https://doi.org/10.5664/jcsm.8976

JCSM | Journal of Clinical Sleep Medicine

SCIENTIFIC INVESTIGATIONS

Multiple Sleep Latency Test: when are 4 naps enough?

John Goddard, BSc, MBBS, FRACP[1]; George Tay, MBChB, FRACP, MHM[2]; Jennifer Fry, BSc[2]; Mark Davis, BSc[3]; Deanne Curtin, MBBS, FRACP[2]; Irene Szollosi, BSc, PhD[2]

[1]Respiratory Department, Sunshine Coast University Hospital, Birtinya, Queensland, Australia; [2]Sleep Disorders Centre, The Prince Charles Hospital, Chermside, Queensland, Australia; [3]Sleep Disorders Clinic, Royal Brisbane and Women's Hospital, Herston, Queensland, Australia

Study Objectives: The Multiple Sleep Latency Test (MSLT) is central to the diagnosis of narcolepsy and idiopathic hypersomnia. This study is the first to assess the impact of a 5-nap protocol on meeting MSLT-derived diagnostic criteria in a general cohort referred for MSLT, without selection bias.

Methods: Data for all MSLTs performed at 2 tertiary sleep units in Australia between May 2012 and May 2018 were retrospectively assessed for the impact of the fifth nap on mean sleep latency (MSL) and sleep onset rapid eye movement periods.

Results: There were 122 MSLTs included. The MSL was 8.7 ± 5.1 minutes after 4 naps, compared with 9.2 ± 5.2 minutes for 5 naps ($P < .0001$). In 8 cases, inclusion of the fifth nap changed the MSL to a value above the diagnostic threshold of 8 minutes. There were no instances in which the MSL moved to ≤ 8 minutes based on fifth nap data. A sleep onset rapid eye movement period occurred in the fifth nap in 9 patients and altered the interpretation in 2 cases.

Conclusions: The fifth nap in an MSLT is associated with an increased MSL, although this difference is rarely clinically significant. In patients with borderline MSL or 1 sleep onset rapid eye movement period after 4 naps, a fifth nap can alter the outcome and should be performed. However, for many cases, a 4-nap MSLT protocol will suffice, potentially allowing resource savings without compromising diagnostic accuracy. We propose the adoption of a conditional 4-nap or 5-nap protocol based on specific criteria.

Keywords: multiple sleep latency test, narcolepsy, idiopathic hypersomnia, central disorders of hypersomnolence

Citation: Goddard J, Tay G, Fry J, Davis M, Curtin D, Szollosi I. Multiple Sleep Latency Test: when are 4 naps enough? *J Clin Sleep Med*. 2021;17(3):491–497.

BRIEF SUMMARY

Current Knowledge/Study Rationale: There is institutional variation in performance of a 4-nap or 5-nap protocol for the Multiple Sleep Latency Test, a key measurement used in the assessment of disorders of hypersomnolence. This study is the first to specifically assess the impact of a 5-nap protocol on Multiple Sleep Latency Test-derived diagnostic criteria in a general cohort with routine performance of a fifth nap.

Study Impact: In our cohort referred for Multiple Sleep Latency Test, the fifth nap data did not alter the overall interpretation of the test for a significant number (60%) of cases. We propose a conditional 4-nap or 5-nap protocol based on criteria for mean sleep latency and sleep onset rapid eye movement periods obtained after 4 naps.

INTRODUCTION

The Multiple Sleep Latency Test (MSLT) is a validated objective assessment of sleepiness for the evaluation of suspected narcolepsy or idiopathic hypersomnia. Narcolepsy is an uncommon disorder of the sleep-wake cycle that affects approximately 0.05% of the population.[1] It is characterized by excessive daytime somnolence and may have associated cataplexy (in narcolepsy type 1), hypnagogic and hypnopompic hallucinations, and sleep paralysis. The pathogenesis of narcolepsy remains uncertain, but, for narcolepsy type 1, is suspected to involve hypocretin-producing neurons in the hypothalamus.[2] The diagnosis of narcolepsy can be challenging, especially in cases without cataplexy (narcolepsy type 2). There is overlap of clinical features with idiopathic hypersomnia, a rare primary disorder of hypersomnolence distinguished from narcolepsy by the absence of rapid eye movement (REM) sleep disturbance as well as other sleep characteristics (ie, continuity).[3]

The MSLT is central to the diagnosis of narcolepsy and idiopathic hypersomnia following assessment of comorbid conditions and other contributing factors. Patients are monitored for a series of supervised daytime nap opportunities, typically of 20-minute duration, following polysomnography (PSG) the night prior. Data regarding sleep latency and staging is collected. A reduced mean sleep latency (MSL) of ≤ 8 minutes and the presence of 2 or more sleep onset rapid eye movement periods (SOREMP) on MSLT is diagnostic of narcolepsy in the appropriate context.[4] Idiopathic hypersomnia is considered if the MSL is similarly reduced but without SOREMPs or other features of narcolepsy. Current practice parameters recommend 5 nap opportunities, performed at 2-hour intervals.[5,6]

