

Evaluation of excessive daytime sleepiness

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Summary – Measures for assessing daytime sleepiness can be categorized into four general types – behavioral observation, laboratory performance, introspection, and physiological techniques. Each approach has its advantages and disadvantages. Thus, for example, observational techniques may provide a minimally ‘contaminated’ sample, but inferences may be quite difficult; laboratory performance measures may indicate vulnerabilities associated with sleepiness, but may be limited because of practice effects; introspection provides a personal perspective, but that point of view may be influenced by past history or ability to articulate; physiological measures may provide the most ‘objective measure’, but are difficult to apply to field studies. The Multiple Sleep Latency Test (MSLT) is the most thoroughly studied physiological measure of sleepiness relying upon serial assessments of the speed of falling asleep in standard conditions intended to optimize the sleep onset process. Procedures for administering, analyzing, and interpreting the MSLT are presented.

somnolence / multiple sleep latency test

Résumé – Évaluation de la somnolence. Les mesures pour évaluer la somnolence diurne sont de quatre types: observation comportementale, performance de laboratoire, autoquestionnaire et technique physiologique. Chaque approche a ses avantages et ses inconvénients. Par exemple les observations peuvent fournir des mesures écologiques mais elles sont perturbées par l'observation elle-même. Les performances en laboratoire peuvent indiquer des faiblesses en relation avec la somnolence, elles sont d'intérêt limité. L'autoquestionnaire donne une vue personnelle, il peut être influencé par l'histoire et les capacités du patient. Les mesures physiologiques peuvent fournir des paramètres objectifs mais sont difficiles à généraliser. Le test des multiples latences d'endormissement (MSLT) est la mesure physiologique la plus largement étudiée. Il repose sur des mesures successives de la vitesse d'endormissement dans des conditions standard favorisant le sommeil. Les procédures d'administration d'analyse et d'interprétation sont rapportées dans cet article.

somnolence / test des multiples latences d'endormissement

Categories of assessment

The assessment of daytime sleepiness can take myriad forms, although four categories of measurement subsume most approaches. The first of these categories is behavioral observation. We have come to associate many types of behavior with sleepiness. In one informal poll, for example, we queried university students to discover the behavior they say that they typically exhibit in the classroom when they are alert, sleepy, or neither alert nor sleepy. Figure 1 illustrates the results. Such behavior as yawning, closing eyes, and so forth was reported as being characteristic of sleepiness; whereas erect posture, alert appearance, and active note-taking characterized alert behavior. Observing such behavior may be useful for measuring one aspect of sleepiness. An analogous approach is the observation of social interactions, which are generally diminished in a sleepy person. For example, one might observe the quality and length of doctor-patient interactions to estimate whether long hours of on-call duty affect physicians' work with patients. There are, however, a number of drawbacks to behavioral measurement approaches including: setting conditions of observation to avoid interfering with the behavior itself; difficulty making assump-

