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Original article

Prediction of the final MSLT result from the results of the first three naps

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Abstract

Objectives: To determine if the mean sleep latency (mSL) and the presence of significant sleep onset rapid eye movement periods (SOREMPs) can be predicted from the results of the first three naps in selected patients undergoing multiple sleep latency test (MSLT).**Methods**: Retrospective analysis of a number of MSLTs to identify the tests in which the mSL category and the presence of ≥2 naps with SOREMPS can be accurately predicted from the sleep latencies (SLs) of and SOREMPs in the first three naps.**Results**: The study included 588 consecutive MSLTs performed on 552 patients during a 3-year period. (1) The mSL was normal (≥10 min) for all MSLTs ($n = 90$, 15%) if either (a) the SL was normal in each of the first three naps, or (b) SL was 20 min for any two of the first three naps. (2) The mSL was low (<5 min) or borderline (≥5 and <10 min) for 99% MSLTs with SL in the low or borderline categories, respectively. (3) The accuracy of predicting ≥2 naps with SOREMPs was 100% (normal SL), 96% (borderline SL), and 89% (low SL). (4) The mSL category (normal or low) and the presence of ≥2 naps with SOREMPs were predicted with 100% accuracy in 23% of all MSLTs.**Conclusions**: The category of mSL can be predicted with >99% accuracy, if SL is normal, borderline, or low in each of the first three naps, or if the patient does not sleep in any two of the first three naps. MSLT can probably be shortened to three naps in up to 23% to reduce time, labor, discomfort, and cost of the test.

Keywords: Multiple sleep latency test; Sleep latency; Methodology; Excessive daytime sleepiness; Sleep onset rapid eye movement period; Narcolepsy

1. Introduction

Excessive daytime somnolence (EDS) is one of the most common symptoms of patients presenting to a sleep disorders center. The multiple sleep latency test (MSLT) is the most commonly used objective test and is considered the 'gold standard' for assessment of EDS. It is also used to diagnose narcolepsy, in which a sleep onset rapid eye movement period (SOREMP), defined as the presence of an epoch of REM sleep during the first 15 min of sleep, occurs in two or more naps out of four or five naps of MSLT.

The standard MSLT has been described by the association of sleep disorders centers task force on daytime sleepiness and in the report from the American Sleep Disorders Association on the clinical use of the test [1,2]. Currently a MSLT requires close monitoring and administration of the test by a sleep laboratory technologist for 6.5–8.5 h. Based on previous studies, the test–retest reliability of a four-nap MSLT over a 4–14-month interval is excellent (correlation coefficient 0.97). However, decreasing the number of naps to three or two reduces the correlation coefficient for mean sleep latency (mSL) to 0.85 and 0.65, respectively [3]. Hence, an MSLT with two or three naps is not considered an acceptable alternative to the standard MSLT in every patient.

Our hypothesis was that in selected patients undergoing MSLT, the mSL could be accurately predicted from the results of the first three naps. The purpose of this study was to identify the groups of patients in whom mSL can be accurately predicted from the sleep latency and presence of SOREMPs in the first three naps, as it may be possible to shorten the MSLT in these patients. To our knowledge, there has been no such study reported in the literature.

2. Methods

We reviewed the medical records of all patients who underwent MSLT at our sleep disorders center for evaluation of EDS during the 3-year study period. The MSLT was performed on the day following an all-night polysomnogra-

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phy to provide accurate documentation of the preceding night's sleep. Four- or five-nap tests of up to 35 min each were conducted at 2-h intervals over the day. The minimum recording montage included a central (C3 or C4) and occipital (O1, O2, or OZ) referential electroencephalogram, two electrooculograms (right and left outer canthi), and a submental myogram (chin), as recommended in the established guidelines [1,2,4]. If a patient remained awake throughout a nap, the SL was 20 min. When there was one SOREMP in the first four naps, the patient underwent a fifth nap.

An MSLT was excluded if it did not meet any of the above-described criteria or the standard recommendations for MSLT [1,2], e.g. a patient drank a caffeine-containing beverage, or took an anxiolytic, sedative or hypnotic medication just before or during the test, or did not complete the required number of naps for any reason.

