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Night-to-Night Variability in Sleep Apnea and Sleep-Related Periodic Leg Movements in the Elderly

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Summary: The amount of night-to-night variability in sleep apnea (SA) and sleep-related periodic leg movements (PLMs) is largely unknown but, despite this, clinical decisions are based on single-night studies in many clinical sleep laboratories. We examined variability in SA and PLMs over three nights in 46 community-resident seniors. No evidence was found for either a first-night effect or a directional trend across nights in either the Respiratory Disturbance Index (RDI) or the Movement Index (MI), despite a prominent first-night effect on pattern of sleep. Duration of apneas/hypopneas and degree of associated heart rate change and oxygen desaturation in subjects with SA and intermovement interval in subjects with PLMs also failed to show systematic change across nights. However, if a cut-off score of 5/h for RDI and MI was used, the classification recorded on the first night did differ from the classification given on at least one of the other nights in 43% of the subjects. The magnitude of fluctuation in RDI or MI from night to night was large enough in some subjects that, in a clinical situation, decisions based on one night would have been entirely different had the subject been studied on a different night. Night-to-night variability in RDI and MI within subjects also was associated with significant alterations in the sleep pattern. We conclude that caution should be taken in drawing conclusions from single-night studies, especially in individuals with relatively mild forms of SA and PLMs where nightly variations could easily place them above or below an arbitrary cut-off score. **Key Words:** Sleep apnea—Sleep-related periodic leg movements—Nightly variability—Elderly.

The first night of polysomnography is commonly viewed as an adaptation night when research findings are reported because of a well known "first-night effect" on sleep pattern in the sleep laboratory (1–3). In contrast, clinical decisions are based on first (single)-night studies in many clinical sleep laboratories. Since the extent of night-to-night variability in common sleep disorders, such as sleep apnea (SA) and sleep-related periodic leg movements (PLMs), is largely unknown, this discrepancy raises important questions about (a) whether sleep disorders also show a first-night effect and (b) the compatibility of inferences drawn from single- versus multiple-night studies.

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The small number of studies that have addressed night-to-night variability in SA have arrived at different conclusions. Bliwise et al. (4) reported a small (<2/h) but significant increase in the Respiratory Disturbance Index (RDI) from the first to the second study night in healthy subjects. In male patients, Wittig et al. (5) found that the greatest variability occurs in milder cases. In a study of patients with snoring or excessive daytime sleepiness, Kramer and Silva (6) concluded that 15% would have been diagnosed differently the second versus the first study night. In contrast, Lee and Giblin (7) concluded that a one-night study appeared to be a reliable diagnostic protocol to rule out SA in healthy men, and Ancoli-Israel et al. (8) found a very high degree of night-to-night consistency in the Apnea Index using portable recordings in a mixed sample of patients and nonpatients. It is likely that differences in subject characteristics (e.g., patient versus healthy samples) and differing bases for assessing and interpreting variability contribute to the aforementioned lack of consensus. No in-laboratory studies of variability in PLMs have been reported. The only published study (8) reported substantially greater variability in PLMs than SA, based on a comparison of portable recordings performed at home and in the laboratory. Clearly, in-depth investigations are needed to clarify not only the amount but also the significance of variability in SA and PLMs in both symptomatic and asymptomatic individuals with disorders of varying severity.

The high incidence of SA and PLMs reported recently in samples of the elderly population, including groups of asymptomatic individuals (9–18), has led to a high level of current interest in these particular disorders in older populations. Based on three consecutive nights of polysomnography, we investigated a first-night effect and night-to-night variability in SA and PLMs, and related sleep disturbance, in 46 relatively healthy, community-resident seniors recruited independent of whether or not they had any sleep-wake complaints.

