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Microsleep and sleepiness: a comparison of multiple sleep latency test and scoring of microsleep as a diagnostic test for excessive daytime sleepiness

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Abstract

Study objective: To compare multiple sleep latency test (MSLT) and scoring of microsleep (presence of sleep electroencephalograph between 3 and 15 s in an epoch) as a diagnostic test for excessive daytime sleepiness (EDS).

Design: A retrospective study.

Setting: Sleep center at a tertiary care teaching hospital.

Subjects: Patients referred to a sleep center who had an MSLT and one or more of the following symptoms; tiredness, sleepiness, memory loss, accidents/near accidents and gap driving.

Interventions: Full night polysomnography (PSG) and next day MSLT were performed. Patients were classified as 'microsleep-positive' or 'microsleep-negative' according to presence or absence of microsleep.

Results: Patients ($n = 92$) were divided into three groups according to their MSLT results; group A had an MSLT ≤ 5 min ($n = 38$), group B had an MSLT = 6–10 min ($n = 26$), and group C had an MSLT > 10 min ($n = 28$). The number of patients with symptoms of tiredness and memory loss were statistically higher in group A compared with groups B and C ($P = 0.036$). The number of patients with symptoms of EDS, in groups B and C, was significantly higher in patients with microsleep than without microsleep ($P < 0.05$). By a paired McNemar's test, the better performance of adding microsleep to MSLT (sensitivity 42.9%; specificity 63.6%) to assess EDS was statistically significant ($P = 0.0096$).

Conclusions: Microsleep determination during an MSLT is a more sensitive and specific test for EDS as compared to MSLT alone.

Keywords: Microsleep; Polysomnography; Excessive daytime sleepiness

1. Introduction

Excessive daytime sleepiness (EDS) – excessive sleep or difficulty in maintaining the desired wakefulness [1] – is one of the most common complaints of patients seen at sleep–wake disorders clinics in the US, with a prevalence between 0.5 and 5% in general population [2,3]. EDS is a major cause of morbidity, and even mortality due to its role in industrial and transportation accidents [4], and impaired cognitive and intellectual functioning with serious psychosocial consequences to interpersonal, marital, work and social relationships [4,5].

Tests of sleepiness include; pupillometry, Stanford sleepiness scale (SSS), Epworth sleepiness scale (ESS), brainstem evoked potential studies, performance tests such as the Wilkinson vigilance test, continuous ambulatory monitoring techniques and actigraphy, and the multiple sleep latency test (MSLT) which is the most scientifically validated objective test of EDS [6]. Other tests for assessment of EDS are less sensitive, non-specific, or have not been adequately subjected to scientific evaluation [6]. The MSLT is considered to be a 'gold standard' to measure sleepiness in clinical practice [14]. The technical aspects and normal values of the MSLT have been standardized [7], and test–retest reliability of MSLT has been studied in healthy subjects [8] and in patients with complaint of EDS [9,10]. The MSLT has been shown to differentiate several types of partial and complete sleep deprivation occurring on either an acute or chronic basis. It is shown to be sensitive to sleep fragmentation, time of day and to several types of medications [15].

The measurement of the MSLT consists of a series of four to five nap opportunities spaced at 2-hourly intervals, with termination of each nap after either 20 min of wakefulness or 15 min of sleep. The sleep latency value is recorded as a

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mean of the sleep latencies of all naps, and is generally interpreted as follows: mean latency less than 5 min signifies pathological sleepiness, more than 10 min is considered normal, and between 5 and 10 min is indicative of indeterminate sleepiness [7].

Sleep state on the MSLT is scored if an epoch contains more than 50% of electroencephalograph (EEG)-defined sleep. Less than 50% is scored as wakefulness. Episodes of sleep intrusion called microsleep (between 3 and 15 s) in epochs are ignored. An episode of microsleep spanning two epochs can last almost 30 s, during which the perception of an external stimulus may be impaired. The polysomnography (PSG) suddenly shifts from waking characteristics to sleep, but then returns to wakefulness before the epoch is scored.