Despite the routine use of MSLTs, data assessing the overall utility of the fifth nap opportunity is limited. Arand et al[7] established a significant difference in MSLs obtained when comparing studies using a 4-nap or 5-nap protocol. In the only study to date that examined the utility of the fifth nap in a within-subject comparison, the majority of MSLTs at that institution were performed using a 4-nap protocol and thus excluded.[8] The remaining 14% of participants included in the analysis that underwent a 5-nap protocol may have represented a biased

sample. The aim of the present study was therefore to examine the utility of the fifth nap in the MSLT in the absence of any selection bias in patients referred for investigation of hypersomnolence. Our objectives were to assess the impact of the fifth nap on both MSL and SOREMPs and to provide clear recommendations as to when the fifth nap is necessary. It was hypothesized that a 4-nap protocol would suffice for the majority of MSLTs performed, potentially reducing resource usage without compromising diagnostic accuracy.

METHODS

A retrospective review was conducted of all patients who underwent an MSLT over a 5-year period at The Prince Charles Hospital and the Royal Brisbane and Women's Hospital in Queensland, Australia. Both institutional ethics committees deemed the study exempt from full ethical review. Institutional databases were interrogated for all MSLTs performed from May 2012 to May 2018. During this period, both centers performed a 5-nap protocol routinely according to the practice parameters published by the American Academy of Sleep Medicine (AASM),[5] including the use of sleep diaries, withdrawal of stimulant, or REM-suppressant medication prior to testing where possible, and urine drug screening. Data from MSLT reports and associated PSG were retrieved. Additional information was obtained from review of clinician letters.

All patients underwent a Level 1 overnight laboratory PSG performed according to AASM criteria[5] prior to the MSLT. Those with obstructive sleep apnea (OSA) used continuous positive airway pressure for the PSG and subsequent MSLT. Five 20-minute nap opportunities were provided at 2-hour intervals with sleep onset defined as the first epoch of any stage of sleep. Naps were terminated 15 minutes after sleep onset or 20 minutes after no sleep. Sleep stages and events were scored according to AASM criteria[9] on both the overnight PSG and MSLT. Data were collated into a Microsoft Excel 2016 spreadsheet and statistical analysis was performed using the *Data Analysis Toolpack*. MSL and SOREMPs were calculated for each study using data from 4 and 5 naps. MSLs were compared using paired *t* tests and correlation was calculated using linear regression and agreement compared using Bland–Altman analysis.

Subgroup analysis was conducted to determine whether apnea-hypopnea index (AHI) on the proceeding PSG influenced MSL or number of SOREMPs at AHI thresholds of 5, 10, and 15 events/h. The residual AHI was recorded if patients were using continuous positive airway pressure. Additional subgroup analysis was performed to assess whether MSL or number of SOREMPs was influenced by the known use of REM suppressant or stimulant medication at the time of the study. If data regarding cessation were missing, patients were included in the group labeled as remaining/unsure on medication to ensure a group confirmed to be free from EEG influencing medications was formed. Independent samples *t* test was used to compare mean MSL between subgroups and chi square test was used to evaluate differences in SOREMPs.

RESULTS

A 5-nap protocol was used for 95% of MSLTs; other cases were excluded from analysis. The characteristics for the 122 patients included in the analysis are presented in **Table 1**. There was a slight female preponderance in the cohort aged 39·0 ± 13·6 years, and subjective hypersomnolence was reported with an Epworth Sleepiness Scale of 14.8 ± 4.8. Nearly one-third were using continuous positive airway pressure in the preceding PSG. OSA was well controlled with AHI of 2.5 ± 4.6 events/h for the group, and adequate sleep duration (≥ 6 hours) on the preceding PSG was present in 93% of cases. A final diagnosis of narcolepsy was reached in 10 patients and idiopathic hypersomnia in 42 patients.

The group MSL data from the 4-nap protocol was 8.7 ± 5.1 minutes compared with 9.2 ± 5.2 minutes for the 5-nap protocol ($P < .0001$). On average, the fifth nap increased MSL by 0.5 ± 1.0 minutes. Bland–Altman plot (**Figure 1**) shows good agreement between the 4-nap and 5-nap protocols with limits of agreement between −1.3 to 2.4 minutes. The bias was not systematic; there was excellent agreement at the lower and upper ranges of sleep latency, however there was less agreement between MSL of 5 and 15 minutes as indicated by a greater scatter in this range.

