NECK ANTHROPOMETRY AND THE PREDICTION OF SLEEP APNEA IN ADULT FEMALES

by

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A DISSERTATION

Presented to the Faculty of

The Graduate College at the University of Nebraska

In Partial Fulfillment of Requirements

For the Degree of Doctor of Philosophy

Major: Interdepartmental Area of Psychological
and
Cultural Studies

Under the Supervision of Professor Wesley E. Sime

Lincoln, Nebraska

December 1997

UMI Number: 9815909

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Ann Arbor, MI 48103

DISSERTATION TITLE

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University of Nebraska, 1997

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This observational laboratory study was designed to evaluate neck size and subdermal neck fat as predictors of obstructive sleep apnea syndrome (OSAS) in adult females. Forty (n = 40) female patients referred to the sleep lab for apnea screening were evaluated for body mass index (BMI), neck circumference, predicted percent of neck circumference (PPNC), submental skinfold thickness, neck skinfold thickness, situational sleepiness (Epworth Sleepiness Scale), and self-rated abnormal sleep breathing behavior. Subjects received a standard all-night clinical polysomnogram. Scored sleep studies were interpreted and obstructive apnea diagnosis severity codes were assigned based on respiratory disturbance index (RDI). Data were also collected on a non-random, non-sleeper sample of adult females (n = 40) for comparison to the sleeper group.

It was hypothesized that neck circumference, submental skin-fold, and Epworth Sleepiness Scale Score would be predictor variables for RDI and could improve previously published multiple regression models. Confidence intervals were set at 0.95, and level of significance at $p \leq 0.05$ for all tests. Forward selection stepwise regression analysis showed that neck circumference and composite self-rated sleep breathing behavior score were the only significant predictor variables for RDI (CI 0.95, $r^2 = 0.2979$, $p < 0.01$). The Epworth Sleepiness Scale was not a predictor variable in any regression model evaluated. Improvement of a predictive regression model for obstructive apnea in adult females was not achieved.

Two-sample, unpaired, multiple t-tests (Bonferroni corrected $p \leq 0.0045$) showed significant differences between non-OSAS diagnosed sleepers and OSAS diagnosed sleepers for respiratory disturbance index (RDI) only.

DEDICATION AND ACKNOWLEDGEMENTS

A colleague and friend once said to me, "A dissertation is never done alone...it is a group effort." This remark is a poignant reflection of my own recent experience. Many fine scholars and teachers, advisors, special friends, trusted associates, university staff, research subjects, and most of all beloved family members are vested in the journey and the product.

Special thanks to Diane Smaling for assistance with collecting and collating data and, to Becky Fasnacht-Pugsley for word processing assistance. Sincere appreciation to Dr. Bob Bleicher for his excellent sleep study interpretation skills and for his encouragement.

The expertise and dedication of the technical and nursing staffs at Somnos Laboratories and the Bryan Memorial Sleep Lab were invaluable.

To Dr. Michael Riley and Dr. Ram Bishu I give my appreciation and respect for their willingness to accept a "book" with a very unusual cover. To my long time friend, Dr. Richard Schmidt, scholar, teacher, and devoted parent, I extend my deep admiration and respect. His advice and encouragement helped me recognize and embrace a new direction. And, to Dr. Douglas May and Dr. Sharon Evans, I

am indebted to you both for so graciously agreeing to serve on my committee and for assisting me with my doctoral plan and research direction.

For Dr. Wesley Sime, who understood me so well and who was always willing to listen and find a way to make things work in supporting my goal, I give my sincerest appreciation and respect. We have many more roads to travel.

And, finally to my sons, Troy and Tim for their steadfast belief in a late-blooming father. I love you both and I will always cherish our time together in our work and in our play. To my beloved wife Connie...who has endured this long process with joy, loneliness and sometimes frustration; always, in the end, with remarkable patience, understanding, and love. Thank you so much for your gifts of time and hope.