Recently, the accuracy of the MSLT has been challenged as it has been suggested that the MSLT is an incomplete measure of sleepiness [11]. There is a suggestion that the MSLT is measuring more than simple sleep tendency. We hypothesize that scoring of microsleep in patients with normal or indeterminate mean latencies increases the diagnostic value of the MSLT.

2. Methods

Patients presenting to the Institute for Sleep–Wake Disorders at the Hackensack University Medical Center between January and December 1997 with complaints of sleepiness were assessed clinically, and then underwent PSG and MSLT. The inclusion criteria in this retrospective study included: age more than 18 years and one or more of the following symptoms: sleepiness, memory loss which in the absence of another etiology was attributed to sleepiness, sleep related accidents/near accidents and memory gaps while driving (gap driving). The exclusion criteria included: (1) patients using continuous or bilevel positive airway pressure (CPAP or BiPAP) therapy; (2) patients with Chronic obstructive pulmonary disease (COPD) and other organ failures; (3) patients on home oxygen; and (4) patients on medications, such as hypnotics and stimulants, which would impair the sleep–wake cycle. The reason for exclusion is the potential for variability in sleep and wake cycle and the impact on sleep continuity and sleep fragmentation.

The patients were asked to fill out a modified Stanford questionnaire prior to evaluation by a physician. A board certified sleep physician[1] conducted an initial intake interview which included questions about (1) falling asleep at inappropriate times and places, (2) among inactive patients, a tiredness assessment based on complaints of exhaustion or fatigue (in the absence of psychological or medical illness as the cause of tiredness), (3) memory loss, (4) accidents/near accidents and driving gaps.

Out of the 92 subjects 17 were women, and 75 were men.

[1] Board Certified Physician is Dr. Ashtyani.

Table 1
Clinical diagnosis of the patients included in the study

Clinical diagnosis	Number of patients
Sleep apnea syndrome (SAS) or IUARS	74
Narcolepsy	1
Primary snoring	1
Periodic limb movement syndrome	8
Alcohol effect on sleep pattern	1
Idiopathic hypersomenlence	2
Cheyne-stokes breathing	1
Normal study	2
Gastroesophageal reflux disease	1
Depression	1

Table 1 lists the clinical diagnosis of the patients included in the study. The clinical diagnoses of sleep apnea syndrome (SAS), narcolepsy, primary snoring, periodic limb movements in sleep (PLMS) and idiopathic hypersomnolence are made by the diagnostic criteria laid out in the international classification of sleep disorders (ICSD) diagnostic and coding manual by American Sleep Disorders Association. Increased upper airway resistance syndrome (IUARS) is diagnosed by (1) the presence of persistent snoring, (2) evidence of increasing inspiratory efforts, including excessive intercostal muscle activity, (3) the presence of arousals which were attributed to snoring and (4) oscillations of oxygen saturation more than 3%, in the absence of other etiologic diagnoses such as overt SAS. The other clinical diagnoses are as per the ICD classification.

2.1. Procedure and measures

Full night polysomnography (PSG) along with next day multiple sleep latency test (MSLT) was performed on 92 patients who met the inclusion criteria. At least 2 weeks before the PSG all sedatives and anti-depressant medications were discontinued and the patients kept sleep logs from which the average of sleep hours was obtained. Average hours of sleep varied from 6 to 9 h (average 7 h), suggesting that there was no sleep deprivation prior to the study.

Two patients had an average sleep time of less than 5 h. One had microsleep in two naps out of four, the other had no microsleep. The majority of patients had an average of 7 h (32 subjects) and 8 h (30 subjects) of sleep per night. Fifteen patients had an average of 6 h, ten patients an average of 9 h, two patients 5–6 h, and one patient 10 h.

No caffeinated or alcoholic beverages were permitted 6 h before bedtime. Sleep was monitored using a standard 14 channel montage which included four EEG channels, two horizontal electrooculography (EOG) channels, submental electromyography (EMG), nasal flow by thermistor, two channels for thoraco-abdominal movements, an electrocardiography (ECG) channel, two channels for right and left leg movements, and an oxygen saturation channel. The PSG was recorded on a Sandman computer system.

