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Sleep and Normal Subjects

Frequency of EEG Arousals from Nocturnal Sleep in Normal Subjects

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Summary: Brief arousals are clinically important and increasingly scored during polysomnography. However, the frequency of arousals during routine polysomnography in the normal population is unknown. We performed overnight polysomnography in the 55 of 59 control subjects from a family practice list who were approached and agreed to undergo polysomnography. Awakenings were scored according to the criteria of Rechtschaffen and Kales and briefer arousals according to three different criteria, including the American Sleep Disorders Association (ASDA) definition. There was a mean of 4 [95% confidence interval (CI), 1–15) Rechtschaffen and Kales awakenings per hour, whereas the ASDA definition gave 21 (95% CI, 7–56) per hour slept. Arousal frequencies increased significantly ($p < 0.001$) with age in our subjects, who ranged from the late teens to early 70s. The high upper limit of the frequency of brief arousals was not altered by exclusion of patients who snored or had witnessed apneas or daytime sleepiness. It is important that those scoring arousals on routine polysomnography recognize that high arousal frequencies occur in the normal population on 1-night polysomnography. **Key Words:** Arousals—Polysomnography—Sleep.

In the sleep apnea/hypopnea syndrome, the degree of cognitive deficit (1) and the severity of sleepiness (2) relate to the frequency of arousals. Nocturnal elevations in blood pressure, both in the sleep apnea/hypopnea syndrome (3) and the periodic limb movement disorder (4), also relate to arousals. The upper airways resistance syndrome is defined in terms of recurrent arousal associated with increased respiratory effort (5). Thus, arousals are increasingly being scored as part of routine assessment of clinical sleep studies.

The frequency of arousals during an overnight sleep study in the normal population needs to be known to allow adequate interpretation of sleep study results. Previous studies have examined the frequency of brief awakenings in normal subjects (6) but have not looked at the frequency of briefer arousals in the normal population on the first night in a sleep laboratory—the situation found in clinical practice.

We have, therefore, determined the frequency of arousal in normal subjects during a 1-night sleep study in our laboratory. Arousal may be determined by many criteria, including electroencephalographic (EEG), cardiovascular or respiratory. We have chosen to investigate EEG criteria because these are currently the most widely used in sleep laboratories. We have examined the criteria of Rechtschaffen and Kales (7) for classical awakenings, along with three different definitions of briefer arousals. The first is the American Sleep Disorders Association (ASDA) definition (8), based on a 3-second change in EEG. The second is the ASDA definition, modified so that briefer (1.5-second) EEG changes constitute an arousal. The third is a definition that we have previously derived and validated against deficits in cognitive function (1).

METHODS

Normal subjects living within 5 miles of our sleep laboratory were recruited from a general practitioner's register. These subjects were chosen as age-, sex-, height- and weight-matched controls for another study (9). Each was approached by us and asked to participate in this study. We approached 59 subjects, of whom 55 agreed to participate. None of the subjects had a previously diagnosed sleep disorder. All were invited for a single night polysomnography in our sleep laboratory.

Polysomnography used our standard procedures (10), including recording EEG, electrooculogram, submental electromyogram (EMG) and anterior tibial EMG. In addition, airflow at the mouth and nostrils was measured by thermocouples, thoracoabdominal move-

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TABLE 1. *Median and 95% confidence interval (CI) of sleep variables in all 55 subjects*

Sleep parameter	Median	95% CI
Time in bed (minutes)	428	377–457
Time awake (minutes)	46	9–250
NREM[a] stage 1 (minutes)	17	5–53
NREM stage 2 (minutes)	165	53–255
NREM stage 3 (minutes)	16	2–39
NREM stage 4 (minutes)	70	5–142
REM (minutes)	67	2–113
Movement time (minutes)	0	0–24
Sleep period time (minutes)	409	340–455
Total sleep time (minutes)	356	103–423
REM latency (minutes)	113	53–310
Sleep efficiency (%)	84	23–95

[a] NREM = non-rapid eye movement; REM = rapid eye movement.