We grouped the MSLTs based on our hypotheses for predicting the final MSLT results. The SLs and number of naps with SOREMPs in the first three naps were used to predict the overall mSL for the four- or five-nap sequence. The SL and mSL categories were defined as normal ($\geq$10 min), borderline ($\geq$5 and $<$10 min), low ($<$5 min), and abnormal ($<$10 min).

Our three hypotheses were the following: (1) if all three sleep latencies are in the same category, then mSL is also in that category; (2) if a patient does not fall asleep in at least two naps, then mSL is normal; and (3) the presence of a SOREMP in at least two naps increases the accuracy of predicting mSL in tests with low or abnormal SL in the first three naps. Mean SL for the first three naps was compared with that of all four or five naps using Pearson's correlation coefficient and a two-tailed paired student's *t*-test.

Accuracy of predicting the presence of $\geq$2 naps with SOREMPs in all four or five naps, based on the first three naps, was also calculated for the same MSLT groups. Finally, groups of MSLTs were combined to define those in which mSL category and the presence of significant ($\geq$2) SOREMPs would be accurately predicted from the first three naps.

The final clinical diagnoses of the patients who underwent these MSLTs were not analyzed. Many of these diagnoses were dependent on symptoms, signs, and clinical follow-up after therapeutic trials, in addition to the results of the MSLTs.

3. Results

A total of 645 MSLTs were performed during the 3-year study period. Fifty-seven (8.8%) MSLTs that did not satisfy the criteria described above were excluded from the study. The remaining 588 MSLTs performed on 552 patients were analyzed; 36 MSLTs were repeat studies. The mean age $\pm$ SD of the patients was 45.1 $\pm$ 0.6 years and the mean body mass index was 31.6 $\pm$ 14.0 kg/m^2. There were 328 (59.4%) men and 224 (40.6%) women. The most common clinical diagnoses included obstructive sleep apnea, upper airway resistance syndrome, narcolepsy, idiopathic hypersomnolence, and periodic limb movement syndrome.

3.1. Analysis of sleep latency and presence of SOREMPs

mSL was low in 212 (36%), borderline in 197 (34%), and normal in 179 (30%) MSLTs. In 56 (9.5%) MSLTs, a fifth nap was required to evaluate for the presence of a second SOREMP. There was at least one nap with SOREMP in 152 (26%) and $\geq$2 SOREMPS in 103 (18%) MSLTs. There was no SOREMP in the remaining 436 (74%) tests. The mSL ($\pm$SD) of all four- or five-nap MSLTs was 7.9 $\pm$ 5.0 min, while the median SL was 6.8 min.

3.2. MSLT groups and hypotheses for prediction of mSL

Table 1 shows the groups of MSLTs and hypotheses for prediction of mSL based on the first three nap results.

Table 1
MSLT groups evaluating the hypotheses predicting mSL based on the results of the first three naps (n = 588 MSLTs)[a]

Group	MSLT criteria	Number of MSLTs (% total)	mSL $\pm$ SD (min)	Prediction of mSL	
				Category	Accuracy (%)
Hypothesis 1. If all three SLs are in the same category then mSL is also in that category					
N3	SL normal in all three naps	73 (12%)	16.2 $\pm$ 2.6	Normal	100
B3	SL borderline in all three naps	24 (4%)	7.3 $\pm$ 1.4	Borderline	100
L3	SL low in all three naps	127 (22%)	2.2 $\pm$ 1.1	Low	99.2
Abn3	SL abnormal in all three naps	307 (52%)	4.1 $\pm$ 2.2	Abnormal	99.7
Hypothesis 2. If the patient does not fall asleep in at least two naps then mSL is normal					
SL 20 $\times$ 2	SL = 20 min in $\geq$2 naps	51 (9%)	17.0 $\pm$ 2.1	Normal	100
Hypothesis 3. If at least two naps have SOREMPs, then the accuracy of prediction of mSL is in increased in MSLTs with low or abnormal SL category					
L3R2	L3 and SOREMP in $\geq$2 naps	48 (8%)	1.8 $\pm$ 1.1	Low	100
Abn3R2	Abn3 and SOREMP in $\geq$2 naps	71 (12%)	2.7 $\pm$ 2.0	Abnormal	100

[a] MSL, mean sleep latency; SL, sleep latency; SL categories: normal $\geq$10 min; low $<$5 min; borderline $\geq$5 and $<$10 min; abnormal $<$10 min.