Table 2
Demographic data[a]

	Group A (MSLT ≤ 5 min)	Group B (MSLT = 6–l0 min)	Group C (MSLT > l0 min)
Number of patients (*n*)	38	26	23
Age in years;	48.3 ± 2.35	50.7 ± 2.1	47.9 ± 2.1
Mean ± SEM (range)	(16–77)	(31–75)	(17–79)
Sex; male:female	33:5	20:6	22:6
RDI	35.02 ± 3.2	29.7 ± 2.7	23.75 ± 2.3
Mean ± SEM (range)	(2–114)	(2–94)	(1–94)
MSLT	3.2 ± 0.2	7.4 ± 0.6	13.7 ± 1.1
Mean + SEM (range)	(2–5)	(5.4–9)	(11–19)

[a] Abbreviations: MSLI, multiple steep lsency test; SEM, standard error of mean; RDI, respiratory disturbance index; *P*-value <0.04 as compared to group C.

MSLT protocols were adopted from the recommendations made by Association of Sleep Disorders Centers task force on daytime sleepiness [7]. The patients were given four opportunities to sleep at 2 h intervals, starting between 9:30 and 10:00 AM. Each nap was terminated 15 min after the first unequivocal epoch of sleep, or after 20 min if no sleep occurred. Patients remained out of bed between the naps, and were instructed not to sleep. The data was recorded at 10 mm per second, and the duration of each epoch was 30 s.

Two registered PSF technologists, both unaware of the study, scored the PSGs and MSLTs separately. The inter rater variability was less than 5%. A physician board certified in sleep medicine reviewed all the studies. No patient was moved to another group after the review. If there was a conflict, it was resolved by the physician. The sleep stages were scored by the Rechtschaffen and Kales scoring method with 30 s epochs [12]. Sleep latency for each nap of MSLT was measured as the time from the onset of the test (lights out) to the first sleep epoch. Rapid eye movement (REM) latency was measured as the time from the onset of sleep to the first REM period. The mean sleep latency was calculated for the four naps.

Microsleep, an episode of sleep intrusion (3–15 s) occurring within the first 10 min of an epoch prior to sleep onset, would have been scored as wake stage according to the standard criteria. Illustration 1 is a tracing of microsleep.

The patients were classified as 'microsleep-positive' or 'microsleep-negative' according to the presence or absence of microsleep. We did not, however, divide the patients depending on the number of episodes of microsleep per nap. Therefore, this study encompasses qualitative assessment of microsleep and sleepiness and not a quantitative measurement, which would need further study. A single episode of microsleep was ignored. Patients classified as 'microsleep-positive' had two or more episodes of microsleep during the MSLT. Further study is being done to quantitatively assess tiredness according to the number of microsleep episodes.

Participants were divided into three groups based on the individual MSLT scores. Group A had a mean sleep latency ≤5 min, group B had a mean sleep latency >5 and <10 min, and group C had a sleep latency ≥10 min. Calculations were performed using the SPSS statistical software package. Values were considered statistically significant when *P*-values were less than 0.05. A prevalence of 5% for sleepiness in the community [2,3] was used to calculate the positive and negative predictive values.

Illustration 1: an episode of microsleep (ROC, LOC, outer canthus of the right and left eye, respectively; CHIN, electromyography; EKG, electrocardiography).

3. Results

Of the total 92 patients included in the study, group A consisted of 38 patients, group B consisted of 26 patients and group C consisted of 28 patients. Table 2 shows the demographic data of these groups. There was no statistical difference of number, age and sex among the three groups. The mean (SEM) respiratory disturbance index (RDI) of 35.02 ± 3.2 in group A was statistically different from group C ($P < 0.04$), but not from group B. The mean sleep latency of groups A, B, and C were 3.2 ± 0.2, 7.4 ± 0.6, and 13.7 ± 1.1 min, respectively.