Regression analysis (**Figure 2**) confirmed excellent correlation between the 4-nap and 5-nap protocol ($r^2 = .97$, $P < .0001$). Inclusion of the fifth nap changed the MSL from ≤ 8 minutes (the diagnostic threshold) to > 8 minutes in 8/122 tests; in no cases did the MSL change from > 8 minutes to ≤ 8 minutes due to the fifth nap.

Only 4 MSLTs were associated with a SOREMP in the preceding PSG. The frequency of SOREMPs across the nap opportunities is presented in **Figure 3**. The propensity for REM sleep was greatest in naps 2 and 3, with 10% and 11% of tests demonstrating REM in these naps, respectively. Nap 4 was associated with reduced REM propensity. SOREMP occurred in the fifth nap in 9/122 tests; however, this influenced the diagnosis in only 2 cases. For these 2 patients there was only 1 SOREMP after 4 naps and the diagnostic criteria for narcolepsy were met with the inclusion of the fifth nap. Four of the 9 studies had demonstrated 2 or more SOREMPs by the fourth nap. In 3 of these cases, there were 3 or more SOREMPs before the fifth nap. Taking into consideration the impact of the fifth nap on both MSL and SOREMPs, 10 of 122 tests performed resulted in a change in either the diagnostic criteria for narcolepsy being met (2/122) or the MSL being reclassified (8/122).

The AHI was < 5 events/h on the preceding PSG for 106 (87%) cases. A further 9 (7%) patients had an AHI between 5 and 10 events/h, 3 (2%) between 10 and 15 events/h, and 4 (3%) greater than 15 events/h. There was no difference in MSL based on AHI using any of the thresholds considered. The number of SOREMPs with 5 naps was significantly different using an AHI threshold of 15 events/h, Yates^2 (df 5, n = 122) = 21.12, $P < .001$. Three of 4 patients (75%) with residual AHI > 15 events/h had 1 SOREMP, whereas 98 of 118 (83%) with AHI < 15 events/h had no SOREMP with 5 naps.

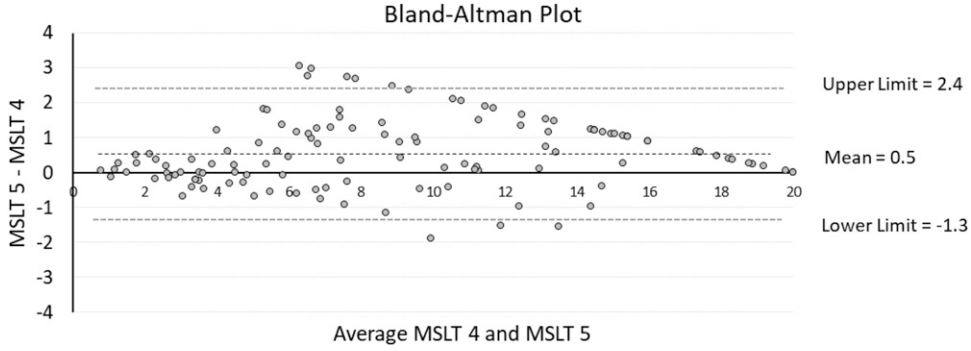
Eighty of 122 (66%) patients were not taking antidepressant medication at time of testing, 27 (22%) were known to be taking

Table 1—Demographic and polysomnographic characteristics of patients with MSLT.

Characteristic	Results
Age (years)	39.0 ± 13.6
Sex (male/female)	56/66
BMI (kg/m^2)	28.4 ± 6.8
Epworth Sleepiness Scale score	14.8 ± 4.8
PSG (diagnostic/CPAP)	82/40
PSG total sleep time (minutes)	422.3 ± 56.3
PSG sleep efficiency (%)	83.9 ± 8.6
PSG apnea-hypopnea index (per hour sleep)	2.5 ± 4.6
PSG arousal index (per hour sleep)	17.7 ± 10.1
Narcolepsy diagnosis	10
Idiopathic hypersomnia diagnosis	42

Data shown as mean ± standard deviation. PSG data obtained from prior night recording. BMI = body mass index, CPAP = continuous positive airway pressure, MSLT = Multiple Sleep Latency Test, PSG = polysomnography.

Figure 1—Bland-Altman Plot showing difference of the 2 paired measurements on *y*-axis (MSL 5–MSL 4), plotted against the mean of the 2 measurements.



There is a bias of 0.55 minutes (ie, inclusion of the fifth nap increases the MSL by an average of 0.55 minutes). The limits of agreement are narrow and show that in 95% of cases, the difference will be between −1.34 and 2.43 minutes. The bias is not systematic. There is excellent agreement at the lower and upper ranges of sleep latency however there is less agreement between a mean of 5–15 minutes as indicated by a greater scatter in this range. MSL = mean sleep latency, MSLT = Multiple Sleep Latency Test.