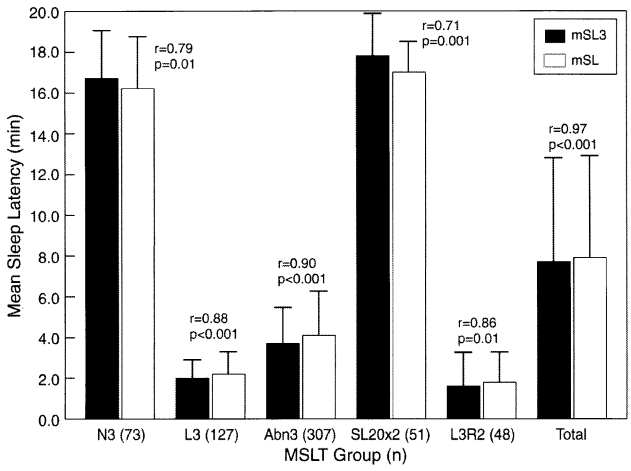

Fig. 1. Comparison of the SLs of the first three naps versus that of all four or five naps: mean, standard deviations, correlation coefficients, and *P* values for statistical difference on two-tailed paired student's *t*-test.

Groups N3, B3, L3, and Abn3 include MSLTs for which the SLs were in the same category – normal, borderline, low, and abnormal, respectively, to evaluate hypothesis 1 (*if all three SLs are in the same category, then mSL is in that category*). Group SL 20 × 2 included MSLTs in which the SL was 20 min in at least two naps to evaluate hypothesis 2 (*if a patient does not fall asleep in at least two naps, then mSL is normal*). Groups L3R2 and Abn3R2 included MSLTs in which SLs were low and abnormal, respectively, and ≥2 SOREMPs were present to evaluate hypothesis 3 (*the presence of SOREMPs increases the accuracy with which mSL is predicted in MSLTs with low or abnormal sleep latencies*).

The mSL category was predicted with perfect accuracy when the SL was normal or borderline for each of the first three naps. It was predicted with more than 99% accuracy when the SL was low or abnormal. The predictive accuracy increased to 100% in these two groups when SOREMPs were present in at least two of the first three naps (Table 1).

The accuracy in predicting normal mSL was high (91%) even for MSLTs with normal SL for any two of the first three naps. In MSLTs with low SL for any two of the first three naps and at least two SOREMPs, accuracy of predicting mSL category was 95.6%. Fig. 1 shows the comparison of mean SL of the first three naps versus that of all four or five naps. The accuracy of predicting the presence of two or more SOREMPs based on the first three naps is shown in Table 2.

3.3. Selection of MSLTs for prediction of the final MSLT result

The mSL can be predicted with >99% accuracy in patients with low, borderline, and normal SL in each of the first three naps. MSLTs with predicted normal mSL (group N, Table 3) do not need subsequent naps because sleep latency category and presence of significant naps with SOREMPs are predicted with 100% accuracy. Additionally, the clinical significance of SOREMPs in patients with normal mSL is unknown. In patients with abnormal and low SL who have ≥2 SOREMPs (groups Abn3R2, L3R2), mSL category is predicted with 100% accuracy (Table 3). Hence, depending on the clinical criteria used to make the diagnosis of narcolepsy, these patients do not need subsequent naps after the third. Thus, 23% MSLTs may be reduced to three naps without compromising the final MSLT results. Significant SOREMPs may occur after the third nap in up to 6.3% of MSLTs with abnormal SL and the diagnosis of narcolepsy may be missed if the MSLT is truncated to three naps.

4. Discussion

Although considered the gold standard for evaluation of EDS, the MSLT is time-consuming, labor-intensive, and expensive. A simpler, shorter, and less costly modification of the MSLT may be clinically useful.

