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Across-Night Lengthening of Sleep Apneic Episodes

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Summary: Systematic trends in the length of apneas were investigated in 8 sleep apnea patients, all of whom had more than 200 apneas per night. Regression analysis performed on the length of apneas by thirds of the night revealed significant linear trends for apneas in sleep stage 2, and for apneas in all sleep stages pooled together. There were no significant trends in the index of apnea density. We suggest that the across-night lengthening of apneas reflects a progressive increase in the arousal threshold, either by a compensatory deepening of sleep or by progressive changes in respiratory chemoreceptor sensitivity. The lack of significant trends in rapid eye movement (REM) sleep supports the conclusion that apnea termination in REM sleep is mediated by a different mechanism than in non-REM sleep. **Key Words:** Sleep apnea syndrome—Linear trend—Apnea termination.

Sleep apnea syndrome (SAS) is a sleep laboratory diagnosis which presents a characteristic clinical picture in the symptomatic patient (Guilleminault et al., 1976). It is defined by the appearance of periodic sleep-induced apneas. The apneas in SAS are usually described in terms of their overall number, distribution by sleep stages and type, and length. Alroy and Lavie (1978) reported their impression that in some subjects there is a gradual lengthening of the apneas across the night. We therefore decided to determine if there are systematic across-night trends in the length and/or number of apneas in sleep apnea patients.

MATERIALS AND METHODS

The 8 SAS patients who were included in the present study were selected according to the following criteria: their polysomnographic recordings were of reasonably good quality, their total bedtime was at least 400 min, each experienced at least 200 apneas, and apneas appeared immediately after each patient's falling asleep.

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All patients were males, aged 32–70 (mean = 54.1 ± 13.3). All were overweight, but none was morbidly obese. Except in one, no severe hypoventilation was found during wakefulness. Mean P_aO_2 was 73.8 ± 7.9, and mean P_aCO_2 was 41.1 ± 5.6. None of the patients was grossly hypertensive, nor did any of them have signs of right heart failure. All patients complained of excessive daytime sleepiness, frequent headaches, snoring, and various combinations of other complaints.

Patients were studied according to our standard protocol: anamnesis, physical examinations, routine laboratory and respiratory functions, and 1–2 nights of polysomnographic recording. Sleep stages were scored according to Rechtschaffen and Kales (1968), and the apneas were scored by an experienced member of our staff (EH).

The analysis of the apneas was done by thirds of the night. Apneas from each third were analyzed separately for sleep stage 2 and rapid eye movement (REM) sleep, and for all sleep stages pooled together. Similar analysis was performed regarding the sleep apnea index: that is, the number of apneas per hour of sleep.

RESULTS

Sleep structure of the present SAS patients was similar to the sleep structure commonly reported for these patients. Total bedtime ranged from 415 to 507 min (mean = 457 ± 32.7), and the mean sleep latency was 5.8 ± 1.0 min. REM sleep and sleep stages 3 and 4 were reduced, and there was a large amount of wakefulness within sleep. The total number of apneas was 3868, of which 90% were obstructive or mixed and the rest central. Fig. 1 presents the mean lengths of apneas (±SD) in each third of the night for stage 2, REM sleep, and for all sleep stages pooled together. Regression analysis revealed a significant linear trend for the length of apneas in sleep stage 2 ($F = 9.61$, $df = 1,21$, $p < 0.01$), and for all sleep stages ($F = 19.96$, $df = 1,21$, $p < 0.01$). The apneas in REM sleep were significantly longer than the apneas in sleep stage 2 ($p < 0.003$), but there was no significant linear trend for apneas in REM sleep.

The mean apnea index was 69.9 (range = 49.1–88.8). Although there was some across-night decrease in apnea index, this trend was not significant.

DISCUSSION

The present observations demonstrate for the first time significant lengthening of apneas across the night in non-REM (NREM) sleep, without change in their density. Although we do not have an immediate explanation for this finding, we would like to suggest that the progressive lengthening of the apneas resulted from a progressive delay in the arousal response that usually terminates the apneas. According to Phillipson and Sullivan (1978), apnea termination in NREM sleep is accomplished by a buildup of afferent respiratory input during the apnea (due to hypercapnia, or hypoxia) to levels that are sufficient to initiate respiration and/or produce arousal. There are some indications that sleep fragmentation, which is typical of SAS patients, causes impairment of the arousal response (Karacan et

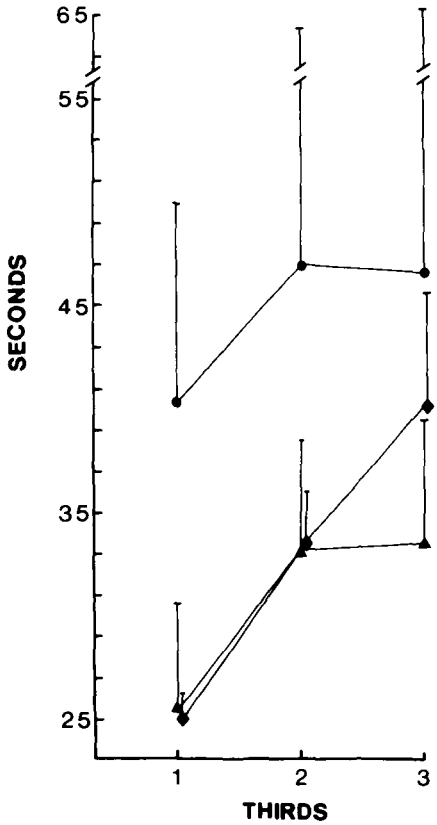

FIG. 1. Length (±S.D.) of apneas in sleep stage 2, and REM sleep, and in all sleep stages by thirds of night. ▲, Sleep stage 2; ●, REM sleep; ◆, mean of all sleep stages.

al., 1978; Johnson et al., 1979; Frederickson and Rechtschaffen, 1978). The accumulated effect of the recurrent sleep interruptions on the arousal response of SAS patient probably is best exemplified by their notable difficulty in waking up in the morning. It should be determined, however, whether the delayed arousal response is caused by a critical number of apneas, or is related to progressive changes in the level of blood gases.

The lack of any significant trend in the length of apnea in REM sleep supports the previous conclusion that apnea termination in REM is mediated by a different mechanism than that in NREM sleep. Phillipson and Sullivan (1978) concluded that since breathing during REM sleep is driven by inputs unrelated to the automatic control system, apneas in REM probably are related to dysfunction of a specific pontine REM sleep-generating mechanism. Therefore, apnea termination is mediated by a similar mechanism. Since, however, hypoxic hyposensitivity is intact during REM sleep, it is possible that apneas long enough to produce hypoxia are terminated by inputs from peripheral chemoreceptors. We also can-

not exclude the possibility that the lack of significant linear trend in REM sleep reflects a "ceiling effect," as apneas in REM were significantly longer than those in NREM sleep.

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