METHODS

Subjects studied were 30 women and 16 men, 60–95 years of age [mean age, 68.7 ± 6.7 (SD) years], recruited from senior citizen centers in Orange County, California, without reference to sleep-wake complaints. The subjects were the first 46 volunteers for a 5-year, longitudinal study of aging that included potential participation in the Foster Grandparent (FGP) Program at Fairview State Hospital in Orange County, California. All subjects met qualifications for the FGP program (as set forth in Section 625 of the Economic Opportunity Act of 1964), which specify that persons be at least 60 years old, have a total income at or below the national poverty level, and be "mentally and physically able" to serve as FGPs. The latter restriction was minimal and excluded subjects only if they had severe conditions, such as acute myocardial infarction. A detailed description of the subjects' health and medications has been reported elsewhere (19). Only six subjects reported any use of medication taken for sleep that, as specified by the longitudinal study, they were not instructed to discontinue. Sixty-five percent of the subjects studied were female. This high percentage simply reflects the fact that 73% of individuals in the same county living below poverty level income are female (according to 1980 census data, Orange County, California, U.S.A.).

A sleep history was obtained for each subject by interview, followed by three consecutive nights of polysomnography, including EEG (C3/A2), bilateral EOGs, chin EMG, bilateral anterior tibialis EMGs, combined oronasal airflow (thermister), and

chest and abdominal wall excursions (strain gauges). Ear oximetry (Biox III) recordings were limited to 33 subjects for one to three nights (because of limited availability), with priority given to subjects with a history of snoring. Sleep stages were scored according to accepted criteria for young adults (20). Epochs of REM sleep interrupted by ≤15 min were considered the same REM period. One Clinical Polysomnographer scored all polysomnograms for sleep stages, apneas/hypopneas, and PLMs to eliminate the problem of interscorer reliability.

Apneas were scored, as is customary, on the basis of absence of airflow lasting ≥10 s. No accepted criteria exist for the scoring of hypopneas. We scored hypopneas on the basis of decreased amplitude airflow lasting ≥10 s, with cortical arousal (i.e., burst of K-complexes and/or alpha or beta activity) terminating the event. We did not apply a specific amplitude criterion to airflow, as some researchers have done, for two reasons: thermister sensitivity varies with placement, which can vary during the night; and, in our experience, otherwise definitive hypopneas (i.e., episodes of visibly decreased airflow associated with oxygen desaturation and terminated by arousal) can be excluded by imposing an arbitrary amplitude criterion. Hypopneas and apneas were added to determine the RDI, i.e., the average number of hypopneas/apneas per hour of sleep.

The PLMs were scored on the basis of rhythmic trains of four or more bursts of activity on either or both leg EMG channels, each lasting 0.5–5 s, and separated by at least 5 and up to 120 s. Movements separated by >120 s established separate bouts. Total number of PLMs were counted to determine the Movement Index (MI), i.e., the average number of PLMs per hour of sleep.

Since the frequency distributions of raw scores for both RDI and MI were highly skewed (Fig. 1), natural logarithm transformations (of raw scores adjusted by +1 to avoid zero values) were used for all parametric statistical tests. The same transformations were applied to other variables with skewness values ≥2.0.

RESULTS

First night effect on sleep pattern

Sleep on night 1 differed in many respects from nights 2 and 3, whereas sleep patterns were similar on the latter two nights (Table 1). Sleep improved on nights 2 and/or 3 in terms of greater total sleep time, shorter sleep latency, less waking after sleep onset,

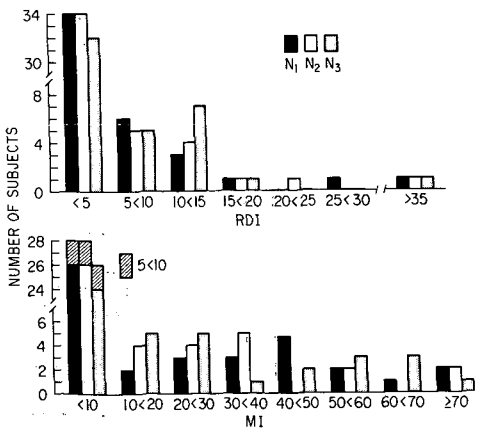

FIG. 1. Frequency histogram of raw scores for RDI (top) and MI (bottom) on study nights 1, 2, and 3.

