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Test–Retest Reliability of Two Consecutive Mean Sleep Latency Tests in Patients with Hypersomnia

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Abstract

Reliability of mean sleep latency testing (MSLT) over consecutive days in patients with hypersomnia is unknown. We reviewed MSLTs of patients with hypersomnia without cataplexy who underwent our two consecutive MSLT protocol (N=29). Average MSLs were 10.9 and 10.9 minutes for days 1 and 2, respectively. Agreement for pathological hypersomnia (defined as MSL $\geq$ 8 minutes) between MSLT days showed $k=0.85$ for all (N=29) and $k=0.76$ for those without sleep apnea (N=20). In patients with subjective complaints of hypersomnia, a single MSLT is sufficient (vs. addition of 2nd day MSLT) in the setting of carefully implemented protocol controlling for potential confounding variables.

Keywords

hypersomnia; mean sleep latency test; narcolepsy; sleep disorder

Introduction

The multiple sleep latency test (MSLT) is a commonly performed adjunctive diagnostic tool to objectively quantify sleepiness when evaluating for pathological hypersomnia including narcolepsy. High test-retest reliability of MSLT has been demonstrated over the short term (weeks to months) in patients with narcolepsy and in healthy subjects [1, 2]. In contrast, test-retest reliability in general population as well as in patients with narcolepsy without cataplexy or idiopathic hypersomnia are low over the long term (years) [3, 4]. In practice it

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is common to see conflicting results from subsequent MSLTs, leading to diagnostic uncertainty.

Variability of MSLT results can be partly attributed to factors such as unrecognized chronic sleep deprivation, obstructive sleep apnea (OSA), circadian phase misalignment, medications and testing environment [5–8]. Objective measurement of hypersomnia with MSLT requires a well-planned testing protocol controlling for these factors using assessment of preceding sleep intake and timing, and nocturnal polysomnography (PSG) prior to MSLT [9]. The purpose of the study was to evaluate the immediate test-retest reliability of the MSLT performed over two consecutive days under optimal settings in patients presenting with hypersomnia.

Materials and Methods

We reviewed all cases (N=29) in which patients presented with refractory hypersomnia despite stimulant therapy, but without history of cataplexy or major psychiatric disorders, and underwent two consecutive MSLTs at Hennepin County Medical Center sleep center between 2000 and 2015. The two day study protocol was typically reserved for a limited number of selected patients who presented with hypersomnia of unclear underlying etiology. In some cases, the protocol was implemented to clarify the diagnosis in light of medico-legal implications.

The pre-protocol diagnoses were narcolepsy without cataplexy (N =13), idiopathic hypersomnia (N=7), and OSA with residual hypersomnia (N=6). Pre-protocol diagnosis was indeterminate in the remaining three patients. Eighteen patients, including those with pre-protocol diagnosis of narcolepsy without cataplexy, were on stimulants at the time referral. The remaining 11 patients had been their stimulants discontinued prior to presentation.

Our protocol required two to three weeks of sleep diaries and actigraphy, termination of stimulants and antidepressants for two weeks prior to PSG, and a negative urine drug screen performed during MSLT. All patients underwent two consecutive sets of overnight PSGs and daytime MSLTs and remained in the lab for the two day period. In patients with prior diagnosis of OSA, continuous positive airway pressure (CPAP) at an established pressure was applied during both overnight PSGs and both MSLTs. If OSA (apnea hypopnea index ≥ 10) was discovered during the initial PSG, CPAP was titrated in a split night manner on the first night and applied during first MSLT and throughout the second period of testing. All patients were allowed to wake spontaneously to terminate the PSGs. Eight minutes was used as the cutoff to assess correlation and agreement of mean sleep latencies (MSLs). We used the following definitions; narcolepsy without cataplexy: MSL ≤ 8 min and ≥ 2 sleep onset rapid eye movement periods (SOREMPs), idiopathic hypersomnia: MSL ≤ 8 min and < 2 SOREMPs, no pathological hypersomnia: MSL > 8 min.[9] Nocturnal PSG REM latency was also evaluated and included in SOREMP criteria. We repeated analysis on the 20 remaining subjects, after excluding those with OSA. The study was approved by the institutional review board at Hennepin County Medical Center and a waiver of informed consent was obtained for this chart review-based study.

