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Sleepiness and vigilance tests

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Summary

Objective assessments of subjective complaints such as sleepiness, tiredness or fatigue using sleepiness and vigilance tests aim to identify its causes and to judge the fitness to drive or to work of the affected person. "Vigilance" comprises wakefulness, alertness and attention and is therefore not merely reciprocal to sleepiness. Since it is a complex phenomenon with several dimensions it is unlikely to be appropriately assessed by one single "vigilance test". One important dimension of vigilance discussed here is wakefulness with its counterpart of overt sleep and the whole spectrum of various levels in between. The transit zone between full wakefulness and overt sleep is mainly characterised by the subjective complaint of sleepiness, which cannot be measured directly. Only the consequences of reduced wakefulness such as a shortened sleep latency, slowed cognitive function and prolonged reaction time can be measured objectively. It is, therefore, more promising to combine a battery of subjective and objective tests to answer a specific question in order to achieve the most appropriate description for a given clinical or medico-legal situation. However even then we must keep in mind that many other important aspects of fitness to drive / fitness to work such as neurological, psychiatric and neuropsychological functions including risk taking behaviour are not covered by vigilance tests. A comprehensive, multidisciplinary approach is essential in such situations.

Key words: vigilance; sleepiness; fatigue; tiredness; MSLT; MWT

Excessive daytime sleepiness (EDS), tiredness and fatigue

Sleepiness, tiredness or fatigue are frequent complaints which must be thoroughly analysed and scrutinised by the treating physician with respect to both its causes and its consequences.

Sleepiness is a basic physiological need comparable to hunger or thirst, which is satisfied by sleeping, eating or drinking respectively and thus serves survival of the organism. Physiological sleepiness, also called "sleep pressure", increases whilst being awake and underlies a circadian rhythm according to the two process model [1]. The subjective feeling of sleepiness characterises a poorly defined transit zone between full wakefulness and overt sleep. This subjective sleepiness can only be described by the individual and is not amenable to direct measurement. Strictly spoken, the assessment is restricted to causes and consequences of sleepiness. The sleepiness state also includes functional impairments of concentration, wandering thoughts, blurred vision, heavy eye lids and the increasing craving for sleep. The behavioural indicators are yawning, reduced activity, ptosis, eye rubbing, head and eyelid drooping and the like. The consequences include shortened sleep latency, attention deficits, slowed cognitive functions and reaction times with consecutively impaired performance, leading to work or motor vehicle accidents. The only physiological method to reduce sleepiness is to get sleep.

Distinguishing between "sleepiness" on the one hand, and "tiredness" and "fatigue" on the other hand is an important diagnostic step. **"Tiredness"** is a common complaint of depressed patients and means lack of energy and initiative, which can be improved by rest, not neces-

List of abbreviations

EDS	Excessive Daytime Sleepiness
ESS	Epworth Sleepiness Scale
CPAP	Continuous Positive Airway Pressure
KSS	Karolinska Sleepiness Scale
MSLT	Multiple Sleep Latency Test
MWT	Maintenance of Wakefulness Test
OSLER	Oxford Sleep Resistance
PVT	Psycho-Vigilance Test
REM	Rapid Eye Movements
R&K	Rechtschaffen and Kales
SAS	Sleep Apnoea Syndrome
SOREM	Sleep Onset REM
SSS	Stanford Sleepiness Scale
VAS	Visual Analogue Scale

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sarily by sleep. It is notable that patients with insomnia suffer from "tiredness" rather than sleepiness during the day. Typically, they are not able to fall asleep when given the opportunity to do so in spite of feeling tired.

"Fatigue" is a physiological phenomenon also described as "time-on-task-performance decrement". This phenomenon – at least theoretically – can be relieved by changing the task. In clinical medicine it refers to an abnormally great deterioration of performance during psychic or physical tasks, as exemplified in chronic fatigue syndrome.

Prevalence rates of **excessive sleepiness** (EDS) up to 15% were reported in young adults and elderly people. The major causes include sleep insufficiency syndrome, irregular sleep-wake rhythm (shift work, jet lag), sedative drugs, sleep apnoea syndrome (SAS), narcolepsy, idiopathic hypersomnia and non-organic hypersomnia. It is generally assumed that EDS in narcolepsy is, on average, more severe than in other conditions of hypersomnia. Yet type and severity of EDS also show great variability among narcoleptic patients.

