

Daytime Consequences of Sleep Apnea in REM and NREM Sleep

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Introduction

There is controversy as to whether the daytime consequences of sleep apnea are different depending on whether the apnea occurs predominantly in the state of REM (rapid eye movement) or NREM (non-rapid eye movement) sleep. Apnea is the partial or complete closure of the airway which occurs during sleep and is ended in part by arousal. Many patients exhibit differences in the amount and frequency of these events during REM and NREM sleep. Patients with apnea present with symptoms of daytime sleepiness and changes in concentration and memory.

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Background and Significance

Research suggests that these daytime consequences might be worse with REM related apnea than NREM (Kass et al., 1996). The generalizability of this study is compromised, however, by the small subject pool (n=34) and inclusion criteria of disease severity; which necessitated an overall AHI (apnea hypopnea index) of less than 10. Recently, in a larger sample of subjects, Punjabi et al. (2002) found no significant association between sleep-disordered breathing in REM sleep and daytime sleepiness as measured by the Multiple Sleep Latency Test (MSLT), an objective measure of daytime sleepiness. Instead he pointed to findings demonstrating a possible correlation between NREM AHI and daytime sleepiness.

While previously mentioned studies have statistically adjusted for gender in their analysis, it is unclear what role, if any, sex may have played in their results. Findings suggest gender differences in severity of respiratory events in REM and NREM sleep. Preliminary findings of a multi center, National Institute of Health (NIH) funded study examining sleep apnea and existing cardiopulmonary functioning, indicate that women tend to have less severe sleep apnea than men during NREM sleep; but are not significantly different during REM sleep. Thus REM-only sleep apnea appears to be more common in women. The New York University (NYU) Sleep Disorder Center is a participant in this study, which is in progress. Our research efforts have the potential for contribution to this line of work, and for a more detailed exposition of sex differences in sleep apnea.

The NYU Sleep Disorder Center has data on more than 3,000 sleep studies. Thus, we have an opportunity to add significant input to these controversies. To begin, we propose a retrospective chart review to further assess this issue in preparation of an ongo-

ing prospective study of sleep apnea across gender, time of night, and state of sleep.

Hypothesis

We hypothesize that REM sleep related respiratory events negatively impact daytime functioning, as measured by the Epworth Sleepiness Scale (ESS); more than NREM sleep related respiratory events. The ESS is a reliable and valid subjective measure of daytime sleepiness. Further, in those patients who have had objective measures of daytime sleepiness in the forms of a Multiple Sleep Latency Test (MSLT), Maintenance of Wakefulness Test (MWT), or Osler Psychomotor Vigilance Reaction Time Task; REM sleep apnea will be correlated with impaired wakefulness and/or reaction time.

Method

We plan to conduct a retrospective chart review of patients who have been diagnosed with sleep apnea (n=240). Relevant data (see data analysis) will be extracted and placed into a database in which all patient identity will be removed and study subjects will be recoded. Selected polysomnographic records will be checked for analysis accuracy, ensuring consistent standards for definition of sleep and respiratory event. If there is any ambiguity, the entire record will be subjected to reanalysis.

Subjects will be included in the study if they have had a complete diagnostic night of sleep, are free of psychotropic or sleep influencing medications, and are otherwise healthy or have stable illnesses such as diabetes, hypertension or coronary disease. Diagnostic data less than 6 hours and excessively long studies (more than 9 hours) will be excluded from the analysis. This will eliminate possible confounds of both insufficient and abnormally long sleep cycles. Subjects will be excluded if they have unsta-

ble medical illnesses, or have had a stroke or other neurological illness such as epilepsy and REM sleep behavior disorder.

Selected records will be entered into a database with attention to the nature and characterization of a patients' sleep disordered breathing and measures of daytime alertness. This is a retrospective study analyzing our sleep center's existing data only, which will be de-identified for the public. Our process will insure complete anonymity and an absence of risk to patients.

Data Analysis

Sleep disordered breathing is an inherently multivariate problem. Most people who have the disease exhibit respiratory events in both REM and NREM sleep stages. Thus a multitude of variables will be considered including gender, menopausal and hormone replacement status (women), age, body-mass index (BMI), severity of apnea in REM and NREM sleep (as measured by apnea count and degree and duration of oxygen desaturation), time in REM/NREM sleep stages, medications, ESS score, mean latency to sleep on MSLT or MWT, reaction time, and lapses of attention as measured by the Osler Psychomotor Vigilance Task.

Variables we intend to isolate for primary analysis are REM AHI, NREM AHI, and Epworth Sleepiness Scores. Our main hypothesis posits that REM AHI, but not NREM AHI, will be significantly associated with the elevated Epworth Sleepiness Scale (ESS) scores; our dependent variable. REM and NREM AHI (apnea hypopnea index) are our independent variables. Epworth scores represent an interval level of data thus a linear, parametric analysis will apply. If the data allows, as expected, 3 groups will be formed: group 1 will consist of those patients who have respiratory events only in REM sleep. Group 2 will be composed of patients who have events during all stages of sleep, but are markedly worse while in REM. And finally, group 3 will be rep-

resented by patients who exhibit events during all sleep stages, but are better in REM. Preliminary estimates of the effect on ESS that we are trying to detect necessitates an N of 240 ($p < .05$; power of .95).

Subgroups will then be formed according to gender. Any confound of gender will be eliminated. If possible, these groups will also be used to examine sleep disordered breathing and its relation to a) sex differences, b) menopausal/hormone replacement status in women.

Summary

Findings of this retrospective study will add significant information to this important issue and provide pilot data for ongoing research efforts.

References

- Kass, J.E., Akers, S.M., Bartter, T.C., & Pratter, M.R. (1996). Rapid-eye-movement-specific sleep-disordered breathing: a possible cause of excessive daytime sleepiness. *American Journal of Respiratory Critical Care Medicine*, 154, 167-169.
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