repeat study in same subjects after disease has progressed.
2. Repeat study in a different group of COPD subjects all with disease severity similar to subject 63.
3. Study a larger sample and include other arousal stimuli, i.e., changes in tidal volume coughing or other movement, noise, etc.
4. Comparative study using normals and COPD subjects.

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APPENDIX I

SUBJECT	AGE (yrs)	HEIGHT (inches)	WEIGHT (lbs.)
28	62	71	177
31	66	71	198
33	59	73	164
58	69	72	122
63	65	67	160
Mean	64.2	70.8	164.2

Physical Characteristics of 5 COPD Subjects

APPENDIX II

SUBJECT	PaO_2 (mmHg)	SaO_2 (%)	$PaCO_2$ (mmHg)	pH
28	55	92.5	47	7.39
31	53	87	47	7.38
33	61	91.3	40	7.40
58	65	93	30	7.41
63	56	88	51	7.38
Mean	58	90.36	43	7.392
SD	4.9	1.16	8.27	.016

Arterial Blood Gases of 5 COPD Subjects

APPENDIX III

SUBJECT	VITAL CAPACITY (L)		FORCED EXPIRATORY VOL. (L)		FEV_1/VC	RESIDUAL VOL. (L)	
	obs	% Pred	obs	% Pred		obs	% Pred
28	2.8	66	0.76	22	27	5.4	216
31	2.2	52	0.76	23	35	4.4	176
33	3.5	75	1.1	30	31	6.2	248
58	2.6	60	0.87	26	35	6.8	251
63	2.2	61	0.76	27	34	no data	no data
Mean		62.8		25.6	32.4		222.75
SD		8.46		3.17	3.44		34.96

Pulmonary Function Data
for 5 COPD Subjects

APPENDIX IV

SUBJECT	NIGHT	MOVEMENT AROUSALS N-REM	MOVEMENT AROUSALS REM	ALPHA AROUSALS N-REM	ALPHA AROUSALS REM	TOTAL AROUSALS N-REM	TOTAL AROUSALS REM
28	2	19	4	32	7	51	11
	3	12	4	25	11	37	15
31	2	49	4	13	0	62	4
	3	26	4	2	1	28	5
33	2	78	2	33	10	111	12
	3	122	11	17	3	139	14
58	2	69	7	6	0	75	7
	3	93	9	23	0	116	9
63	2	33	4	7	4	40	8
	3	43	2	4	0	47	2

Frequency of Arousals
in 5 COPD Subjects for 2 Nights

APPENDIX V

SUBJECT	NIGHT	MOVEMENT AROUSALS per hour N-REM	REM	TOTAL
28	2	4.31	2.43	6.74
	3	2.65	3.40	6.05
31	2	9.50	3.81	13.31
	3	6.37	4.88	11.35
33	2	15.60	3.08	18.68
	3	20.54	9.32	29.86
58	2	13.69	6.80	20.49
	3	18.20	10.00	28.20
63	2	7.69	4.44	12.13
	3	9.93	1.77	11.70
Mean		10.85	4.99	15.84
SD		5.97	2.99	6.90

Frequency of Movement Arousals
per hour of NREM and REM Sleep
in 5 COPD Subjects

APPENDIX VI

SUBJECT	NIGHT	ALPHA AROUSALS per hour N-REM	REM	TOTAL
28	2	7.26	4.27	11.53
	3	5.53	9.36	14.89
31	2	2.57	0	2.57
	3	0.49	1.22	1.71
33	2	6.60	15.38	21.98
	3	2.86	2.54	5.40
58	2	1.19	0	1.19
	3	4.50	0	4.50
63	2	1.63	4.44	6.07
	3	0.92	0	0.92
Mean		3.55	3.72	7.07
SD		2.45	5.07	6.95

Frequency of Alpha Arousals
per hour of NREM and REM Sleep
in 5 COPD Subjects

APPENDIX VII

SUBJECT	NIGHT	Movement Arousal Epochs in N-REM Mean Minimum SaO2	SD	Alpha Arousal Epochs in N-REM Mean Minimum SaO2	SD
28	2	86.06	1.602	85.97	1.305
	3	87.84	1.276	88.05	1.364
31	2	83.98	2.072	85.39	1.544
	3	83.92	1.344	84.51	-
33	2	87.60	1.620	88.69	1.521
	3	88.40	2.126	87.83	1.849
58	2	88.58	1.066	88.51	1.488
	3	91.29	1.806	91.40	.998
63	2	80.60	2.147	78.42	1.699
	3	82.00	1.842	82.19	.473
Mean		86.03		86.10	
SD		3.036		3.618	

Mean Minimum SaO_2 of Movement
and Alpha Arousal Epochs
in N-REM Sleep for 5 COPD Subjects

APPENDIX VIII

SUBJECT	NIGHT	Movement Arousal Epochs in REM Mean Minimum SaO2	SD	Alpha Arousal Epochs in REM Mean Minimum SaO2	SD
28	2	83.45	1.360	86.10	4.81
	3	85.38	1.720	86.49	1.96
31	2	80.63	2.100	-	-
	3	79.79	2.932	82.22	-
33	2	83.61	-	81.76	3.039
	3	81.36	3.302	82.08	1.498
58	2	85.05	1.720	-	-
	3	87.26	3.216	-	-
63	2	75.18	7.424	70.99	4.464
	3	73.07	-	-	-
Mean		81.48		81.44	
SD		4.478		5.367	

Mean Minimum SaO_2 of Movement
and Alpha Arousal Epochs
in REM Sleep for 5 COPD Subjects

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