Fig. 1 shows the distribution of symptoms in groups A, B, and C. The number of patients with symptoms of sleepiness and memory loss was statistically higher in group A

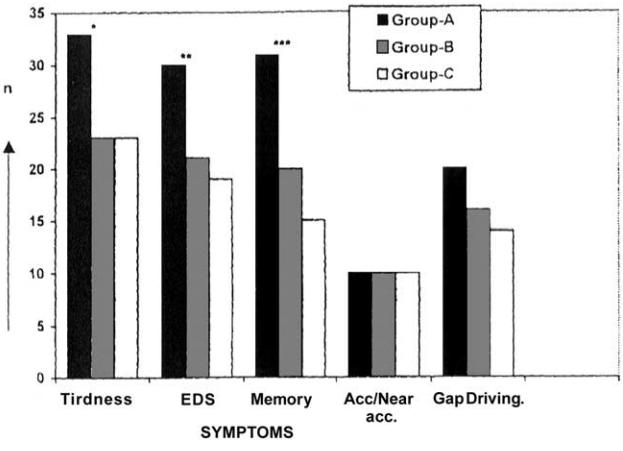

Fig. 1.

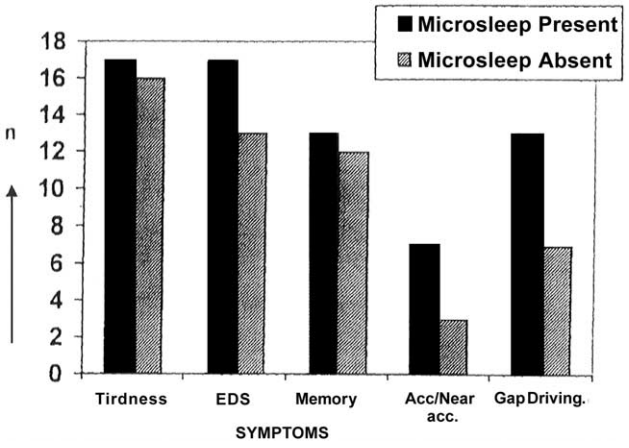

Fig. 2.

compared to groups B, and C ($P = 0.036$). The number of patients with symptoms of tiredness, accidents/near accidents and gap driving (occasions or episodes of driving without explicit memory, which can be attributed to automatic behavior) were not different in the three groups.

In group A (Fig. 2) there was no difference in the number of patients, with or without microsleep, in reference to any symptoms. In groups B, and C the number of patients with symptoms of sleepiness, accidents/near accidents, and gap driving was statistically higher in patients with microsleep than without microsleep. In addition, the number of patients in group C with complaints of tiredness accompanied by occurrences of microsleep was significantly higher than the number of those who did not have microsleep. Microsleep occurred in a higher number of patients with tiredness and memory loss in group B, and patients with memory loss in group C, but it was not statistically significant.

The performance of tests (sensitivity, specificity, positive predictive value and negative predictive value) of MSLT and microsleep for EDS in all patients is shown in Table 3. Of patients included in the study 70 (76%) reported having sleepiness and 22 (24%) did not. In 17 out of 70 (24.3%) patients with complaints of sleepiness the symptoms correlated with MSLT and microsleep results. The complaints of sleepiness in nine (12.8%) patients did not correlate with either test, and in 44 (62.8%) patients the

Table 3
Performance of tests for sleepiness in all patients[a]

Test	Sensitivity (%)	Specificity (%)	Positive predictive value (PPV) (%)	Negative predictive value (NPV) (%)
MSLT	42.9	83.8	78.9	25.9
Presence of microsleep[a]	68.6	81.8	92.3	45.0

[a] The better performance of microsleep was statistically significant by a paired McNemar's test (two-tailed $P = 0.0096$).

Table 4
Performance of test (presence of microsleep) for sleepiness in three groups

Group	Number of patients		Sensitivity (%)	Specificity (%)	Positive predictive value (PPV) (%)	Negative predictive value (NPV) (%)
	EDS	Total				
A	30	38	56.70	75.00	89.50	31.60
B	21	26	71.40	100	100	45.50
C	19	28	84.20	77.80	88.90	70.00

symptoms correlated with one but not the other. Of these 44 patients, 31(70.5%) had symptoms correlating with microsleep and 13 (29.5%) had symptoms correlating with MSLT, in a ratio of 2.3 in favor of microsleep. The better performance of microsleep (sensitivity of 68.6%) as compared to MSLT (sensitivity of 42.9%), with a ratio of 31:13, was statistically significant by a paired McNemar's test ($P = 0.0096$).