Results and Discussion

Mean age of patients was 40.3 years (SD=14.8) and 22 subjects were female (76%). Based on sleep diary and actigraphy assessment, there was no evidence of behaviorally induced insufficient sleep, as defined by average total sleep time of less than 6 hours per night, or circadian phase misalignment.

Two patients met criteria for narcolepsy without cataplexy based on the first MSLT and remained consistent on the second MSLT (Supplemental Figure). No SOREMPs or nocturnal SOREMPs were observed in any other patients. Mean MSLs were 10.9 (5.8) and 10.9 (5.9) minutes for first and second MSLT, respectively ($p=NS$). A total of nine patients were found to have OSA based on the first night PSG. Pre-protocol diagnosis of these nine patients included OSA ($N=5$), narcolepsy without cataplexy ($N=1$), idiopathic hypersomnia ($N=1$) and indeterminate ($N=2$). One of the six patients originally presenting with OSA did not have OSA during the protocol. When patients with OSA were excluded, mean MSLs were 11.7 (5.6) and 12.1 (5.7) minutes for first and second MSLTs, respectively ($p=NS$). The Pearson correlation was high ($R=0.86$, $p<0.001$) between the two MSLs. The Bland-Altman plot showed moderate agreement in absolute MSLs between the first and second day MSLTs (Figure 1). However, agreement in diagnosis based on MSL 8 min cut-off was high (Kappa=0.85, SE of Kappa=0.10; Table 1). After excluding those with OSA, correlation ($R=0.83$, $p<0.001$) as well as agreement (Kappa=0.76, SE of Kappa=0.16) remained high. Diagnosis remained consistent across MSLTs in all but two patients. One patient who met idiopathic hypersomnia criteria on the first MSLT (MSL=7.2 minutes) did not meet criteria on the second MSLT (MSL=15.8 minutes). The other patient did not demonstrate pathological hypersomnia on the first MSLT (MSL=9.8 minutes), but met idiopathic hypersomnia criteria on the second MSLT (MSL=6.1 minutes). There was modest correlation in total sleep time between first and second overnight PSGs ($R=0.45$, $p=0.01$).

This study shows high immediate test-retest reliability of the MSLT in patients presenting with refractory hypersomnia without history of cataplexy. Results were similar when patients with OSA were excluded. We speculate that this, at least in part, owes to the strict protocol we implemented to control for confounders in MSLTs. Alternatively, it may imply that in contrast to significant long term variability, there is low immediate variability for MSLT. In fact, even taking different protocol into account, MSLT results can inherently change over time due to various factors including age-related changes, progression of underlying disease and development of other comorbidities. It is noteworthy that two-thirds of the patients did not meet pathological hypersomnia criteria despite presenting with a history of difficult to treat, persistent hypersomnia. Finally, the MSLT may not identify all non-narcoleptic pathologic hypersomnia. The International Classification of Sleep Disorders 3 requires objective testing in addition to history for the diagnosis of 'hypersomnias of central origin', but ultimately, clinical judgment is tantamount.[10] Our study is limited by potential biases inherent to retrospective analyses. The two day study protocol was not intended to assess test-retest reliability but was often administered to patients with persistent hypersomnia who required of confirmatory diagnosis. Therefore, it should be noted that selection bias is likely present and the findings of our study may not be generalizable to all patients with hypersomnia. In addition, the study was not powered to determine factors

predictive of concordant vs. discordant results due to the small number of discordant cases. The focus of the results should be mainly centered on the consistency of MSL rather than on that of SOREM given few patients with SOREM. Finally, the purpose of this study was to evaluate for immediate stability of the MSLT rather than to assess its value as a diagnostic tool to discriminate underlying causes of hypersomnia. Long term stability of MSLT results when implemented with similar strict protocol as employed in this study is uncertain and deserves future investigation.

Conclusions

The MSLT showed high immediate test-retest reliability when performed in a two consecutive day manner in patients with refractory hypersomnia. Based on the results of the study we propose that a single MSLT is generally sufficient (vs. addition of 2nd day MSLT) in the setting of carefully implemented protocol controlling for potential confounding variables.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1.
Bland-Altman Plot of MSL Day 1 vs. Day 2 (N=29).
MSL, mean sleep latency (Units: min)

Table 1

Agreement between MSLT Day 1 and Day 2 (N=29)

Number of Patients		2nd MSLT	
		MSL $\geq$ 8 min	MSL < 8 min
1st MSLT	MSL $\geq$ 8 min	10	1
	MSL < 8 min	1	17

MSLT, mean sleep latency test