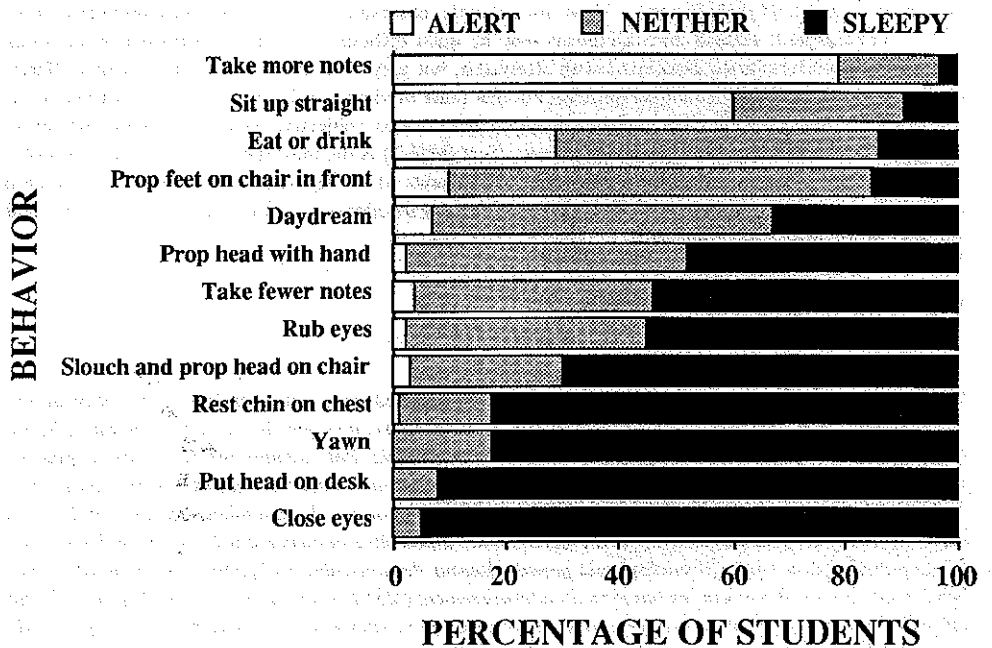


Fig 1. The results of a survey of university undergraduate students who were asked to indicate behavior they were most likely to exhibit in the classroom when they were sleepy, alert, or neither sleepy nor alert.

Table I. Advantages and disadvantages of the MSLT.

Advantages of the MSLT

Test results are not easy to fake either way, either to appear more sleepy or more alert. Thus, denial or mulling are unlikely to contaminate results.

The test involves no practice effects; day-to-day reliability is high.

Subjects and patients in most age groups are able to be tested with equal ease, with the exception of children too young to follow the simple instructions.

Motivation to perform is not relevant to outcome on the test.

Disadvantages of the MSLT

The technique requires a full day to perform and is therefore relatively time consuming for the patient, subject, and laboratory staff.

Outside of the confounds of a sleep laboratory setting, the technique is difficult to execute, since it relies upon technological expertise.

Results are not valid if the subject or patient is ill or in pain.

tions about the meaning of behavior that is observed; difficulty controlling environmental factors that may extraneously affect the behavior; and difficulty establishing standard conditions of observation.

A more common approach to measuring sleepiness – though somewhat indirect – is with laboratory performance. A variety of tests have been used, and traditionally the most sensitive seems to be long (*ie*, over 60 min), non-arousing, and subject paced. Dinges and Powell (1989) however, have recently validated a much shorter task that seems quite sensitive to variations of alertness/sleepiness. In many types of performance tests, sleepiness-related decrements are seen as lapses in performance. In my laboratory experience – based upon simultaneous recording of EEG and performance behavior – lapses are usually associated with microsleep episodes (Carskadon and Dement, 1979). Difficulties using performance as a measure of sleepiness include the following factors: making inferences about sleepiness from an individual's performance level at any given time is difficult, since performance is the product of a variety of factors of which sleepiness is just one; in certain performance testing paradigms, practice effects are large and often difficult to overcome; many tests lack an effective normative database with which to compare the performance level of a given patient; sensitivity of many performance tests to sleepiness level is uncertain.

A third, more common approach to assessing sleepiness is introspection. This type of measure can take many forms, including a simple inquiry: Are you sleepy or how sleepy are you? More sophisticated measures have been used, such as the Stanford Sleepiness Scale (SSS), developed by Hoddes *et al* at Stanford in the 1970s (Hoddes *et al*, 1973). A number of pitfalls to such measures have been identified including: the measure may be liable to denial on the part of certain individuals (Carskadon and

Dement, 1985); by contrast, introspective measures are also prone to deliberate falsification by malingerers who exaggerate sleepiness or by individuals who have a vested interest in appearing less sleepy and exaggerate alertness; the SSS in particular relies heavily on verbal skill level and is therefore difficult for individuals without well-developed verbal skills, such as children; many patients who have been excessively sleepy for a long period of time may have a skewed frame of reference for introspective analysis that may influence their response in a manner incompatible with comparison to normative samples; finally, the dimension of sleepiness/alertness *per se* may directly affect the ability to introspect.

Several types of physiological measures have been used to provide a more direct assessment of sleepiness. The earliest of these was pupillometry, which was used extensively in the Mayo Clinic for many years to evaluate sleepiness in narcolepsy and hypersomnolence (Yoss *et al*, 1969). Pupillometry takes advantage of the variations in pupil size – particularly instability of pupillary diameter – that accompany reductions in levels of alertness. Few strictly normative studies have been performed with this technique; therefore, it remains difficult to assess individual differences when using this technique. Nevertheless, several clinical centers are currently using pupillometry to gauge treatment efficacy in patients with narcolepsy. Evoked EEG potentials have also been related to levels of daytime sleepiness in clinical populations as well as experimental paradigms (Broughton, 1982; Broughton *et al*, 1982; Pressman *et al*, 1982). Such studies have been limited and the technique has yet to be applied widely.