> The city sleeps and the country sleeps,
> The living sleep for their time,
> the dead sleep for their time.
> The old husband sleeps by his wife
> and the young husband sleeps by his wife;
> And these tend inward to me, and I tend outward
> to them,
> And such as it is to be of these more or less I am,
> And of these one and all I weave the song of
> myself.
>
> WALT WHITMAN (1819-92), Song of Myself, sct.15
> in *Leaves of Grass*.

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CHAPTER ONE

INTRODUCTION

The purpose of this chapter is to introduce the topic of study, provide study relevance and a statement of problem, identify basic assumptions and limitations, and summarize the general organization of the dissertation.

Background

A description of normal human sleep would contribute to a better general understanding of sleep disorders, and to better comprehension of the features and effects of obstructive sleep apnea syndrome (OSAS). The following two subsections provide an introduction to normal human sleep followed by an overview of obstructive sleep apnea. The remaining sections address study needs, relevance, problem statement, assumptions, limitations, and organization of dissertation.

Normal Human Sleep

Sleep is a reversible behavioral state in which the sleeper is disengaged from and unresponsive to the environment. Human sleep is a complex mixture of physiological and behavioral processes. Both sleep and awake states are thought to be driven by the upper brain stem region or ascending reticular activating system

(ARCS) mediated by body core temperature cycling, growth hormone, serotonin, melatonin, and the external light environment. Humans possess both a manifest sleep drive (sleepiness due to external environmental cues or so-called "zeitgebers") and physiological sleep drive (sleepiness due to internal drive mechanisms). The normal diurnal sleep-wake cycle, which coincides closely with body core temperature cycling, and the natural availability of light, is only one of more than 2000 distinct circadian cycles identified in humans (Carskadon & Dement, 1994; Anch, Browman, Mitler, & Walsh, 1988).

Sleep is usually, but not always, experienced in the recumbent posture, quiescent, eyes closed, and the outward appearance of sleeping. Normal sleep consists of two separate states: NREM or non-rapid eye movement sleep, and REM or rapid eye movement sleep. These two states are physiologically different from each other and measurable. All mammals and birds exhibit this dichotomy of physiological state (Carskadon & Dement, 1994; Anch, Browman, Mitler, & Walsh, 1988).

NREM sleep is arbitrarily divided into four stages which are discernable by measuring cortical activity of the brain by means of scalp electrodes and an electroencephalograph (EEG). EEG activity for NREM sleep is synchronous with characteristic waveforms such as sleep spindles, K-complexes, and high voltage slow waves. NREM stages 1-4 roughly equate to the depth of sleep in an individual. It is easiest for a sleeper to arouse from stage 1 and hardest from stage 4. NREM represents a brain with very low mental activity in a body that is still movable and regulated by the brain.

REM sleep is an EEG active stage of sleep in that there is pronounced brain activity similar to the awake state, loss of muscle tonus, and episodes or bursts of

rapid eye movement. REM is not divided into stages like NREM, but into two types of REM called "tonic" and "phasic". The most common phasic REM activity in humans are the bursts of rapid eye movement associated with the mental activity of dreaming. In essence, during REM sleep there exists a highly activated brain inside of a paralyzed body (Carskadon & Dement, 1994; Anch, Browman, Mitler, & Walsh, 1988).

Sleep onset is the precise moment when an individual passes from awake to asleep. The onset of sleep in normal humans and under normal circumstances is through NREM sleep. Sleep onset through REM sleep is abnormal and often a marker for certain sleep disorders such as narcolepsy. At sleep onset identifiable behavioral and physiological changes occur. These changes include synchronous eye movements or "rolling eyes" and an EEG (electroencephalographic) pattern that transitions from a clearly rhythmic alpha of 8-13 cycles/second to a relatively low voltage mixed frequency pattern called stage 1 sleep.

In a normal sleeper there is a stage progression or pattern through the night. For normal, young healthy sleepers there does not seem to be a difference in this progression between males and females. The first sleep cycle lasts about 80 minutes and begins as the sleeper passes from awake to stage 1 with an increase in arousal threshold. Stage 1 persists for only about 1-7 minutes and throughout the night will reoccur as a "transition" stage in the overall sleep cycle progression (Anch, Browman, Mitler, & Walsh, 1988).