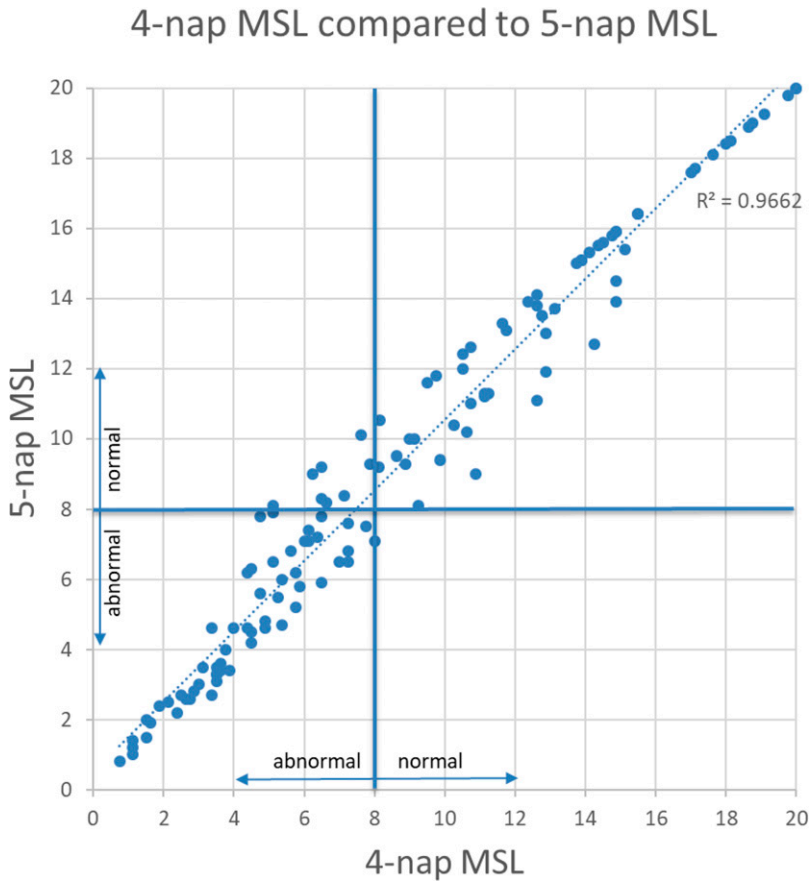
antidepressants, and 15 (12%) had records where antidepressants use was uncertain at time of testing. Most patients (113/122, 93%) were not on stimulant medication at time of testing; 13 (11%) had ceased in preparation for testing and the remaining 9 (7%) had records where the use of stimulants was uncertain. When considering the effect of medications individually or as taking either antidepressants or stimulants, there were no significant differences between the groups in either MSL or number of SOREMPs.

DISCUSSION

This study is the first to examine the utility of the fifth nap without selection bias, using a routine 5-nap MSLT protocol in a generalizable cohort referred for investigation of hypersomnolence. Our results confirm previous findings that a 5-nap protocol tends to increase the MSL when compared to a 4-nap protocol. Our results, from a within-subject study design, confirm and strengthen these findings given previous investigators compared MSLs obtained from different studies using a 4-nap or 5-nap protocol[7] or included a highly selected cohort.[8] Importantly, we also confirm that the fifth nap opportunity has the potential to impact diagnosis in select cases, with a tendency normalize the MSL or provide the second SOREMP to meet the diagnostic criteria for narcolepsy. However, we have demonstrated this fifth nap impact is relatively infrequent and propose a conditional 4-nap protocol that will suffice for a significant number of patients.

Early research established sleep latency as a valid measure of physiological sleep tendency[10] and the association between SOREMPs and narcolepsy.[11,12] Formal protocols for the MSLT were developed,[13] and the test has since been applied in the assessment of a variety of disorders and effects of treatment.[7] Normative data for the MSLT can vary, as the test is prone to influence from methodological differences, age, and prior sleep time. An earlier review of normative values suggested a normal MSL of 10 to 11 minutes from pooled analysis, although with broad confidence intervals.[7] Most patients with type 1 narcolepsy have a significantly reduced MSL of around 3 minutes,[14,15] and 2 or more SOREMPs.[16,17] The MSL for patients with

Figure 2—Regression of 4-nap MSL vs 5-nap MSL (r^2 = .97).



The chart has been divided into quadrants along the 8-minute MSL thresholds to indicate abnormal and normal test results. MSL = mean sleep latency.