TABLE 2. *Median (95% confidence interval) arousals per hour in different subject groups using different arousal definitions*

Definition	Arousals per hour: All subjects (55)[a]	<60 years old (47)	Asymptomatic (31)	Total sleep time >4 hours
R&K[b]	4[c] (1–15)	4 (1–12)	4 (1–10)	4 (1–8)
ASDA 3 sec	21[c] (7–56)	16 (6–33)	21 (6–63)	19 (6–58)
ASDA 1.5 sec	26[c] (5–67)	24 (6–42)	26 (3–75)	24 (4–67)
Cheshire	14[c] (3–55)	10 (5–30)	14 (2–67)	13 (3–58)

[a] The number in parentheses in this row is the number of subjects.
[b] R&K = Rechtschaffen and Kales (7), and ASDA = American Sleep Disorders Association (8); Cheshire indicates criteria defined by Cheshire et al. (1).
[c] Comparisons show significant differences between all definitions ($p < 0.0001$).

ment by inductance plethysmogram and ear oxygen saturation by an Ohmeda Biox 3700 oximeter. All the data were recorded in a 16-channel polygraph (Specialised Laboratory Equipment) at 15 mm/second. Sleep and respiratory event scoring was done manually, per standard criteria, with a 20-second epoch length (7). From this scoring, an awakening was defined as follows:

Rechtschaffen and Kales (7) definition

Contiguous epochs scored awake with less than 10 seconds intervening sleep were counted as one awakening. Each noncontiguous epoch scored awake was counted as one awakening. Awakenings could be scored during an epoch of recording scored awake by the Rechtschaffen and Kales criteria. Awakenings were not scored on the basis of submental EMG changes alone. Artifacts including those by pen blocking, K complexes or delta waves were not scored as awakenings unless accompanied by a contiguous EEG frequency shift. Nonconcurrent but contiguous EEG and EMG changes individually less but together more than 10 seconds' duration were not scored as awakenings. Last, transitions from one sleep stage to another alone without an intervening defined arousal were not scored as awakenings.

Arousal scorings were done on each sleep record by the same observer using three different definitions. Each definition required the subject to be asleep for at least 10 continuous seconds before an EEG arousal could be scored.

ASDA 3-second definition

Any shift in the EEG frequency to alpha or theta for at least 3 seconds irrespective of any change in submental EMG during nonrapid eye movement (NREM) sleep but accompanied by a concurrent 3-second increase in submental EMG amplitude during rapid eye movement (REM) sleep (8) was scored as an awakening by the ASDA 3-second definition.

ASDA 1.5-second definition

Any shift in the EEG frequency to alpha or theta for at least 1.5 seconds, irrespective of any change in submental EMG during NREM sleep, but always accompanied by a 1.5-second increase in submental EMG amplitude during REM sleep was scored as an awakening by the 1.5-second ASDA definition.

Cheshire definition

Any change in the EEG frequency to alpha or theta for at least 1.5 seconds, associated with a rise in submental EMG, however brief (1), was scored as an awakening by the Cheshire definition.

Statistical analysis

Arousal indices, defined as total number of arousals per hour slept, were calculated for each definition used. Data was analyzed using the SPSS-PC program and arousal frequencies compared between definitions by repeated measures analysis of variance with subsequent paired t testing. Local Ethics Committee approval was obtained for the study.

RESULTS

A total of 55 subjects (27 males) were recruited for the study. They had a mean age of 37 [95% confidence interval (CI) 20–70 years] and a mean body mass index of 23 (95% CI 20–32 kg/m^2). The classical Rechtschaf-