TABLE 1. *Descriptors of nocturnal sleep*

	Night 1	$\bar{X}$ Nights 2 and 3
Total bed time (min)	405.6	416.0
Total sleep time (TST) (min)	276.6	313.5[a,b]
Sleep latency (min to Stage 2)	26.7	19.9[a,b]
Waking after sleep onset (min)	88.4	70.3[c]
Sleep efficiency index	0.68	0.75[a,b]
No. stage changes	104.6	115.8[b,d]
No. stage changes/TST	0.39	0.38
No. awakenings >1 min	10.6	9.9
% of TST		
Stage 1	23.5	20.5
Stage 2	55.3	54.4
Stage 3	1.0	1.4
Stage 4	0.2	0.3
Stage REM	19.6	22.9[a,b]
REM Latency (min)		
With waking	99.5	71.7[a,b]
Without waking	77.2	62.6[b]
No. REM periods	2.9	3.3[b]

Table values reflect means of 46 subjects. Newman-Keuls procedure was applied for descriptors exhibiting significant trends across the three study nights (one-way ANOVA, $p = 0.042$–<0.0001). For Newman-Keuls posttest: [a]Night 1 vs. Night 2, $p < 0.01$, [b]Night 1 vs. Night 3, $p < 0.01$, [c]Night 1 vs. Night 3, $p < 0.05$, [d]Night 1 vs. Night 2, $p < 0.05$.

better sleep efficiency, more REM sleep, shorter REM latency, and a greater number of REM periods. The number of stage changes was higher on both nights 2 and 3, but normalization for total sleep time (i.e., ratio of number of stage changes to total sleep time) eliminated night-to-night differences. Nights 2 and 3 did not differ significantly on any sleep descriptor.

Night-to-night variability in SA and PLMs

Frequency histograms for RDI and MI on each night are presented in Fig. 1. Pairwise comparisons of the nightly distributions (i.e., night 1 vs. 2, 2 vs. 3, and 1 vs. 3) failed to reveal significant night-to-night differences in the shapes of the distributions for either RDI or MI (Kolmogorov-Smirnov tests, $p > 0.05$). All subjects had one or more apneas/hypopneas on at least one night, whereas 18 subjects failed to exhibit PLMs on any night. For all 46 subjects, the mean RDI across all three nights was 4.8 ± 7.2 (SD)/h, with a range of 0.2–42.0/h across subjects. The mean MI across three nights for all 46 subjects was 18.3 ± 29.8/h, ranging up to 164.3/h in individual subjects. Of those 28 subjects with PLMs on at least one night, mean MI across three nights was 30.1 ± 35.2/h.

Means and ranges of scores for RDI ($n = 46$) and MI ($n = 28$) for affected subjects on individual nights are presented in Table 2. A one-way analysis of variance (ANOVA) and F_{max} test of homogeneity of variances indicated that neither mean levels nor variances in RDI and MI showed systematic trends across nights (Table 2). We also looked for evidence that values for RDI and MI obtained on nights 2 and 3 might be more representative than those obtained on night 1 by comparing strengths of correlations of transformed scores (see Methods section) for consecutive nights. Although correlations were higher on nights 2 vs. 3 than 1 vs. 2 for both RDI (night 2 vs. 3, Pearson $r = 0.76$; night 1 vs. 2, $r = 0.70$; $n = 46$) and MI (night 2 vs. 3, $r = 0.78$; night 1 vs. 2, $r = 0.59$;

TABLE 2. *Night-to-night variability in RDI and MI*

	RDI (/h)	MI[a] (/h)
Night 1	4.7 ± 7.2 (0–35.4)	32.0 ± 34.8 (0–141.2)
Night 2	4.3 ± 7.4 (0.1–40.3)	26.6 ± 31.1 (0–144.8)
Night 3	5.3 ± 8.3 (0–50.3)	31.6 ± 40.1 (0–207.3)
All nights	4.8 ± 7.6 (0.2–42.0)	30.1 ± 35.2 (0.4–164.3)

Table entries reflect group means and standard deviations. Ranges in scores across individual subjects are in parentheses. No significant trends across nights (one-way ANOVA) in RDI ($F = 0.40$, $p = 0.67$) or MI ($F = 0.37$, $p = 0.69$) were found using transformed scores (see Methods section). Variances in RDI and MI also failed to change systematically across nights ($p > 0.05$, F_{max} test for homogeneity of variances).