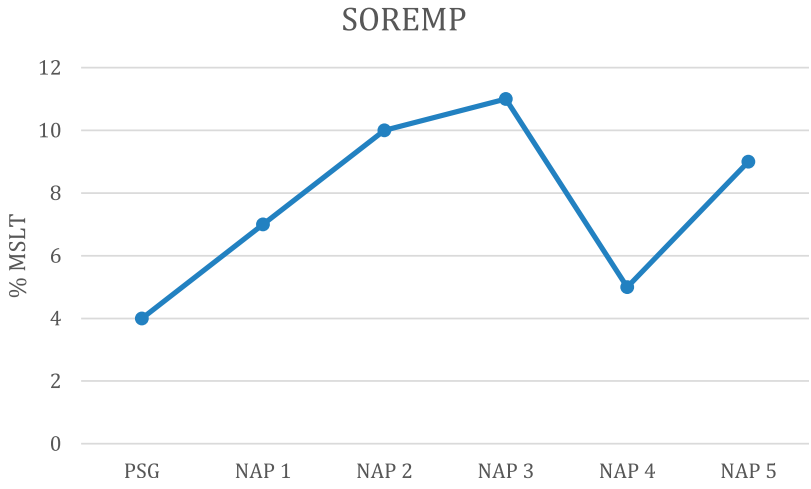
idiopathic hypersomnia falls in an intermediate range between type 1 narcolepsy and normal controls.[18,19] There is good test-retest reliability for the MSLT in type 1 narcolepsy, but less so for type 2 narcolepsy and idiopathic hypersomnia.[20–22]

Current practice parameters recommend 5 nap opportunities, performed at 2-hour intervals, noting that a 4-nap protocol may be applied.[5] Given the paucity of research, clear guidelines on when the fifth nap should be applied are lacking. As such, institutional practices for the MSLT vary between 4 or 5 nap opportunities.[23] In support of a truncated MLST is the fact the fifth nap may increase the time and resources required to complete the test. Patients could conceivably have heightened anxiety around finishing and attending to travel arrangements.[24] This "last test" effect has been proposed to contribute to the increased sleep latency seen with the fifth nap, although posttest arrangements did not appear to influence results in a prior study.[25]

On the other hand, the diagnosis of hypersomnolence can be challenging, and it may be argued that the additional information afforded by the fifth nap is worth the extra resources required. While demonstration of low hypocretin-1 levels in cerebrospinal fluid can support the diagnosis of type 1 narcolepsy, there is no definitive pathobiological marker for type 2 narcolepsy or idiopathic hypersomnolence.[26] The results of the MSLT are therefore crucial to the diagnostic algorithm for hypersomnolence. The specificity of the MSLT for narcolepsy increases with each additional observed SOREMP.[17] Moreover, SOREMPs are not evenly distributed between the different nap opportunities, with lowest incidence during the fourth nap,[27,28] a pattern replicated in our cohort. Factors such as circadian rhythm and homeostatic drive, in addition to age and sex, may influence the MSLT. For instance, a recent analysis of a large database has reported a U-shaped distribution of both mean sleep latency and SOREMPs for patient age.[28]

The 2 key parameters in an MSLT are the MSL and the occurrence of SOREMPs. The fifth nap can alter the conclusions of the test if the sleep latency differs substantially from earlier naps or if an additional SOREMP is observed. Our results reaffirm the finding that sleep latency is increased in the fifth nap,[7,28] with a statistically significant increase in MSL for 5-nap data. This statistical difference was rarely clinically significant in our cohort. In 7% of cases, the MSL was reclassified to above the diagnostic threshold compatible with narcolepsy or idiopathic hypersomnia (using a cut-off of 8 minutes), based on the fifth nap opportunity. An MSL of around 8 minutes is an equivocal result with overlap between diagnoses, including normal participants, and must be interpreted within the clinical context. However, there could be implications, including access to subsidized medication, for patients with an MSL in this range. There was more consistent agreement for 4-nap and 5-nap data for MSL at both extremes (ie, clearly normal or clearly abnormal), highlighting

Figure 3—Propensity for REM sleep across the nap opportunities as assessed by the presence of sleep onset REM periods.



REM = rapid eye movement.

the importance of careful consideration of clinical features in the diagnosis of patients when the MSL is in the intermediate range.

A SOREMP during the fifth nap is most significant in the situation where 1 prior SOREMP has been recorded, including during the overnight PSG. A patient in this scenario, with low MSL, could thus meet the diagnostic criteria for narcolepsy. In our study, a SOREMP was noted in 7% of fifth naps. Most occurrences were for patients who had already satisfied or in some cases exceeded the criteria for narcolepsy after 4 naps. Overall, less than 10% of the patients in our cohort had a different conclusion on the MSLT due to the fifth nap, and in the majority of cases the conclusion favored a normal MSLT.