Theoretically, the causes of sleepiness or impairment of vigilance can be divided into two major categories, those which increase sleep pressure (REM and NREM) and those which reduce vigilance. The term vigilance has been used somewhat variably, but is now mostly used synonymously with sustained attention or tonic alertness [2]. Following this usage it is not quite correct to subsume the multiple sleep latency test (MSLT) under the term "vigilance tests", since no active performance and attention is required during the MSLT, which basically assesses sleep pressure. As such MSLT is nevertheless a prerequisite to interpret the results of vigilance tests. Factors modulating the capacity to maintain tonic alertness or vigilance include individual motivation, task derived physical and intellectual activation, monotony, temperature, light conditions, whole body vibrations and heavy meals. These factors are not regarded as direct causes of EDS but rather unmask an underlying increased sleep pressure.

Assessments

Since sleepiness, wakefulness and vigilance combine to give a rather complex picture, how then can this multidimensional phenomenon be assessed? We should learn not to search for the *one* gold standard assessing method but rather search for the optimal test battery with respect to the individual situation. In order to choose the appropriate methods, one must first and always define the goal of an assessment: Is it to establish (1) the presence of, or (2) the absence of sleepiness, or (3) to monitor changes in sleepiness in a given patient? Furthermore, we must consider the actual purpose of the assessment: Is it for (4) clinical purposes, (5) research, or (6) for medico-legal purposes (such as assessing fitness to drive)? Finally and most importantly, we must always consider the possibility of unspoken or ulterior motives: Are there psychological factors or is there even a hidden agenda aiming at a (7) primary or (8) a secondary gain of the disorder (e.g., malingering narcolepsy to acquire access to amphetamines or pretending good alertness in order to regain a driving licence)?

Questionnaires

The history obtained by the experienced sleep specialist including an interview with the patient's partner is certainly the most important source of information needed to reach a comprehensive judgement of EDS in the clinical context. Standardised scales are specifically designed to assess sleepiness and also help to distinguish sleepiness from fatigue.

The *Epworth Sleepiness Scale* [3] (ESS) is at present the most widely used subjective sleepiness scale in clinical practice. This questionnaire is based on the likelihood of falling asleep, which has to be rated by the patient for eight different social situations. The popularity of the ESS is due to its simplicity and brevity and to the fact that the test can be done by the patient without help from the physician. Furthermore, in treatment studies of sleep apnoea patients and patients with narcolepsy [4] it shows a good test-retest reliability, correlates with other subjective sleepiness scales and can measure improvement. The ESS correlates negatively with health related quality of life scale in SAS [5] and correlates positively with the likelihood of falling asleep at the wheel [6] and with the risk of suffering a work injury [7]. This underlines the usefulness of this simple instrument in practical medicine, as long as it is used in the context of the clinical picture and together with complementary vigilance tests. One disadvantage is that the test is not useful for re-administration in short intervals e.g., when evaluating circadian sleepiness. No studies using the ESS have shown a clear group difference between sleepiness in narcolepsy and other causes of EDS, although the average score in narcolepsy is often among the highest of all patient groups [3]. Normal values as assessed by Johns in the original work [3] were set at 5.9 ± 2.2 or between 2 and 10 of the maximum of 24 scoring points.

The weak or lacking correlation between ESS and MSLT [8, 9] and between ESS and MWT [10] should not be taken as a shortcoming of these tests, but rather as pointing at the different facets of sleepiness which are differentially assessed [10]. In a clinical setting one therefore cannot rely on a single method of assessing sleepiness. We agree with Sangal et al. [10] that more than one method is required for making clinical decisions.

The *Stanford Sleepiness Scale* [11] (SSS) is based on a Likert self-rating Scale with seven degrees of severity. This method can be applied repetitively to assess the momentary subjective (introspective) sleepiness and can even be repeated at short intervals, for instance, to study

circadian sleepiness. Comparison between subject or patient groups using the SSS are problematic, since normative data do not exist. The *Karolinska Sleepiness Scale* (KSS) [12] and the visual analogue scale (VAS) are other possibilities to assess subjective sleepiness. Cognitive test procedures are also sensitive to sleep deprivation, but these tests need specific training and are not suitable for standardised bed-side tests.

Multiple sleep latency test (MSLT)

The MSLT consists of a series of four to six nap opportunities at two hour intervals during the day beginning approximately two hours after morning awakening. The test measures the propensity for falling asleep in a comfortable situation lying in bed in a dark and quiet room with explicit permission to fall asleep. Two different versions of the MSLT exist, a clinical and a research version [13]. In the research version the accumulated sleep during the tests is minimised by always wakening the sleeper after sleep onset, defined as either the occurrence of one epoch of sleep stage 2 to 4 or REM sleep, or the occurrence of three subsequent epochs of sleep stage-1. In the clinical version, the patient is not awakened after sleep onset because a second objective of the test is to detect possible early REM sleep, so called sleep onset REM periods (SOREM). If a REM sleep episode occurs within 15 minutes after sleep onset, it is defied as SOREM. Therefore, each test session continues for 15 minutes after sleep onset, defined here as one epoch of any sleep stage. If no sleep occurs, the nap opportunity is terminated after 20 minutes in both versions of the MSLT.