[a] Values for MI refer to those 28 subjects with MI >0 on at least one night; RDI >0 for all 46 subjects on at least one night.

n = 28), this was not a significant trend for either index ($p > 0.05$, t test for difference between correlations, ref. 21).

Regression analyses of RDI and MI scores on consecutive pairs of nights can be used to estimate a score for a subsequent night given a single night's score. Ideally, one would like to create a confidence interval that would have a given probability of containing the score on a subsequent night. Such an interval can be created using the formula provided in Draper and Smith (22). This interval was computed for the log scores used in the regression equations that related night 1 to night 2 and night 2 to night 3 for both RDI and MI. These intervals were then converted to the original metric using an exponential transform. The 95% confidence intervals for RDI derived from nights 1 vs. 2 appear in Table 3 and could be used clinically in the interpretation of single-night scores. The confidence intervals derived from the regressions of nights 2 vs. 3 were highly similar. Unfortunately, the computed intervals for MI were too wide to be informative: The confidence interval was greater for MI scores because the standard error of the estimate for MI was greater than for RDI (1.26 vs. 0.69 in log units for nights 1 vs. 2) and the MI regression was based on a smaller sample size (28 subjects for MI,

TABLE 3. *Confidence intervals for RDI*

Obtained RDI (/h)	Predicted RDI (95% confidence interval)
0	0.0–4.7
5	0.1–17.8
10	0.7–27.8
15	1.1–36.7
20	1.5–45.0
25	1.8–52.9
30	2.2–60.4
35	2.5–67.7

Confidence intervals were derived from regression equations based on nights 1 vs. 2 and specify intervals that would contain scores for RDI on a second night 95% of the time, given the single obtained scores listed. The exponential function was applied to transform upper and lower confidence limits to the original units per hour.

46 for RDI). However, the intervals for MI would probably be wide even for a very large sample because of the magnitude of the standard error of the estimate, which reflects substantial night-to-night variability.

Night-to-night variability in RDI and MI can also be described in terms of the commonly used cut-off score of 5/h. Five subjects with an RDI score <5/h on night 1 exceeded this cut-off on nights 2 and/or 3; in two of these cases, RDI on night 2 and/or 3 fell between 10 and 20/h. Similarly, six different subjects with a MI score <5/h on night 1 exceeded this cut-off on nights 2 and/or 3, and in five of these cases, MI fell between 10 and 40/h. Conversely, four subjects with an RDI score ≥5/h and five different subjects with a MI score ≥5/h on night 1 had indices <5/h on nights 2 and/or 3. Thus, based strictly on cut-off scores of 5/h, 20 of 46 subjects (43%) were classified differently on nights 2 and/or 3 compared with their first study night. That the number of subjects classified differently on nights 2 and/or 3 vs. night 1 was similar for those reclassified above (n = 11) and below (n = 9) these cutoffs is consistent with the absence of a significant directional trend across nights in either RDI or MI, as previously shown. When nights 2 and 3 were considered separately, 17 subjects (37%) were classified differently on nights 1 vs. 2, 8 subjects (17%) on nights 2 vs. 3, and 15 subjects (33%) on nights 1 vs. 3.

Ignoring the order of nights, substantial variations in RDI or MI, large enough to affect diagnosis or treatment plan in a clinical setting, were observed in several subjects. For example, one subject with no PLMs on one night had a MI of 37.1/h another night. Another subject with no PLMs on two nights had a MI of 20.4/h on the third night. A third subject with an RDI <5/h on one night had an index of 25.3/h another night.

We also explored night-to-night variability in other commonly reported measures of SA and PLMs. Thirty-one subjects exhibited apneas/hypopneas on all three nights, and each night for these subjects we calculated the mean duration and extreme duration of apneas/hypopneas, the mean and extreme change in heart rate associated with apneas/hypopneas, and the mean and extreme oxygen desaturation. One-way ANOVAs revealed no systematic trends across nights in the mean levels of any of these six variables (Table 4). For each of these same variables, the difference between the two extreme values across the three nights was determined to obtain ranges of each subject.