The secondary analyses suggest that use of REM-suppressant medication or stimulants did not significantly impact MSL or SOREMPs for 4-nap or 5-nap data. Based on usual clinical practice it is likely that very few (if any) patients were on stimulant therapy; the small number of patients assigned to this group for analysis was based on missing data. An association was noted between elevated AHI (> 15 events/h) and the occurrence of a SOREMP. The association of OSA and SOREMPs has been well described previously[29] and highlights the importance of optimizing treatment of comorbid OSA prior to MSLT. Overall, the average AHI for the cohort was normal (2.5 ± 4.6 events/h), with 4/122 patients exhibiting AHI > 15 events/h. When stratifying patients by AHI, there was no significant impact on MSL. Based on the subgroup analyses, the overall conclusions of the study remain consistent when limiting consideration to patients without the confounding factors of medication usage or suboptimally treated OSA.

There are several prior studies that have examined the impact of the fifth nap, although with importance differences to our cohort. A retrospective analysis of a cohort in the United Kingdom who had undergone a MSLT found the fifth nap contributed to a diagnosis of narcolepsy in 16% of cases.[8] This analysis was restricted to the impact of SOREMPs rather than MSL and focused on a selected cohort with a diagnosis of narcolepsy and low MSL. A large majority of patients (86%) had undergone a 4-nap protocol and were excluded from analysis, which may have introduced a selection bias. In a separate prior study of patients with narcolepsy, 10% required the fifth nap to reach the threshold of 2 SOREMPs.[27] It is difficult to extrapolate the results of these earlier studies to an overall cohort with hypersomnolence as only a proportion of those undergoing a MSLT will ultimately have narcolepsy. Our results avoided this selection bias by including all patients referred for MSLT and assessed the influence of the fifth nap on both MSL and number of SOREMPs. It is useful to consider all cases referred for MSLT, rather than just those with narcolepsy, as patients with clearly normal results may be most suited to a shortened 4-nap protocol.

A mathematical approach can be applied to the standard diagnostic criteria for narcolepsy and idiopathic hypersomnia to determine when the fifth nap could change the overall MSLT results. A patient with an MSL < 5 minutes after 4 naps cannot achieve an overall MSL of ≥ 8 minutes even with no sleep (assigned a sleep latency of 20 minutes) on the fifth nap. Similarly, a patient who fell asleep immediately on the fifth nap would retain a normal overall MSL if the average after 4 naps had been > 10 minutes. Therefore, a fifth nap could be reserved for those who have a MSL between 5 to 10 minutes, or 1 SOREMP, after 4 naps have been observed. For simplicity, we suggest patients with an MSL between 5 and 10 minutes and 2 or more SOREMPs after 4 naps also complete a fifth nap. This approach partially mitigates a scenario where there is disagreement over the scoring of SOREMPs.[30]

In our cohort, a 4-nap MSLT could suffice in 60% of cases if applying this rule. Using the proposed algorithm would have resulted in 49 fifth nap opportunities, with the outcome changing in 10/49 of cases (20%). Importantly, this approach does require accurate real-time polysomnographic scoring during the MSLT, which may not be universally available in all sleep laboratories. Error in the real-time analysis could be particularly significant if short periods of REM sleep were not recognized. Adjustments could be made to the decision rule to account for this concern. If greater specificity for the diagnosis of narcolepsy is desired, those with 2 SOREMPs and an MSL < 5 minutes after 4 naps could also proceed to a fifth nap. This situation was uncommon, accounting for an additional 5 patients in our

cohort. A more conservative approach again would include all patients with MSL < 5 minutes in the 5-nap protocol, given reclassification of SOREMPs during subsequent analysis could alter the diagnosis between narcolepsy and idiopathic hypersomnia. In our data set a further 29 patients (24%) would then have required the fifth nap.

For patients and sleep services, a more efficient test may be desirable if diagnostic performance and testing logistics are not compromised. Adopting the model proposed and reserving a fifth nap for select cases after 4 naps could result in time and resource savings. The application of a conditional 4-nap protocol is intuitive and likely being applied in many settings. Specific guidance for when a fifth nap opportunity should be provided would assist sleep laboratories to standardize testing procedures as well as the interpretation of results across laboratories.

The strengths of the current study include the minimization of selection bias by including all patients referred for MSLT from 2 tertiary referral centers, both performing 5 naps routinely during the study period. We have examined the impact of the fifth nap opportunity on both key MSLT parameters, the MSL and occurrence of SOREMPs. This allows the results of the present study to be applied to a general sleep laboratory setting where MSLTs are performed to investigate excessive daytime somnolence not exclusively due to suspected narcolepsy.

Several limitations in the present study should also be noted. Firstly, the data were collected retrospectively using existing clinical data. This study design is appropriate for the comparison of 4-nap and 5-nap protocols on MSL and SOREMPs given that within-subject comparison can be made without inferring cause and effect relationships. However, we are unable to evaluate whether the results of the fifth nap opportunity would have influenced the final diagnosis, given the MSLT is just one aspect contributing to the clinician diagnosis. Thus, we are limited to evaluating the impact of the fifth nap to specific established diagnostic criteria rather than final diagnosis. It was also not possible to explore the "last test" effect. It is unclear whether a dynamic 4-nap or 5-nap protocol could influence the last test effect, with an impact potentially extending to the fourth nap. The need for patients and staff alike to provision for the possibility of proceeding to a fifth nap could also offset some of the theoretical resource savings. However, clinical processes can be developed which take into account these considerations and improve overall efficiency in the case of a 4-nap MSLT.