Several modifications of the MSLT have been proposed. The modified assessment of sleepiness test (MAST) may substitute for the traditional MLST in assessment of EDS, while the maintenance of wakefulness test (MWT) has been used to evaluate treatment efficacy in these patients [5,6]. However, accuracy of the MAST for assessing EDS is not much different from the MSLT, and these two tests have not served the purpose of reducing time, labor, or cost. One of the suggested modifications of the interpretation of the MSLT is to use 'wake efficiency', defined as 100% minus percent time asleep [7]. The authors who proposed the use of 'wake efficiency' consider it to be more strongly correlated with sleep disordered breathing than measures based on sleep latency [7]. Another study examined the use of the

Table 2
Prediction of the presence of ≥2 naps with SOREMPs in all four or five naps, based on results of the first three naps

MSLT group ($n = 588$)	MSLT criteria	MSLTs with ≥2 naps with SOREMPs		Accuracy of prediction (%)
		Present in the first three naps (%)	Present in all four or five naps (n)	
N3 (73)	SL normal in all three naps	5 (6.8%)	5 (6.8%)	100
B3 (24)	SL borderline in all three naps	0	1 (4.2%)	95.8
L3 (127)	SL low in all three naps	48 (37.8%)	62 (48.8%)	89
Abn3 (307)	SL abnormal in all three naps	71 (23.1%)	91 (29.6%)	93.5
SL 20 × 2 (51)	SL 20 min in ≥2 naps	0	0	100

Table 3
Selection of MSLTs that can be reduced to three naps based on the results of the first three naps[a]

Predicted mSL category (*n*)	Group	MSLT criteria	Number of MSLTs (%)	Accuracy of prediction (%)	
				MSL category	≥ 2 naps with SOREMPs in four or five naps
Normal (179)	N3	SL normal in all three naps	73 (41%)	100%	100%
	SL 20 × 2	SL 20 min in any two of three naps	51 (28%)	100%	100%
	N[b]	Criteria of N3 or SL 20 × 2	90 (50%)	100%	100%
Borderline (197)	B3	SL borderline in all three naps	24 (12%)	100%	95.8% (23)
Low (212)	L3	SL low in all three naps	127 (60%)	99.2% (126)	89% (113)
	L3R2	SL low in all three naps and SOREMP in ≥2 naps	48 (23%)	100%	100%
Abnormal (409)	Abn3	SL abnormal in all three naps	307 (75%)	99.7% (306)	93.5% (287)
	Abn3R2	SL abnormal in all three naps and SOREMP in ≥2 naps	71 (17%)	100%	100%

[a] n, number of MSLTs in each category. Abnormal category includes all in low category by definition.
[b] Thirty-four MSLTs are included in both N3 and SL 20 × 2.

median instead of the mean SL as a measure of EDS; however, it was found that both measures were equally acceptable for clinical purposes [8]. None of these modifications have been accepted for routine application.

We hypothesized that one can predict the mSL category based on the results of the previous naps. This may be especially true when the earlier naps have very high SL or very low SL and the presence of naps with SOREMPs. Based on our study results, we believe that the subsequent naps of MSLT may be avoided in the tests for which the results of the first three (or two) naps satisfy the criteria for predicting mSL shown schematically in Fig. 2.

Once the mSL result is reported as normal (≥10 and ≤20 min), the clinical importance of low normal or high normal mSL and the presence of naps with SOREMPs among subjects with EDS is not known [9]. Thus, in patients whose earlier naps predict normal mSL with 100% accuracy (group N, 15% MSLTs), subsequent naps can be omitted probably without compromising results (Table 3).

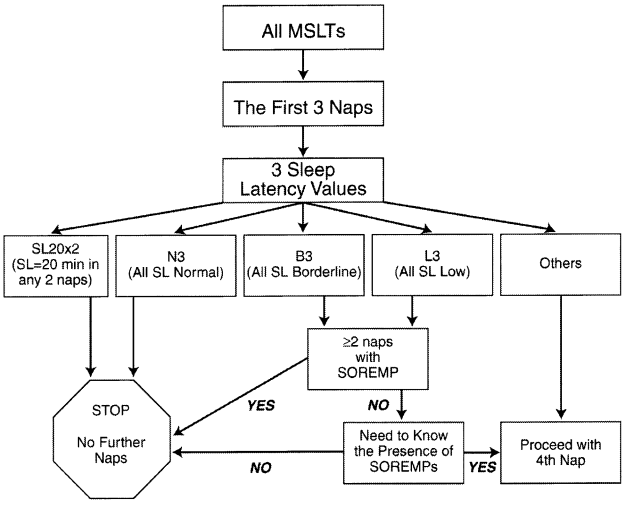

Fig. 2. Algorithm for the truncation of MSLTs based on the results of the first three naps.