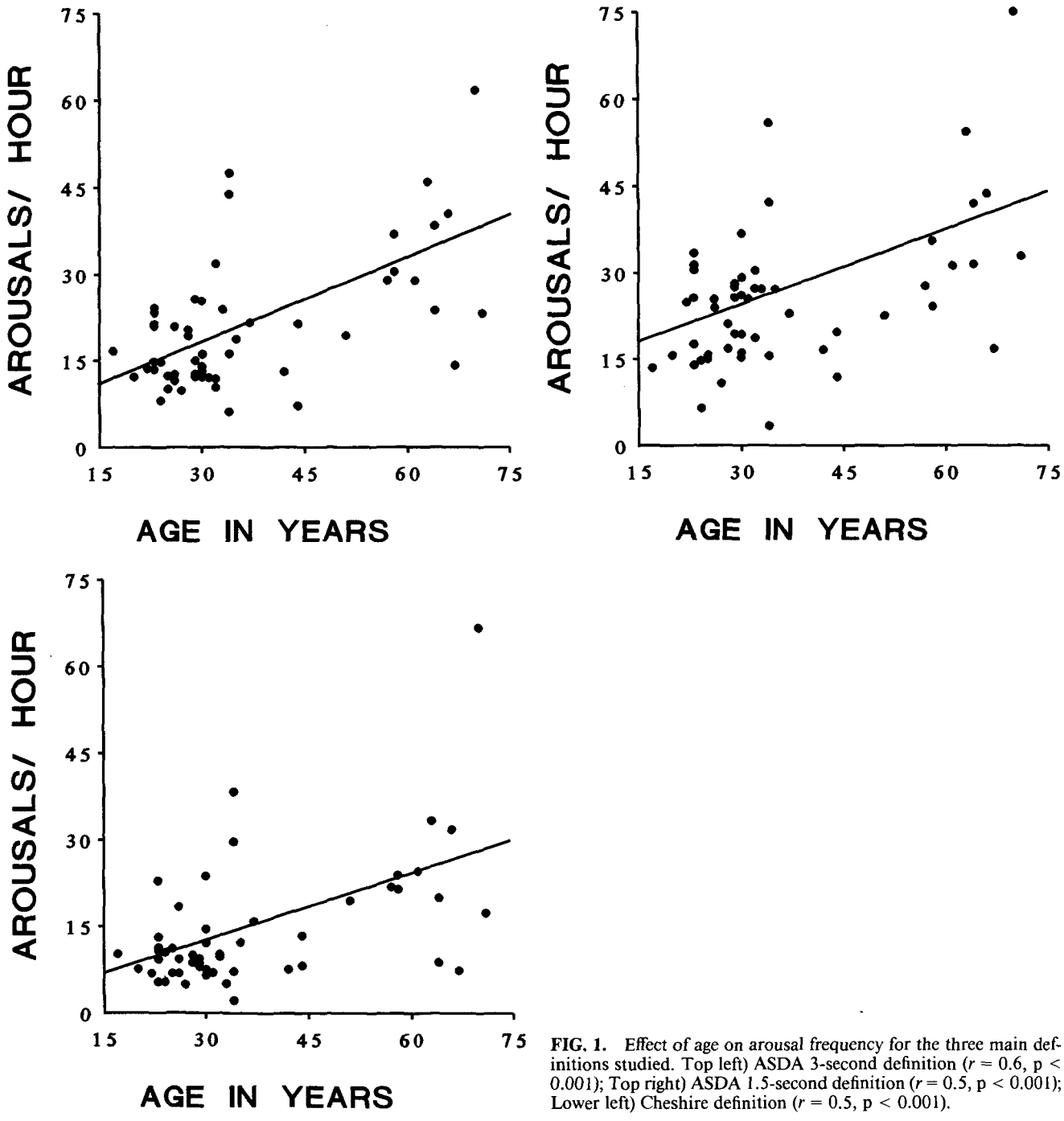

FIG. 1. Effect of age on arousal frequency for the three main definitions studied. Top left) ASDA 3-second definition ($r = 0.6$, $p < 0.001$); Top right) ASDA 1.5-second definition ($r = 0.5$, $p < 0.001$); Lower left) Cheshire definition ($r = 0.5$, $p < 0.001$).

fen and Kales (7) sleep quality data are shown in Table 1.