Due to the rarity of narcolepsy and idiopathic hypersomnia, the sample size is modest but comparable to other reported cohorts. An interesting observation in our cohort is the higher rate of an idiopathic hypersomnia diagnosis compared with narcolepsy. Alternative contributors such as comorbid conditions, shift work, circadian rhythm disturbance, or chronic sleep restriction may have been present but not captured in the data collection for some cases. It is possible that idiopathic hypersomnia may be prone to overdiagnosis and incorporation bias given the relatively high prevalence of reduced mean sleep latency noted in previous population-based cohort studies.[31] Additionally, the continuation of REM-suppressant medications in some cases may have affected discrimination between idiopathic hypersomnia and narcolepsy type 2. Finally, there is growing evidence that the MSLT may be less reliable in the diagnosis of narcolepsy type 2 or idiopathic hypersomnia compared with narcolepsy type 1.[22] Future work in this area could further explore the validity of the MSLT in these conditions, ideally with larger sample sizes, collection of biomarkers, and prospective data to allow accurate phenotyping.

CONCLUSIONS

This study demonstrates that in a cohort of patients undergoing MSLT for investigation of hypersomnolence disorders, the fifth nap opportunity occasionally impacts on MSLT-derived diagnostic criteria. We conclude that a 4-nap protocol is sufficient for the majority of cases and recommend the adoption of a conditional 4-nap protocol. In this model, patients will progress to a 5-nap protocol when there is the potential to impact diagnostic criteria for narcolepsy or idiopathic hypersomnia. The fifth nap is thus completed for only those patients with an MSL between 5 to 10 minutes, or 1 SOREMP, after 4 naps. A more conservative protocol that completes a fifth nap for all patients with a MSL < 10 minutes after 4 naps could also be considered, particularly if there were concerns about real-time scoring of SOREMPs. Adopting a conditional 4-nap protocol, with a fifth nap reserved for select subgroups could allow cost and time savings without compromising the diagnostic fidelity of the MSLT.

ABBREVIATIONS

AASM, American Academy of Sleep Medicine
AHI, apnea-hypopnea index
CPAP, continuous positive airway pressure
MSL, mean sleep latency
MSLT, Multiple Sleep Latency Test
OSA, obstructive sleep apnea
PSG, polysomnography
REM, rapid eye movement
SOREMP, sleep onset rapid eye movement period

REFERENCES

1. Scammell TE. Narcolepsy. *N Engl J Med.* 2015;373(27):2654–2662.
2. Peyron C, Faraco J, Rogers W, et al. A mutation in a case of early onset narcolepsy and a generalized absence of hypocretin peptides in human narcoleptic brains. *Nat Med.* 2000;6(9):991–997.
3. Billiard M, Sonka K. Idiopathic hypersomnia. *Sleep Med Rev.* 2016;29:23–33.
4. Sateia MJ. International classification of sleep disorders-third edition: highlights and modifications. *Chest.* 2014;146(5):1387–1394.
5. Littner MR, Kushida C, Wise M, et al.Standards of Practice Committee of the American Academy of Sleep Medicine. Practice parameters for clinical use of the multiple sleep latency test and the maintenance of wakefulness test. *Sleep.* 2005; 28(1):113–121.
6. Douglas JA, Chai-Coetzer CL, McEvoy D, et al. Guidelines for sleep studies in adults - a position statement of the Australasian Sleep Association. *Sleep Med.* 2017;36(Suppl 1):S2–S22.
7. Arand D, Bonnet M, Hurwitz T, Mitler M, Rosa R, Sangal RB. The clinical use of the MSLT and MWT. *Sleep.* 2005;28(1):123–144.
8. Muza R, Lykouras D, Rees K. The utility of a 5(th) nap in multiple sleep latency test. *J Thorac Dis.* 2016;8(2):282–286.