In 12 (54.5%) of the 22 patients who did not complain of sleepiness, there was agreement between microsleep, MSLT and complaints. In two (9.1%) patients neither microsleep nor MSLT correlated with complaints. In six (27.3%) patients microsleep did not correlate with MSLT or complaints. In two (9.1%) patients MSLT did not correlate with microsleep or complaints. The specificity for better performance of microsleep is 81.8%, as compared to MSLT, which is 63.6%.

Table 4 shows performance of tests (sensitivity, specificity, positive predictive value and negative predictive value) for EDS in subcategories (according to presence or absence of microsleep) in groups A, B, and C. The better performance of microsleep was statistically significant ($P < 0.05$) in groups B, and C.

4. Discussion

This study shows the sensitivity and specificity of MSLT to be 42.9 and 63.6%, respectively in patients complaining of sleepiness. Sensitivity and specificity improves to 68.6 and 81.8%, respectively by scoring microsleep ($P = 0.0096$). Furthermore, in the subgroup of patients with intermediate and 'normal' MSLTs (groups B, and C), the sensitivity (71.4% in group B, 84.2% in group C) and specificity (100% in group B, 77.8% in group C) is significantly better with scoring of microsleep.

A significantly higher number of patients in groups B, and C presenting with symptoms of tiredness, sleepiness, accidents/near accidents and gap driving had the presence of microsleep. This might suggest the presence of microsleep as a predictor of these symptoms. In group A (sleep latency ≤ 5), there was no difference among patients, with or without microsleep, in any of the symptoms. Patients in this

category are already so sleepy that scoring of microsleep is probably not of any additional help.

In our patient population, among those with microsleep, a higher number in all three groups had memory loss, although this did not reach the statistically significant level. The number of patients with a complaint of memory loss was significantly higher in group A, as compared to groups B, and C, suggesting that sleepiness may lead to memory loss. This finding has also been reported previously by other authors [13].

The standard definition of sleep onset on MSLT is based on scoring a full sleep epoch of more than 15 s. However, in normal individuals one does not expect to find short sleep periods of less than 15 s (microsleep). Of further note is the fact that the majority of the patients included in the study were subsequently diagnosed with SAS or IUARS. Microsleep was scored as mentioned before: sleep EEG between 3 and 15 s in an epoch. In SAS patients, these episodes represent microsleep rather than multiple arousals at sleep onset, as all apneas would be longer than 3 s and should not impinge on the criterion to score microsleep.

Several factors affect an individual MSLT score. Sleep propensity may be modulated by internal and external activating factors. Not only the sleep tendency, but also the extraneous factors such as pain, anxiety, motivation or exposure to a hospital environment can influence the results of MSLT [15]. As per Kronholm et al. [16], psychological distress is an indicator of chronic inner psychophysiological arousal, which can prolong sleep latency in the MSLT. It might be that MSLT measures a balance of factors, such as sleep tendency and the level of competing arousal, which impact the score. Among patients with subjective complaints of sleepiness, other factors affecting the state of arousal and causing failure to achieve sleep might prolong the MSLT latency. In such instances microsleep will aid in identifying patients with complaints of sleepiness and normal sleep latency.

Brief transitions from wakefulness to sleep (microsleep) and back to wakefulness, rupture the continuity of cognitive function. The importance of an accurate and sensitive measure of sleepiness is implied by the need for treatment [17].

While we acknowledge that more needs to be done to define and standardize identifying criteria, the presence of microsleep can be used to help identify patients with EDS. MSLT, which alone might underestimate daytime sleepiness, may be a more sensitive and specific test of EDS when combined with microsleep. Although its presence has not been studied in normal population, we conclude that, if combined with MSLT, microsleep may be helpful in determining objective evidence of EDS in patients with normal or near normal MSLT.

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