Stage 2 occurs next with the appearance of distinctive sleep spindles and K-complexes (high voltage, slower wave brain activity) which lasts for 10-25 minutes. Gradually, the brain waves get larger in amplitude and even slower to the point

where this waveform is 20% to 50% of the total activity representing stage 3. Stage 3 lasts for only a few minutes until more than 50% of the sleep record trace shows the large, slow wave forms and stage 4 is reached. Stage 4 can last anywhere from 20-40 minutes. In stage 3 and 4 the sleeper's arousal threshold is at it highest. Some researchers lump stages 3 and 4 sleep together under the name "slow wave, delta, or deep sleep" (Carskadon & Dement, 1994; Anch, Browman, Mitler, & Walsh, 1988).

At the end of stage 4 there is often a series of small body movements that indicates the approaching ascent from deep sleep to lighter sleep. A 1-2 minute episode of stage 3 sleep is followed by 5-10 minutes of stage 2 sleep, and then again interrupted by a series of small body movements that indicate entry into REM sleep. The first REM episode of the night is usually quite short, only 1-2 minutes, and at its conclusion the first sleep cycle has been completed. The next cycle may be punctuated by the briefest of arousals, usually undiscernible to the sleeper, and the "stairway" down again into deeper stages of sleep begins again. As the night progresses the sleeper will experience 3 to 5 more cycles of somewhat shorter duration (60-70 minutes) with each cycle ending in REM and perhaps momentary arousal. During the second half of the night the extent and duration of deep sleep declines while REM sleep incidence and duration increases until the sleeper finally fully awakens in the morning (Carskadon & Dement, 1994; Anch, Browman, Mitler, & Walsh, 1988).

Most healthy young adult sleepers sleep once per 24 hour period with the average daily sleep requirement between 6.5 and 7.5 hours. Age is the most important and consistent factor affecting the pattern of sleep in humans. Infants experience up to 50% of their sleep each day as REM with gradual change toward a more normal

increment of 20% REM and 80% NREM at age 10 or so. As adults age the amount of REM sleep remains relatively constant as a per cent of the total time asleep. However, deep sleep amount and duration declines, sleep is more fragmented, and the total amount of sleep needed each day decreases. Some researchers believe that the changes in sleep pattern seen in humans as they age are part of the aging process. There may be an association between the loss of melatonin production with aging, sleep pattern changes, and eventual death (Carskadon & Dement, 1994; Anch, Browman, Mitler, & Walsh, 1988).

Sleep changes the breathing pattern and respiratory response to external stimuli. These changes may contribute to sleep-related hypoxemia associated with respiratory disease and the pathogenesis of obstructive sleep apnea syndrome. The goal of the respiratory system during sleep is to maintain blood gases in a range so that normal metabolic functions of the body can occur. Respiratory muscles receive impulses from the medulla region of the brain from a center called the respiratory oscillator or respiratory signal generator. When physiological conditions change, respiration changes. The respiratory center can respond to three types of stimuli: chemical receptors for PaO_2, $PaCO_2$, and pH.; mechanical information from receptors in the lung and chest wall; and behavioral information from higher cortical centers (Douglas, 1994).

Humans demonstrate more irregular breathing patterns during REM compared to NREM. Other factors such as chest-abdominal movement, reduced functional residual capacity, and increased airflow resistance can also change ventilatory response in humans. Various breathing abnormalities during sleep have been related to common conditions such as male gender, increased age, excess weight, snoring, and apnea. During a normal night's sleep, humans may occasionally stop

breathing for very short periods of time (called apneas) and/or have reduced breathing rates called "hypopneas" (Douglas, 1994). These terms and their thresholds for normality and abnormality are explained in Chapter 2.

<u>Obstructive Sleep Apnea Syndrome (OSAS)</u>

Congress established the National Commission on Sleep Disorders in 1988 to conduct a comprehensive study of sleep disorders and to develop a long range plan for directing national resources to deal more effectively with sleep disorders research and medicine. The Commission reported that each year millions of Americans are disturbed, disrupted, or destroyed by the consequences of sleep disorders (National Commission on Sleep Disorders Research, 1993; Phillipson, 1993).