TABLE 4. *Night-to-night variability in other measures of SA and PLMs*

	Night 1	Night 2	Night 3
Apneas/hypopneas (n = 31)			
Mean duration (s)	22.3	24.2	23.3
Greatest duration (s)	39.7	38.3	40.0
Mean HR change (/min)	8.5	8.0	8.1
Greatest HR change (/min)	16.3	15.8	15.6
Mean O_2 ↓ (%)[a]	4.1	4.9	4.8
Greatest O_2 ↓ (%)[a]	8.1	9.4	9.8
PLMs (n = 21)			
IMI (s)	31.7	31.7	30.6

HR, Heart rate; O_2 ↓, oxygen desaturation; IMI, intermovement interval.

Table entries reflect group means for subjects exhibiting apneas/hypopneas (n = 31) and PLMs (n = 21) on all three nights. No significant trends across nights were found for any variable (one-way ANOVAs, $p > 0.05$).

[a] n = 11 in ANOVAs for Mean O_2 ↓ and Greatest O_2 ↓ because of limited availability of oximetry. For these variables, *t* tests for nights 1 vs. 2 (n = 16) and 2 vs. 3 (n = 16) for subjects with oximetry on two consecutive nights also revealed nonsignificant differences.

The group mean average in these range scores was 7.4 s for mean duration of apneas/hypopneas, 20.5 s for greatest duration, 5.1/min for mean heart rate change, 9.2/min for greatest heart rate change, 2.6% for mean oxygen desaturation, and 4.7% for greatest oxygen desaturation. The most extreme range scores observed in individual subjects were 20.9 s for mean duration, 65 s for greatest duration, 22.5/min for mean heart rate change, 25.0/min for greatest heart rate change, 5.1% for mean oxygen desaturation, and 9% for greatest oxygen desaturation.

Similarly, for the subgroup of 21 subjects who exhibited PLMs on all three nights, the mean intermovement interval (i.e., the mean interval between PLMs within bouts) was computed nightly for each subject. One-way ANOVA revealed no significant trend across nights (Table 4). The range across nights in mean intermovement interval averaged 7.9 s in this subgroup, and the extreme range for an individual subject was 30.2 s.

Nightly variability in sleep pattern related to SA and PLMs

As reported separately (19), measurable sleep disturbance was recorded across these subjects as a function of SA and PLMs. As RDI or MI increased, the subjects had significantly lower sleep efficiency, more waking after sleep onset, more stage changes, more awakenings >1 min, a higher percentage of Stage 1 sleep, and a lower percentage of Stage 2.

In the present study, we found that the subjects' night-to-night fluctuations in RDI or MI were also associated with measurable changes in their sleep pattern. These night-to-night fluctuations were assessed by running a set of repeated measure ANOVAs using RDI and MI as covariates in the subjects who demonstrated apneas/hypopneas ($n = 46$) or PLMs ($n = 28$) on at least one night. For each analysis, the night of the study was the only factor in the design. The dependent variables were the sleep discriptors listed in Table 1. Each analysis reported both a within-subject and a between-subject slope for each of the two covariates. The within-subject slope addressed the night-to-night fluctuations within individuals, while the between-subject slope reported the relationship across individuals pooled over nights.

Significance tests on the within-subject slopes indicated that each of the covariates was related to multiple dependent variables. Higher RDI values were associated with significantly more stage changes [slope (B) = 9.24, $p = 0.009$], more stage changes per hour of sleep ($B = 0.04$, $p = 0.006$), a greater percentage of Stage 1 sleep ($B = 3.26$, $p = 0.009$) and a lower percentage of Stages 2 ($B = -3.13$, $p = 0.02$) and 3 ($B = -0.12$, $p = 0.04$). Higher MI values were associated with a lower percentage of Stages 3 ($B = -0.14$, $p = 0.003$) and 4 ($B = -0.09$, $p = 0.05$). The fact that more sleep variables were affected by RDI may reflect the greater degrees of freedom associated with RDI than MI.