The Multiple Sleep Latency Test (MSLT) is a physiological measure of daytime sleepiness/alertness developed at Stanford University in the late 1970s (Carskadon and Dement, 1977), and it is now probably the technique most widely used to assess sleepiness/alertness (Roth *et al*, 1989). The MSLT has been validated in numerous studies of normal individuals of various ages and under varying sleep/wake schedules, as well as in clinical populations. The MSLT is an operationally defined measure in which the speed of falling asleep on repeated tests is used to define the level of sleepiness. Its advantages and disadvantages are summarized in table I. The logic of the MSLT relies upon a simple conceptual framework: physiological sleepiness as measured by the MSLT reflects one's underlying predisposition to sleep – the brain's tendency to fall asleep; manifest sleepiness reflects how one feels or performs at a given moment, which can be measured by observation, introspection, or performance. Faster sleep onset parallels greater sleep tendency; slower sleep onset, greater alertness.

Method for administering the MSLT

The methods outlined below are taken from the recommendations of the Task Force on Daytime Sleepiness of the Association of Sleep Disorders Centers (Carskadon *et al*, 1986).

A number of general considerations are important before beginning the MSLT. When performed in a clinical or experimental setting, it is important to have some knowledge of the subject or patient's sleep for at least the preceding week, if not two weeks. This knowledge is usually obtained by having the individual keep a sleep log or sleep diary before coming into the laboratory. The necessity for this procedure results because the MSLT may be influenced not just by the single night preceding the test but by as many as seven nights before the test (Carskadon and Dement, 1981). It is also important to record the individual's sleep on the night immediately prior to the MSLT. In a clinical setting, this recording is made to rule out probable causes of the patients' complaint of sleepiness, such as sleep apnea or periodic leg movements. If an overnight polysomnogram has been previously recorded and ruled out such disorders, then in such instances it is possible to obtain an adequate assessment of the prior night's sleep by another method, such as actigraphy, that can provide sufficient information to determine whether the patient was attempting to sleep on the preceding night.

One of the more important issues to be considered before administering the MSLT is the drug status of the patient. Many drugs are known to affect sleep latency, as well as latency to REM sleep. Such drugs will have the effects during acute and chronic administration and will also affect the individual's sleep during the acute withdrawal period. The MSLT guidelines suggest a two-week withdrawal period for most drugs a sleepy patient is likely to be taking. Such a withdrawal period is difficult for many patients and clinical judgement must be exercised. It cannot be forgotten however, that compounds such as tranquilizers, sleeping pills, and antihistamines will shorten sleep latency while stimulants such as caffeine etc will lengthen sleep latency. When acutely withdrawn from high doses of these compounds, the opposite is likely to occur. Thus, it is important to have a sufficiently long drug-free period to eliminate both the direct and withdrawal effects. By the same token, compounds such as tricyclic antidepressants, monoamine oxidase inhibitors (MAOI), and amphetamines suppress REM sleep while they are being taken, and thus lengthen REM sleep latency, even in patients with narcolepsy. When they are acutely withdrawn, these compounds may result in a rebound of REM sleep and decreased REM latency, which could produce false positive results on the MSLT. Hence, great care in assessing a patient's drug status is important. Occasionally, an individual will come to a laboratory claiming not to be taking any medication, although comments to a technologist may suggest that drugs are indeed being used. In such cases, precautionary urine drug screens may be useful. A final word about caffeine and alcohol may be useful. It is recommended that patients do not consume caffeinated or alcoholic beverages on the day of MSLT testing. In a patient or subject who has become accustomed to high doses of caffeine, however, restricting intake may result in an acute withdrawal syndrome that will have a lengthening effect on sleep latency. Hence, when considering the patient or subject's drug status, gradual withdrawal from caffeinated beverages before the MSLT may be useful.

In general, each MSLT is to be performed in a setting that maximizes the opportunity to fall asleep. Thus, the individual and the environment should be free from com-