Of all sleep disorders, the most serious with respect to morbidity and mortality is obstructive sleep apnea syndrome (OSAS). Obstructive sleep apnea is characterized by repeated episodes of respiratory airflow cessation during sleep caused by the collapse of the soft tissues of the upper airway at the pharynx. Years of heavy snoring contribute to severe narrowing or complete collapse of the airway. Periods of respiratory cessation can last from 15 to 90 seconds and, in severe cases, more than 300 such episodes can occur in a single night. Significant drops in arterial oxygen level often accompanies apnea episodes. Apnea episode termination results in brief arousal, snorting, gasping, choking, which results in brief arousal and the repeated fragmentation of normal sleep architecture. Several deep breathes restore the airway and a return to sleep (Phillipson, 1984; Hudgel, 1992).

Apnea patients often experience debilitating daytime symptoms which include excessive daytime sleepiness (EDS), impaired cognitive function, memory loss, morning headaches, and sometimes depression and personality dysfunction. These symptoms can result in employment difficulties, social disharmony, and emotional disturbance. In severe cases, patients report falling asleep while driving. Highway safety studies related to apnea show that a severe apnea sufferer is two to three times more likely to be involved in a highway road accident than the population at large. Obstructive sleep apnea has been identified as a major contributor to pulmonary hypertension and right ventricular failure. Diagnosis and treatment usually shows a remarkable improvement in cardiac function (Phillipson, 1993; Wheatley, J.R., Mezzanotte, W.S, Tangel, D.J., and White, D.P., 1994; Findley, Fabrizio, M, Thommi, G, & Suratt, P.M., 1989).

A number of studies have examined the prevalence of obstructive sleep apnea in the adult population. Young et al. (1993) used polysomnographic studies of a population based sample (n=602) of men and women from 30 to 60 years of age to estimate prevalence. The results of this study implied that 4 percent of women and 9 percent of men in the age groups studied had 15 or more episodes of apnea and hypopnea (reduced or incomplete airflow cessation) per hour of sleep. From this information, Young et al. extrapolated the conclusion that 2 percent of women and 4 percent of men of the middle-aged work force have clinically significant apnea. Therefore, sleep apnea is probably under diagnosed and represents a major public health risk (Young, 1993; Young, Palta, M., Dempsey, J, et al., 1993).

Obstructive sleep apnea can be effectively diagnosed with an overnight polysomnogram (sleep study). The range of treatment options includes weight loss, physical conditioning, sleep position retraining, oral devices, upper pharynx

surgery, continuous positive airway pressure (CPAP), and tracheostomy. Overnight sleep studies are expensive with the cost ranging from about $1000 to $2000 in most labs. Effective treatment outcomes require long-term patient compliance and physician monitoring (Kryger, 1994; Reite, Nagel, & Ruddy, 1990).

Relevance

Apnea patients are often obese and appear to have short, fat necks. Because of this common observational association, a number of predictor variables for obstructive apnea have been studied. The overall goal has been to improve physician screening methods and reduce the inconvenience and economic risks associated with polysomnographically testing patients who are, in fact, negative for a sleep breathing disorder. Predictor variables of greatest interest and research attention have included weight; body mass index (BMI); external neck circumference; chest, abdominal, hip, and thigh circumferences; radiographic and sonographic internal airway circumference and shape; soft palate dimensions; daytime symptom reports (especially sleepiness); and nocturnal breathing behavior reports (Katz, Stradling, Slutsky, Zamel, & Hoffstein, 1990; Davies & Stradling, 1990; Davies, Ali, & Stradling, 1992; Bohlman, Haponik, Smith, et al., 1983; Flemmons, Whitelaw, Brant, & Remmers, 1994; Horner, et al., 1989; Horner, Sheat, McIvor, et al., 1989; Hoffstein & Mateika, 1992; Horner, et al., 1989).

Radiographic, tomographic, and sonographic anatomical studies have shown that apnea patients seem to have higher levels of fat present in pharyngeal tissues and structures (vellum and tongue), and subdermal in the neck (presented as a larger neck circumference). Which of these two locations of fat deposit, pharynx or neck