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Original Article

Automatic slow eye movement (SEM) detection of sleep onset in patients with obstructive sleep apnea syndrome (OSAS): Comparison between multiple sleep latency test (MSLT) and maintenance of wakefulness test (MWT)

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ABSTRACT

Objective: To determine whether automatic slow eye movement (SEM) analysis performs comparably to standard sleep onset criteria at the multiple sleep latency test (MSLT) and at the maintenance of wakefulness test (MWT) in patients with obstructive sleep apnea syndrome (OSAS).
Methods: We compared sleep latencies obtained upon standard analysis of MSLT and MWT recordings with automatically detected SEM latencies in a population of 20 severe OSAS patients that randomly underwent the two tests 1 week apart.
Results: Eight of 20 OSAS patients had EDS as answered by the Epworth Sleepiness Scale (ESS). Mean SEM latency performed comparably to standard sleep onset in both the MSLT (6.4 ± 5.5 min versus 7.4 ± 5.1 min, $p = 0.25$) and the MWT (25.2 ± 14.5 min versus 24.4 ± 14.0 min, $p = 0.45$) settings. Mean SEM latency significantly correlated with the sleep latency at the MSLT ($r = 0.52$, $p < 0.05$) and at the MWT ($r = 0.74$, $p < 0.001$). Finally, the Epworth Sleepiness Scale score correlated with SEM latency at the MWT ($r = -0.62$, $p < 0.01$), but not at the MSLT.
Conclusions: Automatic SEM detection performed comparably to standard polysomnographic assessment of sleep onset, thus providing a simplified technical requirement for the MSLT and the MWT. Further studies are warranted to evaluate SEM detection of sleep onset in other sleep disorders with excessive daytime sleepiness.

1. Introduction

Excessive daytime sleepiness (EDS) is defined as the inability to stay awake and alert during the major waking episodes of the day [1]. The prevalence of EDS among adults has been reported as high as 12% [2]. The significant impact of EDS on car accidents, work safety and public health has been widely reported in the literature [3–5].

Objective measurements of EDS have proven problematic. Several methods have been used in evaluating EDS, from subjective scales such as the Stanford Sleepiness Scale [6] and the Epworth Sleepiness Scale [7], that attempt to measure state and trait sleepiness, respectively, to objective laboratory based tools that evaluate sleep latency in different conditions. Among the latter are the multiple sleep latency test (MSLT) [8] and the maintenance of wakefulness test (MWT) [9], the recommended objective tests for the evaluation of EDS for clinical and experimental purposes [1].

The MSLT measures a subject's ability to fall asleep; in each session the subject is instructed to "please lie quietly, assume a comfortable position, keep your eyes closed, and try to fall asleep" [1,8]. The MWT measures a subject's ability to stay awake in a quiet, non-stimulating situation for a given period of time; in each session the subject is instructed to "please sit still and remain awake for as long as possible, look directly ahead of you, and do not look directly at the light" [1,9]. Therefore, the MSLT assumes that sleepiness is equivalent to a high proneness to sleep in an appropriate setting, whereas the MWT considers an inability to maintain wakefulness in a boring situation. Each MSLT and MWT session involves the recording of EEG, EOG and EMG for the detection of sleep onset.

As recommended by the Task Force of the American Academy of Sleep Medicine [1], the MSLT is not specifically aimed at the investigation of sleepiness in patients with OSAS, but represents a major diagnostic tool for the differential diagnosis of hypersomnias of central origin (with emphasis on sleep onset Rapid Eye Movement

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[REM] period detection for the identification of narcolepsy). Conversely, the MWT is better adapted to evaluate individuals who must remain awake for public safety reasons (such as truck drivers or pilots), as well as to assess the response to treatment in patients with EDS [1]. MSLT and MWT are expensive, all day tests; they require a laboratory setting that vaguely resembles real life, and they need the obligatory and dynamic presence of an expert laboratory technician.

Slow eye movements (SEMs) are low frequency (mainly 0.2–0.6 Hz), rolling, horizontal, bidirectional and conjugate movements of the eyes [10]. SEMs are a phenomenon typical of the wake–sleep transition [10–16]. Several studies have correlated SEM appearance with the EEG counterpart [15,17–19] and with the behavioural responses typical of drowsiness [20]. SEM could thus represent a useful marker of drowsiness, sleep onset and consequently EDS.

We already developed an automatic method for the detection of SEM [21–23] that has been validated against visual scoring on either 8- or 24-h polysomnographic recordings. Recently, we applied our technique to MSLT recordings performed in subjects with normal MSLT and in OSAS patients, disclosing equal performance of SEM detection versus standard measurements of sleep onset [24].

The aim of the present study was to perform an automatic SEM detection on both the MSLT and the MWT recordings of a new set of patients with severe OSAS (i.e., having an apnea–hypopnea index [AHI] higher than 30) [25,26], associated or not with EDS, in order to test our automatic method on the MSLT recordings and to assess its relative performance versus the MWT recordings.