PROTOCOL FOR MSLT

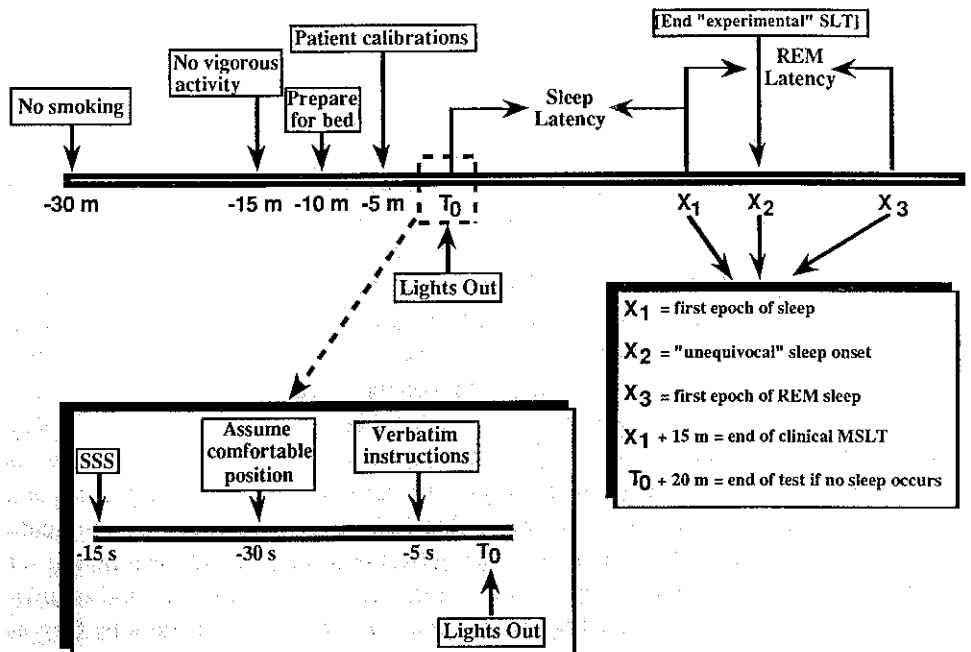


Fig 2. The specific procedures recommended for each test in a day's Multiple Sleep Latency tests. The inset expands the time-line for the minute preceding the start of the test.

peting stimuli. The person should not be hungry, should have relieved the urge to use the toilet, and the environment should be a comfortable bedroom that can be darkened and protected from external noises.

The recommended recording montage for the MSLT includes the parameters as described in the standard manual of Rechtschaffen and Kales (1968): central electroencephalogram (EEG), right and left electro-oculogram (EOG), and mental/submental electromyogram (EMG). In addition, the ASDC Task Force recommended continuous monitoring during the MSLT of the following parameters: i) electrocardiogram (EKG); ii) EEG from an occipital placement in order to assist in the visualization of alpha rhythm (useful for identifying the onset of sleep); iii) a vertical electro-oculographic (EOG) lead, which is frequently useful for identifying REM sleep in individuals with narcolepsy; iv) sounds of respiration noises, which may be useful in patients with sleep apnea to identify when such breathing noises may have caused an arousal. Recording of other measures is at the discretion of the individual laboratory. Another parameter that might be useful, for example, is anterior tibialis EMG in a patient with restless leg syndrome who may demonstrate prolonged sleep latencies in association with excessive leg movements.

The specific procedures used in the MSLT are depicted in figure 2, which illustrates the recommended time-line for an individual test. It should be borne in mind that the ASDC Task Force recommends a minimum of four tests occurring at two-hour intervals during a single day. The tests should begin within three hours following the termination of nocturnal sleep. The Task Force emphasized that the patient or subject should be up and dressed in street clothes before the start of the procedure. In addition, a meal (breakfast) is commonly given to the subject or patient before the day's first MSLT.

As shown in figure 2, the subject or patient should be asked not to use tobacco within 30 min preceding the start of each sleep latency test (SLT). The technologist should explain this procedure to patients in advance so that they are not surprised by the denial of smoking privileges. During the 15 min before the start of each SLT, the patient should refrain from vigorous activity and begin preparing for the test. During this interval, the technologist should perform an impedance test to verify continued viability of the electrode hook-up. The immediate preparation for a test involves having the patient remove his or her shoes and loosen restrictive clothing, in order to be as comfortable as possible during the test. Changing into sleepwear or pyjamas is not recommended. Approximately five min before the beginning of the test, the patient should be in bed to perform a standard set of 'patient calibration' procedures. Most laboratories have an established standard procedure for evaluating the efficacy of the recording; this procedure actually serves as a part of the MSLT that tends to relax the patient.

Following patient calibrations, it is usual to ask the subject to give an introspective rating of alertness/sleepiness. Although this rating is not crucial to the MSLT *per se*, it may take on relevance in the clinical context. Thus, the physician can use the MSLT measure as a way of gauging the patients' subjective characterization of alertness. Before the MSLT instructions are given and the test starts, the patient should be asked to get comfortable. In my laboratory, we request that subjects get into their 'favorite going-to-sleep position'. At this time, a standard script is repeated verbatim to the patient instructing him/her to lie still with eyes closed and try to fall asleep. The wording of this instruction should be identical on repeated test occasions. Whoever administers the test, therefore, it is important that the laboratory have a script for this part of the procedure to be used consistently by all technical staff. The salient features of the instructions for the MSLT are that the patient is asked to try to remain immobile with closed eyes and not to resist falling asleep. After reading the instruction script, the technologist extinguishes the bedroom lights, leaves the room, and closes the door, thus marking the start of the Sleep Latency Test.