The MSLT has sometimes been considered to be the "gold standard" for measuring sleep pressure [14]. However, the standard polysomnography, which has to be performed in the preceding night, does not take into account the individual sleep duration, which in turn can affect the MSLT, particularly in long sleepers. For this reason, it is useful to have the patient keep a sleep diary [14]. This should be done one week prior to the MSLT, since MSLT values can be influenced by sleep loss up to seven nights beforehand [15]. A simultaneously performed actigraphy additionally helps to detect unusual sleep-wake habits.

An average sleep latency of five minutes or less is assumed to indicate abnormal sleepiness, whilst an average sleep latency of over ten minutes is considered normal with a diagnostic grey area between five and ten minutes. As expected, the sleep latency as assessed by the MSLT correlates with the sleep latency of polysomnography. On the other hand, the correlation between MSLT and test values of sleep quality obtained by polysomnography or subjective scores of EDS in SAS and narcolepsy were found to be weak or absent. Situational arousal could explain some discrepancies between MSLT results and subjective sleepiness scores in other disorders [16]. Therefore, the debate on what is actually measured by the MSLT, and whether it should be taken as the gold standard for sleepiness, still continues [17].

The MSLT has only limited value in diagnosing a specific EDS causing disorder. Nevertheless, clearly abnormal sleep latencies of less than five minutes are most often found in narcolepsy [18], whereas the sleep latency of sleep apnoea syndrome, idiopathic hypersomnia [18] or sleep insufficiency syndrome [19] more often fall in the "grey area" range between five and ten minutes, whereas the longest latencies are found in insomnia patients [20]. Most patients with depression suffer from insomnia [21] with prolonged MSLT latency, but in atypical depression or in non-organic hypersomnia depression can be accompanied by objective sleepiness.

A hallmark of narcoleptic sleep is the occurrence of sleep onset REM periods (SOREM) i.e., REM sleep within 15 minutes after sleep onset as first described by Vogel et al. [22]. Although an MSLT with ≥2 SOREMs and <5 min mean sleep latency indicates narcolepsy with a sensitivity of 70% and a specificity of 97%, 30% of the subjects with this combination do not have narcolepsy [23]. These features were also found in 4.0% to 25% of sleep apnoea patients [23, 24]. Due to the much higher prevalence of patients with sleep related breathing disorders as compared to narcolepsy in most sleep centres, the false positive results of such patients explain the rather low positive predictive value (PPV) of 70% for narcolepsy. Patients with depression, sleep insufficiency syndrome or inadequate sleep hygiene may also show short sleep latency and SOREMs, and this is not so infrequent. In summary, it can be concluded that the MSLT results typical of narcolepsy are neither sufficient nor obligatory to diagnose narcolepsy, and it should be stressed that the MSLT must be interpreted in conjunction with the clinical and other paraclinical findings.

Limitations of the MSLT

There are essentially two critically discussed aspects of the MSLT:

(1) While the MSLT seems suitable to assess sleep propensity as such, it is not the appropriate method to assess the ability to stay awake if required i.e., to judge the suitability for driving or fitness for duty. In order to answer this question, most experts would rather rely on the maintenance of wakefulness test (see below). Likewise, the inability of the MSLT to detect a possible therapy induced improvement of sleepiness in narcolepsy is a significant shortcoming [25].

(2) A methodologically critical point is the definition of sleep onset in the MSLT. According to the official guidelines [14, 26] sleep latency should be measured from lights off to the appearance of the first sleep epoch i.e., 30 seconds of sleep stage-1. However, to be on the safe side, several experts prefer to rely on 30 seconds of "unequivocal sleep" that is sleep stage 2, 3, 4 or REM

or alternatively three consecutive epochs of sleep stage-1. On the other hand, depending on the objective of the test, the one sleep stage-1 epoch criterion could perhaps also be too strict to be sufficiently sensitive [27]. The criteria introduced by Rechtschaffen and Kales (R&K) in 1963 [28] ignore states of drowsiness or sleepiness when moving from wakefulness to R&K NREM stage-1, which is particularly dissatisfying in the MWT. In order to close this gap, an adapted scoring method has been proposed [29] using a minimal "epoch duration" of 0.5 seconds and including several stages of drowsiness.