DISCUSSION

Our study focused on variability in RDI and MI, since these are the measures most commonly reported in assessments of SA and PLMs. Neither RDI nor MI showed a first-night effect or a systematic change across study nights, despite the presence of a prominent first-night effect on sleep pattern. This means that values for RDI and MI obtained on the first study night are as representative as values obtained on subsequent study nights, a favorable finding for clinical laboratories where practical concerns often dictate single-night studies. However, the magnitude of night-to-night variability ob-

served in both RDI and MI does raise an important question about the reliability of single-night studies. Several subjects exhibited night-to-night fluctuations in RDI and/or MI of sufficient magnitude to affect both the diagnosis and treatment plan in patients. For example, based on a commonly used cut-off score of 5/h for both RDI and MI, 43% of subjects were classified differently on nights 2 or 3, compared with night 1. Ignoring the order of nights, RDI and MI ranged up to 25.3 and 37.1/h, respectively, in subjects with indices <5/h on at least one night. Furthermore, confidence intervals for RDI and MI were established for estimating a second night's score based on a single score, and the width of these intervals revealed substantial night-to-night variability in both indices. For MI, in fact, the intervals were too wide to be informative, reflecting the greater night-to-night variability in MI than in RDI scores.

These findings raise serious concerns about conclusions based on single-night studies and about the judiciousness of applying arbitrary cut-off scores to RDI and MI, as is commonly done. Since there is no directional trend in either RDI or MI across nights, impressions based on single-night studies are equally likely to over- or underestimate severity, as revealed on subsequent study nights. Our findings underscore the need for multiple night studies to accurately assess the severity of SA and PLMs. This is especially true (a) in investigations of the relationship between severity of SA or PLMs and other variables; (b) in samples, such as ours, derived from nonclinical sources, where high rates of relatively mild forms of SA and PLMs might be expected; and (c) in persons with clinical symptomatology characteristic of SA or PLMs, where a first-night study revealed little or no pathology. For example, two of our subjects with a history of restless legs had MI scores <2/h on the first night, but had scores ≥20/h on other nights. Certainly single-night studies would be adequate for most clinical purposes where combined evidence from clinical and laboratory sources demonstrates overwhelmingly that a disorder of clinical proportions is present.

We also examined night-to-night variability in other commonly used measures for describing SA and PLMs. Duration of apneas/hypopneas and degree of associated heart rate change and oxygen desaturation all failed to show a systematic change across study nights. In subjects with PLMs, the intermovement interval also did not vary significantly from night to night. These data provide further evidence that the SA and PLMs recorded on any given study night were as representative as those recorded on other study nights. We also described the magnitude of variability in these same measures as range scores across nights, but since no accepted criteria exist for rating severity of these measures (e.g., for rating observed oxygen desaturation as mild, moderate, or severe), we were unable to appraise these range scores in terms of their possible clinical significance. This dilemma highlights the need for the development of reliable and valid guidelines for assigning severity ratings to all commonly used measures for describing SA and PLMs.

Another important issue raised by our study is the degree to which nightly fluctuations in SA and PLMs affect the individual on a day-to-day basis. Night-to-night fluctuations in RDI and/or MI were associated with measurable changes in sleep pattern, as manifested in frequency of stage changes and relative percentages of non-REM sleep stages. We do not know yet whether these alterations in sleep pattern affect subjective sleep satisfaction or daytime sleepiness on a day-to-day basis. However, we reported elsewhere that neither the mean level in RDI nor MI across the three nights predicted whether or not general sleep-wake complaints were reported by these subjects, and the reverse was also true (19). Given this, it seems unlikely that night-to-night variability within subjects in RDI or MI would affect sleep-wake complaints on a day-to-day basis

either. However, since the relationship between general sleep-wake complaints and subjective satisfaction with sleep on a day-to-day basis has not been established for the elderly, this remains an open question.

In summary, even though no evidence was found for a directional trend across nights in either RDI or MI, the magnitude of night-to-night variability observed in these indices raises important questions about conclusions drawn from single-night studies. This is particularly true for individuals with relatively mild degrees of SA and PLMs, where nightly fluctuations could easily place them above or below an arbitrary cut-off score such as is commonly applied to RDI and MI. Night-to-night variability in SA and especially PLMs has not been studied in depth previously. Further studies will be needed to determine the extent to which our findings can be generalized to other groups of elderly people (e.g., sleep clinic patients) and to younger adults.

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