Ending the MSLTs and measuring latencies

The following descriptions include only those procedures used in a clinical setting, where the MSLT serves a diagnostic/evaluative role. (Instructions for an 'experi-

mental' version of the MSLT are included in the standard guidelines (Carskadon *et al*, 1986). As recommended by the ASDC Task Force, the Sleep Latency Test ends after 20 min if no sleep has occurred. This value (20 min) is assigned as the sleep latency for any such individual test. If the patient falls asleep, the test should be continued for an additional 15 min. The Task Force recommended a 30-s scoring epoch for evaluating the MSLT record. Using a 30-s epoch, therefore, the 15-min episode begins when the subject experiences ≥ 15 s of sleep. At the end of the 15 min, the patient is aroused and the test terminated. Patients must be kept awake between the Multiple Sleep Latency Tests, since the inadvertent occurrence of sleep, especially REM sleep, will likely have a direct impact on subsequent sleep, resulting in a failure to have REM sleep (due to the refractory period) and a false negative test. One common question concerns whether to awaken the patient from an MSLT as soon as REM sleep is observed. This procedure is not recommended due to the difficulties that may be involved with a technologist making an 'on-line decision' of this nature. If the decision to wake is made erroneously, the test is not valid.

The measurement of latencies on the MSLT is depicted in figure 2, in which various events are denoted by the letter X with subscripts. Extinguishing the bedroom lights marks the start of the test or time zero (T_0). Sleep latency is measured as the interval between T_0 and X_1 , the first epoch scored as sleep. (X_2 is the termination point for an experimental MSLT and not relevant for clinical assessment.) X_3 , the first epoch of REM sleep, is an important marker that establishes REM latency: the elapsed time between X_1 (the onset of sleep) and X_3 (the onset of REM sleep). $X+20$ denotes the termination point of the MSLT (20 min after lights out) if no sleep at all occurs.

When writing a report of findings from the MSLT, it is important to include i) the results of the preceding night's recording; ii) a test-by-test listing of sleep latency values; iii) a test-by-test listing of REM latency for the MSLT, as well as the REM latency from the previous night's sleep recordings; iv) a summary score sleep latency across all four tests, which may be either a mean or median value; and v) the REM latency average. Interpretation of the findings on the MSLT is straightforward and involves recalling a key assumption of the test: faster sleep onsets are associated with greater sleepiness and slower sleep onsets with greater alertness. Several studies have suggested an average MSLT value of 5 min or less to indicate a pathological level of sleepiness (Richardson *et al*, 1978; Van den Hoed *et al*, 1981). Data from a number of studies I have performed indicate that this level of sleepiness is associated with performance decrements, unintended episodes of sleep, and difficulty maintaining vigilance in an environment lacking external stimulation (Carskadon and Dement, 1979; Carskadon and Dement, 1981; Carskadon *et al*, 1981; Carskadon *et al*, 1985). Such pathological values are seen in patients with narcolepsy and sleep apnea and may also be seen as 'normal individuals' who have been sleep deprived or who have obtained insufficient sleep. The presence of REM sleep in two or more of the day's MSLTs is clearly supportive of the diagnosis of narcolepsy. The assessment of this sleep-onset structure abnormality should include the previous nights' REM sleep latency, as well as from

the daytime MSLTs. It is very clear, however, that rare cases may show only one sleep-onset REM episode in the face of clear description of the clinical picture by the patient. In such cases, the physician's clinical judgement is vital. Given careful attention to the laboratory procedures, such instances should be extremely rare.

In summary, the Multiple Sleep Latency Test appears to be an effective and useful tool for assessing daytime sleepiness in a variety of situations. Its diagnostic usefulness for narcolepsy has been well established; however, its usefulness in assessing therapeutic outcome is less clear. One of the earliest studies of MSLT involved assessment of sleepiness in patients with sleep apnea syndrome in whom tracheostomy was performed: in every case, a significant increase in sleep latency was observed (Dement *et al.*, 1978). Subsequent studies have also shown lengthening of sleep latencies with treatment, as well as reduction in the number of sleep-onset REM episodes in patients with narcolepsy. Nevertheless, controversy continues, and other types of tests that emphasize resisting falling asleep have been introduced, particularly for evaluating therapeutic outcome.

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