(3) It is obvious that by deliberately or perhaps subconsciously resisting falling asleep, the sleep latency of an MSLT can be falsely prolonged with the possibility of a false negative result.

Maintenance of wakefulness test (MWT)

This test is now frequently used to assess the ability to stay awake in cases where the suitability for driving [30] or fitness for duty is questioned [31]. The subject is usually sitting rather than lying in a bed and, most importantly, is instructed to stay awake. The original test was performed in trials of 20 minutes, but later, because ceiling effects were observed with the 20 minutes trials some experts have proposed 40 minutes instead. Others used a latency criterion of one epoch of any stage [32], whereas in later studies the criterion of three stage-1 epochs was used [30, 33]. With either version, the MWT has now been applied to numerous patients with narcolepsy [33], SAS [30] or both [32]. The first systematic study to define normal values was performed by Doghramji et al. in 1997 [34]. Similar values have been obtained in an Australian study in 31 randomly recruited healthy subjects [35], although they used much brighter light conditions (1 lux). In a large multi-centre treatment trial on patients with narcolepsy free of psychoactive drugs [25], the 20 minutes version of MWT revealed a mean sleep latency of 6.0 ± 4.8 minutes to sustained sleep. Only 1.5% of all narcoleptics were able to remain awake during all four 20-minutes trials compared to 55% of normal controls in Doghramji's study, and 14.5% of the narcoleptics had a mean latency of >12 minutes as compared to 95% of the normal controls.

A mean sleep latency of >15 minutes during the MWT was proposed as a prerequisite for driving ability by some researches, who based their conclusion on normal values [30, 31]. However, in contrast to this rather low limit, we agree with other experts, who demand – at least for professional drivers (taxi, bus, lorry, pilots, engine) – a much higher limit of >30 or even 40 minutes as prerequisite for allowing a patient to drive (M Partinen, J Horne, personal communications). These experts argue correctly that normal MWT values cannot be used to judge fitness to drive, since falling asleep at the wheel obviously has dramatic consequences and therefore improves the motivation to remain awake, whist the MWT measurement is done without any pressure on the participants, such as a punishment for a short latency. Since no pertinent studies are available correlating the MWT results with the risk of motor vehicle crashes, a well-founded limit of MWT measured mean sleep latency cannot yet be proposed. A recent study comparing MWT results with a driving simulator has revealed a sleep latency below 20 minutes to be associated with a greater risk of performance errors in the simulator [36] and this is a commonly applied limit for personal driving. Whereas formal guidelines are available for the performance of the MSLT [37], no universally accepted guidelines exist for performance of the MWT [38]. The condition under which the MWT is performed e.g., with or without stimulants, coffee or naps in between has to be decided depending on the aim of this study.

Recommendations for the practical approach of the physician when facing a sleepy driver were outlined recently by a commission of the Swiss Society of Sleep Research, Sleep Medicine and Chronobiology (SSSSC) [39].

A second indication of the MWT is in the assessment of treatment effects, for which the MWT has been shown to be more suitable than the MSLT [25, 26, 31, 40].

Direct comparison between the MWT and the MSLT performed on the same day [31, 32] showed only a weak correlation between MSLT and MWT results (rho = 0.41). Variance of the MWT values accounted for only 16% of the variance of MSLT values, indicating that the test results were relatively independent. Low to inexistent correlations between different vigilance tests were also found in our own analysis of several hundreds of patients with EDS due to various conditions (unpublished). From these data it has become apparent that sleepiness and alertness cannot be considered as mere reciprocal qualities [31]. It must, on the contrary, be concluded that subjective sleepiness and lack of alertness both include several components, based on various brain mechanisms: (1) The ability to fall asleep when allowed to do so as assessed by the MSLT, (2) the inability to stay awake when required to as measured by the MWT, (3) a reduced attention as measured by cognitive neuropsychological performance tests, reaction time tests, driving simulators, and long latency evoked potentials, (4) tiredness or loss of energy ascertainable only by subjective tests, (5) fatigue in the sense of a time-on-task performance decrement, which may be a separate component or a complex composite of all other components. The MWT is, of course, not immune to the theoretical risk of falsification, when using it for diagnosis of EDS. If a subject deliberately does not resist falling asleep, a false positive result may result.