9. Berry RB, Brooks R, Gamaldo C, et al. AASM Scoring Manual Updates for 2017 (Version 2.4). *J Clin Sleep Med.* 2017;13(5):665–666.
10. Carskadon MA, Dement WC. Effects of total sleep loss on sleep tendency. *Percept Mot Skills*. 1979;48(2):495–506.
11. Rechtschaffen A, Wolpert EA, Dement WC, Mitchell SA, Fisher C. Nocturnal Sleep of Narcoleptics. *Electroencephalogr Clin Neurophysiol.* 1963;15(4): 599–609.
12. Mitler MM, Van den Hoed J, Carskadon MA, et al. REM sleep episodes during the Multple Sleep Latency Test in narcoleptic patients. *Electroencephalogr Clin Neurophysiol.* 1979;46(4):479–481.
13. Carskadon MA, Dement WC, Mitler MM, Roth T, Westbrook PR, Keenan S. Guidelines for the multiple sleep latency test (MSLT): a standard measure of sleepiness. *Sleep*. 1986;9(4):519–524.
14. Richardson GS, Carskadon MA, Flagg W, Van den Hoed J, Dement WC, Mitler MM. Excessive daytime sleepiness in man: multiple sleep latency measurement in narcoleptic and control subjects. *Electroencephalogr Clin Neurophysiol.* 1978; 45(5):621–627.
15. Broughton R, Aguirre M, Dunham W. A comparison of multiple and single sleep latency and cerebral evoked potential (P300) measures in the assessment of excessive daytime sleepiness in narcolepsy-cataplexy. *Sleep*. 1988;11(6):537–545.
16. Amira SA, Johnson TS, Logowitz NB. Diagnosis of narcolepsy using the multiple sleep latency test: analysis of current laboratory criteria. *Sleep*. 1985;8(4): 325–331.
17. Aldrich MS, Chervin RD, Malow BA. Value of the multiple sleep latency test (MSLT) for the diagnosis of narcolepsy. *Sleep*. 1997;20(8):620–629.
18. Bassetti C, Aldrich MS. Idiopathic hypersomnia. A series of 42 patients. *Brain.* 1997;120(Pt 8):1423–1435.
19. van den Hoed J, Kraemer H, Guilleminault C, et al. Disorders of excessive daytime somnolence: polygraphic and clinical data for 100 patients. *Sleep*. 1981; 4(1):23–37.
20. Trotti LM, Staab BA, Rye DB. Test-retest reliability of the multiple sleep latency test in narcolepsy without cataplexy and idiopathic hypersomnia. *J Clin Sleep Med.* 2013;9(8):789–795.
21. Lopez R, Doukkali A, Barateau L, et al. Test-retest reliability of the multiple sleep latency test in central disorders of hypersomnolence. *Sleep*. 2017;40(12).
22. Ruoff C, Pizza F, Trotti LM, et al. The MSLT is repeatable in narcolepsy type 1 but not narcolepsy type 2: a retrospective patient study. *J Clin Sleep Med.* 2018;14(1): 65–74.
23. Pataka A, Yoon CH, Poddar A, Riha RL. Assessment of multiple sleep latency testing in adults in Europe. *Sleep Med.* 2013;14(2):136–139.
24. Roehrs T, Roth T. Multiple Sleep Latency Test: technical aspects and normal values. *J Clin Neurophysiol.* 1992;9(1):63–67.
25. Tashiro J, Stefani A, Hogl B, Brandauer E, Poewe W, Heidbreder A. Influence of a post-test factor on the results of the Multiple Sleep Latency Test. *J Clin Sleep Med.* 2016;12(4):529–531.
26. Kanbayashi T, Inoue Y, Chiba S, et al. CSF hypocretin-1 (orexin-A) concentrations in narcolepsy with and without cataplexy and idiopathic hypersomnia. *J Sleep Res.* 2002;11(1):91–93.
27. Sansa G, Falup-Pecurariu C, Salamero M, Iranzo A, Santamaria J. Non-random temporal distribution of sleep onset REM periods in the MSLT in narcolepsy. *J Neurol Sci.* 2014;341(1-2):136–138.
28. Cairns A, Trotti LM, Bogan R. Demographic and nap-related variance of the MSLT: results from 2,498 suspected hypersomnia patients: Clinical MSLT variance. *Sleep Med.* 2019;55:115–123.
29. Seneviratne U, Puvanendran K. Excessive daytime sleepiness in obstructive sleep apnea: prevalence, severity, and predictors. *Sleep Med.* 2004;5(4):339–343.
30. Ryals S, Berry RB, Girdhar A, Wagner M. Second opinion: does this patient really have narcolepsy? *J Clin Sleep Med.* 2015;11(7):831–833.
31. Goldbart A, Peppard P, Finn L, et al. Narcolepsy and predictors of positive MSLTs in the Wisconsin Sleep Cohort. *Sleep*. 2014;37(6):1043–1051.

SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication July 8, 2020
Submitted in final revised form October 29, 2020
Accepted for publication October 29, 2020
Address correspondence to: Dr. John Goddard, Respiratory Department, Sunshine Coast University Hospital, 6 Doherty St Birtinya, QLD 4575;
Email: john.goddard@health.qld.gov.au and john.goddard@uqconnect.edu.au

DISCLOSURE STATEMENT

All of the authors have seen and approved the manuscript. The authors report no conflicts of interest.