Similarly, once the mSL result is reported as low (≤5 min), the clinical importance of very low (e.g. 0.5 min) or slightly low (e.g. 4.5 min) mSL is unknown. However, further naps may be necessary to detect SOREMPs, as their presence may suggest narcolepsy in patients with compatible clinical scenarios [10]. For example, in 8% of MSLTs, low mSL can be predicted with 100% accuracy and at least two naps with SOREMPs have occurred, obviating the need for subsequent naps (Table 1). However, SOREMPs occurred in the third nap in 79 (62%) MSLTs with predicted low mSL, and although mSL was predicted with 99.2% accuracy, subsequent naps were needed if the patients were to be evaluated for narcolepsy (Table 3).

Sometimes a patient cannot undergo the later naps of the MSLT either due to personal reasons (unwillingness to complete the series of naps, intentional or accidental consumption of caffeine-containing beverages, anxiolytic, or other medication) or rarely technical reasons (e.g. malfunction of the recording montage). In these circumstances the results of this study may be helpful in determining if a full MSLT must be repeated. Low or borderline mSL may be predicted very accurately (>99%) from the first three naps, and these patients probably do not need to undergo subsequent naps, except for the evaluation of narcolepsy if clinically indicated. In our study, the presence of SOREMPs in two or more naps improves the predictive accuracy for low mSL to 100%.

The limitations of this study are as follows. By omitting the later naps, each MSLT may comprise data from a variable number of naps (from two to five), which may cause some confusion in comparing MSLTs on the same patient or with those of other patients. However, this may not have any

adverse consequence on the management of patients with EDS evaluated by MSLTs. The time in which the test will be completed is unpredictable before the actual test is done, so in order to decrease labor costs, staff allocation would have to be somewhat flexible. The scoring of the first two or three naps must be done quickly and accurately, as mistakes leading to inappropriate truncation of the test may result in the need for repeat MSLT. This can be avoided by careful scoring of earlier naps, and in the case of any doubt, continuing with the subsequent naps.

Before our recommendations are generalized for routine use, our results may need to be validated with data from other sleep laboratories. However, there is no obvious reason to believe that the patients undergoing MSLT in other sleep disorders centers will be much different from the patients studied at our center; hence, the same conclusions should be applicable. Another limitation is that although categories like 'low', 'normal', and 'borderline' have some support in the literature, some clinicians also utilize the MSLT as a continuous measure of 'sleep tendency'. By truncating the MSLT, the accuracy of this measure may be reduced.

Truncation of the MSLT is not possible in all patients (Table 3). Among the patients with normal mSL, MSLT can be truncated without compromising the result in 50%. Similarly, among the patients with low and abnormal mSL, MSLT can be truncated in 23 and 17% of tests, respectively. Thus the 'specificity' to predict the final result for MSLT for these groups is from 17 to 50%. 'Specificity' is not expected to be 100% because truncation is possible only in selected groups that meet the above-described criteria.

5. Conclusions

The mSL can be predicted to be normal with 100% accuracy if: (1) each of the first three naps has normal SL, or (2) the patient does not fall asleep in any two or the first three naps. Similarly mSL can be predicted to be low or abnormal with 100% accuracy if each of the first three naps has low or abnormal SL, respectively, along with SOREMPs in any two of these naps. At least one of the later naps can be avoided in these MSLTs (23%) to save time, labor, and cost. In other combinations than those described above, the SL and presence of SOREMPs in the first three naps can be used to predict the mSL with adequate accuracy (although not 100%). This may obviate the need for repeating the test in certain circumstances, e.g. when further naps could not be performed due to personal or technical reasons.

We believe that the conclusions of our study may have important clinical implications in the performance of MSLTs by omitting later naps without compromising final test results. This may allow us to use more efficiently the equipment and also the professional and technological expertise of the physicians and technical staff of the sleep disorders center for evaluating patients with EDS, one of the most common symptoms of multiple sleep disorders.

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