To obtain a more complete picture, a combination of the MSLT with the MWT on the same

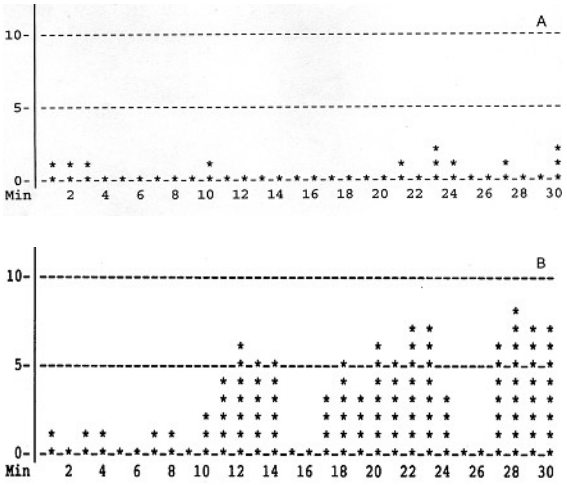

Figure 1

Result from the steer clear reaction time test in a normal, fully awake subject (A) and in a patient with narcolepsy (B) and severe daytime sleepiness. The X axis represents the time axis with a full range of 30 minutes, the duration of the test; the Y axis represents the error rate per minute in % of obstacles.

day was suggested. Yet reducing the number of MSLT trials too much impairs its reliability. In addition, the clinical version of the MSLT allowing up to 15 minutes of sleep may influence the result of the subsequent MWT. We propose alternating MSLT and MWT procedures on the same day only for diagnostic purposes, but not when medico-legal issues of alertness and fitness are in question.

Reaction time tests

In the "Steer Clear"-reaction time test a two lane street is presented on the PC and the subject has to press a button to avoid hitting obstacles, which appear randomly on either lane during the 30 minute test duration. Instead of measuring reaction time, the number of performance failures ("hits") is counted in percentage of all obstacles, representing reaction times above a certain duration (fig. 1).

The Oxford Sleep Resistance test (OSLER), developed as a substitute for the MWT, uses a behavioural element to determine sleep onset [41]. The subjects have to press a switch in response to the flash of a light emitting diode, lightening up every three seconds for one second. Sleep onset is defined as the failure to respond to the light in seven consecutive illuminations. The psycho-vigilance test (PVT) is another simple visual reaction time test [42] with continuous feed back information on reaction time. The number of lapses, defined as a reaction time greater than 500 ms, is counted as a measure of reduced performance. The test is sensitive to circadian changes of sleepiness and effects of sleep deprivation in healthy subjects [43], night shift effects and effects of CPAP treatment in SAS, despite its short duration of only 10 minutes. Such simple reaction time tests requiring an active participation of the subjects are very useful additive tests for assessing performance, but should not be used in isolation, because the results do not allow a discrimination between lack of motivation in depression and increased sleep propensity.

Pupillography

Several studies have shown that the diameter of the pupil is inversely and its variability over time positively related to subjective complaints of sleepiness [44]. The method has been used mainly in a clinical environment to assess EDS because it requires little co-operation and is hence very objective. It has been shown to be sensitive to sleep restriction in healthy subjects [44]. The method provides reliable results when comparing sequential tests in the same individual, but seems less suitable when comparing one subject with another [13] or between different studies.

Driving simulators

Patients with EDS are at a higher risk of motor vehicle accidents due to falling asleep at the wheel [45], and a large proportion of motor vehicle accidents in a driving population are due to sleepiness [46]. Various sophisticated driving simulators exist with the aim to answer the crucial question of whether a patient with EDS (or other impairments) is fit to drive a motor vehicle properly or not. Particularly when testing professional drivers such "realistic" test procedures are indicated.

Actigraphy

Actigraphy cannot be used to assess sleepiness at a specific time of the day. However the inactivity periods, which can be objectively recorded over several days, can help to define an increased "time in bed", which could be a consequence of "hypersomnia". Distinction from liability to remain in bed due to depression or chronic fatigue syndrome must, however, be based on additional clinical information.

In summary, we recommend the use of a *battery* of sleepiness and vigilance tests in conjunction with the clinical findings to identify causes and consequences of EDS and we cannot support the wishful idea, that fitness to drive can be judged by a single short lasting test. Obviously "passive tests" such as the MSLT are preferred when the aim is to objectively measure sleep pressure (= sleepiness tests), while active tests such as the MWT or driving simulators or other reaction time tests (= vigilance tests) are preferred to measure the capacity to remain awake. In addition, it is important to realise, that the tested sleep-wake-axis is only one of multiple dimensions relevant to safe driving. Neurological, psychiatric and neuropsychological functions including risk taking behaviour are not covered by vigilance tests and deserve a comprehensive multidisciplinary approach.

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