The Rechtschaffen and Kales (7) definition of awakenings gave a mean of 4 (95% CI, 1–15 per hour). Using the ASDA 3-second definition of arousal gave a mean of 21 (95% CI, 7–56) arousals per hour, and the ASDA 1.5 second arousal definition gave a mean of 26 (95% CI, 5–67) arousals per hour. The in-house Cheshire definition gave a mean of 14 (95% CI, 3–55) arousals per hour. The frequency of arousals was not different between the sexes but did increase with age irrespective of the definition of arousal.

Ten of the 55 subjects reported snoring, 16 reported at least occasional daytime sleepiness and 2 had witnessed apneas. A total of 24 of the 55 subjects had snoring, daytime sleepiness or witnessed apneas. Exclusion of these 24 made no numerical difference to the mean arousal frequency for any of the three definitions and increased the 95% CIs in each case (Table 2). Six of the subjects had total sleep times of <4 hours.

Exclusion of these six again made no appreciable difference to the arousal frequencies (Table 2).

Comparison of the frequency of arousal/awakening using the different definitions showed that the results obtained by all four definitions were highly significantly ($p < 0.0001$) different from each other (Fig. 1).

DISCUSSION

This study shows that in a random sample of subjects from the normal population, arousal frequencies during 1-night polysomnography are high. The frequency of arousal increases with age but in this study population was otherwise not related to sex or minor sleep related symptoms.

This study does not address the frequency of arousals in the normal population sleeping in an unmonitored fashion. We deliberately did not acclimatize our subjects to sleeping in a monitored situation because we wished to provide comparative data with routine overnight polysomnography. The high arousal frequencies that we have observed with relatively noninvasive polysomnography indicate that recurrent arousals during routine polysomnography may occur in the absence of a major sleep-related illness and that they must be interpreted with caution.

This study used three different definitions to score arousals from sleep. Although inclusion of the submental EMG increase as a mandatory criterion in association with EEG changes in the Cheshire definition roughly halves the number of arousals, it was not our primary intention to compare the results obtained and advocate one definition as preferential to the other two. Rather, we were interested in gathering normative data on arousals for a group of sleep studies in normal subjects using different definitions, including the 3 seconds proposed by the ASDA (8).

In each of the three definitions, arousal from REM sleep required the presence of a simultaneous increase in submental EMG amplitude. This is because spontaneous and isolated bursts of alpha or theta activity during REM sleep are common events and may not necessarily indicate a physiological arousal from this sleep state. Likewise, isolated increases in submental EMG activity without any change in EEG frequency may not indicate arousal and have therefore not been considered as such in any of the definitions concerned.

As a separate definition, we did attempt to count the EEG return to alpha or theta activity of less than 1.5 seconds' duration as an individual arousal, but such an attempt was plagued by methodological difficulties. This was because it proved very difficult to distinguish such small events from sleep spindles. We also attempted to identify any EEG changes such as K complexes or quickening of electrical activity at apnea/hypopnea termination but failed to consistently identify any such EEG marker events in all sleep stages and in most if not all the subjects.

Correlational studies of arousal scoring with respiratory disturbance, with nonrespiratory arousal stimuli and with resulting morbidity are needed to establish the optimum definition of an EEG arousal. The Cheshire definition used in this study does correlate with the degree of cognitive defect but not significantly with the magnitude of daytime sleepiness in patients with the sleep apnea/hypopnea syndrome (1). In contrast to this latter observation, Roehrs et al. (2) found a significant correlation, in a much larger study, between respiratory arousal frequency and multiple sleep latency test (MSLT) scores, although the correlation obtained only explained 13% of the observed variance in MSLT. There is thus a need for further study of the correlation between the morbidity caused by sleep fragmentation and the extent of arousal required to produce morbidity.

Recent studies modeling the sleep fragmentation of sleep apnea in normal subjects are beginning to address this issue (11). It is likely that clinically significant arousals may occur in the absence of a visible change in EEG (2) and that the optimal definition of arousal may be either derived by computer from the EEG or may relate to respiratory or cardiovascular changes.

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