2. Patients and methods

Twenty men with a definite clinical diagnosis of severe OSAS participated in the study. They were consecutive patients selected on the basis of the following selection criteria: (1) diagnosis of severe OSAS established by nocturnal portable monitoring (Embletta®–Embla Systems, Broomfield, CO) performed at the patient's home (showing an AHI over 30) according to current diagnostic criteria [25,26]; (2) acceptance of written informed consent to participate in the study; (3) absence of other significant medical or sleep disorders; (4) absence of chronic use of drugs interfering with daytime alertness; (5) absence of alcohol abuse; (6) no consumption of more than five caffeinated beverages; and (7) smoking not more than 10 cigarettes per day. They had a mean age (±standard deviation [SD]) of 54 ± 9 years, a mean body mass index (BMI) of 31.6 ± 3.6 kg/m^2 and a mean AHI of 48.8 ± 13.6, with an oxygen desaturation index (ODI) of 49.1 ± 16.6 events per hour of sleep and a minimum O_2 saturation of 68 ± 12%.

Daytime sleepiness was not an inclusion criterion per se. The mean ESS score was 9.7 ± 3.6 (range 4–16), with eight patients having an ESS score ⩾11 suggesting EDS (Table 1) [7,28]. MSLT and MWT were performed according to the practice parameters for the evaluation of objective sleepiness for research purposes, with interruption of single tests after the occurrence of three consecutive epochs of stage 1 sleep or any other sleep stage (Sustained Sleep Latency – SusSL) to avoid interfering with the sleep homeostatic process, or after 20′ (for the MSLT) and 40′ (for the MWT) if SusSL did not occur [1,8,9]. Each exam consisted of four single tests performed at 10:00, 12:00, 14:00 and 16:00. MSLT and MWT were performed on two different days, 1 week apart. Patients were randomly assigned to start with the MSLT or the MWT. Each testing day was preceded by one week of sleep diary (with total sleep time and number of awakenings per night) as previously described [27]. A polysomnographic study was not performed the night before the study.

Sleep latency at MSLT and MWT was scored as the elapsed time from lights-out to the occurrence of a single epoch of stage 1 sleep (SL) and of three consecutive stage 1 epochs or any other sleep stage (SusSL) for each test; individual mean sleep latency was the average of the four SL and SusSL [1]. Recordings were visually examined independently by three neurologists trained in sleep medicine (F.P., S.C. and F.C.) who had to agree on the scoring of SL and SusSL.

2.1. EOG signal analysis procedure for the SEM

The MSLT and MWT recordings were acquired according to the recommendations for the MSLT and MWT protocol [1]. Unipolar electrode montage was used for EOG acquisition as recommended by Rechtschaffen and Kales [12]. Therefore, the EOG active electrodes were placed 1 cm below and one above the outer cantus of the left and right eyes, respectively (E1, E2), with the reference electrode placed on the left mastoid (A1) [12]. The EOG traces were subsequently exported in European Data Format (EDF®) for automatic SEM detection via computerized EOG analysis according to the wavelet-based method previously developed [21–23]. The seconds within each 30-s epoch that were occupied by SEM were automatically calculated according to previous methods [22,24]. Subsequently, in analogy with the epoch time for standard MSLT and MWT detection of sleep onset, the epochs that were occupied for ⩾50% of the time by SEM were considered "*SEM events*" in each recording, and a "*SEM latency*" was calculated as the elapsed time from lights off to the first SEM event in each MSLT and MWT recording. Final individual SEM latency was the average of the four MSLT and MWT sessions.

Since MSLT and MWT should be interrupted after the occurrence of three consecutive sleep epochs by the sleep laboratory technician, we excluded from further analysis single naps that had been precociously interrupted and any individual mean result that was not supported by at least 75% (3 out of 4) of correct procedures.

2.2. Statistical analysis

For each MSLT and MWT single session the following data were considered: SL, SusSL and SEM latency. Thereafter, we calculated mean values of SL, SusSL and SEM latency for each patient.

Mean SL and SusSL were compared with mean SEM latencies using the nonparametric Wilcoxon Signed Rank test for paired data ($p < 0.05$) separately for the MSLT and the MWT. Mean SL and SusSL were then correlated with the mean SEM latency using Pearson correlations ($p < 0.05$) separately for the MSLT and the MWT, and all the latencies were correlated with the ESS score.

The Bland–Altman plot was performed between the SL and SEM at the MSLT and MWT, and we also calculated the mean difference (bias) and the 95% limits of agreement between SL and SEM scoring criteria at the MSLT and MWT.

2.3. Local ethics board

The study was performed according to the standards of the local ethics board. All patients gave written informed consent prior to the study and were informed that all results were confidential without any legal impact regarding their drivers licenses.

3. Results

The individual data are reported in Table 1.

3.1. MSLT data

For the whole OSAS population, the mean SL was significantly shorter than the SusSL (7.41 ± 5.11 min versus 10.43 ± 4.65 min,