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Comparison of Sleep Latency Measured by the Oxford Sleep Resistance Test and Simultaneous EEG in Japanese Patients

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Abstract

Excessive daytime sleepiness (EDS) is observed in various pathological conditions associated with sleep disorders. However, objective methods for the assessment of EDS rely on complex electroencephalographic (EEG) recording and are impractical for use in general clinical practice. To address this issue, the Oxford Sleep Resistance Test (OSLER) has been developed for use in clinical practice overseas, though few studies have examined the reliability of the OSLER test for measuring sleep latency in Japanese patients. Thus, in the present study, we aimed to determine whether sleep latency measured via the OSLER test (SL_{OSLER}) is consistent with that measured via EEG (SL_{EEG}) in Japanese patients with obstructive sleep apnea (OSA). Seventeen Japanese men with OSA (mean age: 51.5 ± 9.8 years) underwent simultaneous OSLER and EEG testing a total of four times on the day following polysomnography evaluation. SL_{OSLER} and SL_{EEG} were compared, and the reliability of the former was analysed using Bland-Altman plots. Mean SL_{OSLER} and SL_{EEG} for all patients were 26.9 ± 11.6 and 25.7 ± 12.2 minutes, respectively. A significant positive correlation was observed between these measurements (p<0.0001, r=0.963). Moreover, the Epworth Sleepiness Scale (ESS) scores were not significantly correlated with either SL_{OSLER} or SL_{EEG}. Bland-Altman plot analysis revealed that 94% of the plotted SL_{OSLER} or SL_{EEG} measurements converged within a range of mean ± 1.96 SD. Our findings thus demonstrated that SL_{OSLER} is consistent with SL_{EEG} in Japanese patients with OSA.

Keywords: Excessive daytime sleepiness; Oxford sleep resistance test; Sleep latency; Obstructive sleep apnea

Introduction

Excessive daytime sleepiness (EDS) presents a significant health and safety concern for individuals engaged in hazardous occupations-such as public transportation drivers, pilots, and heavy-equipment operators-as well as the general population. Obstructive sleep apnea (OSA) [1,2] is a prevalent disorder in which repetitive hypopnea or apnea during sleep induces frequent intermittent hypoxemia and electroencephalographic arousal, eventually resulting in EDS. The association between OSA and traffic accidents attributed to EDS has been highlighted as a serious social problem [3]. Sagaspe et al. reported that the frequency of lane departure during driving simulation was significantly higher in participants with a sleep latency of <20 minutes as measured using the Maintenance of Wakefulness Test (MWT) than in the with a sleep latency of ≥ 34 minutes [4]. Karimi et al. also reported that the incidence of motor vehicle accidents among patients with OSA decreases following initiation of continuous positive airway pressure (CPAP) therapy for ≥ 4 hours per night [5]. Thus, objective assessment of EDS is essential for the appropriate screening of patients and evaluation of outcomes following medical and social interventions.

Available methods for EDS assessment include both objective and subjective scales. The Epworth Sleepiness Scale (ESS) [6] and Stanford Sleepiness Scale (SSS) [7] are widely utilized for the subjective assessment of EDS in both daily clinical practice and clinical studies. Objective methods of EDS assessment include the Multiple Sleep Latency Test (MSLT) [8], which measures the time to sleep onset, and the MWT [9], which measures the duration of sustained wakefulness.

In the MSLT and MWT, sleep latency and the duration of sustained wakefulness are repeatedly measured by recording electroencephalogram (EEG) activity four to five times per day under soporific conditions (e.g., in an examination room with low light) in the daytime, respectively. Not only are these tests time-consuming, but they also require the use of complex EEG equipment and constant observation by an EEG technologist. Due to the substantial human and economic burden of such tests, they are difficult to perform for many patients in general clinical practice. Moreover, previous studies have indicated that the results of subjective assessments do not always correlate well with those of objective scales such as the MWT [10]. Thus, simpler and more objective techniques for the assessment of EDS are required.

To address the aforementioned issues, researchers have proposed the Oxford Sleep Resistance Test (OSLER test), which measures the duration of sustained wakefulness via simple behavioural observation rather than EEG recording [11]. In the OSLER test, the examinee is required to operate a switch in response to a 1-s light-emitting diode (LED) stimulus presented in intervals of 3 s in a dimly lit examination room, and task performance is recorded to assess the state of wakefulness during the test.

Although the OSLER test has been compared to the MWT and used to evaluate clinical cases of EDS in Europe and the United States [11-13], no such studies have been conducted in Japanese populations. As such, whether the time to sleep onset measured using the OSLER test is comparable to that measured via EEG recording in Japanese individuals remains to be elucidated. Therefore, in the present study, we aimed to compare sleep latency measured via EEG (SL_{EEG}) and the OSLER test (SL_{OSLER}) in Japanese patients with OSA.

Materials and Methods

Participants

The present study was approved by the ethics committee of Iwate Medical University School of Medicine (permission number H26-51), and written informed consent was obtained from all participants following a thorough explanation of the study. The study included 17 Japanese men (mean age: 51.5 years ± 9.8 years) referred to the Division of Behavioural Sleep Medicine at Iwate Medical University Hospital for further evaluation of sleep-disordered breathing based on objective (e.g., snoring and/or apnea) or subjective symptoms (e.g., EDS and/or lethargy). The mean ESS score for all patients was 9.8 ± 5.4, and the mean Apnea/Hypopnea Index (AHI) was 61.4 ± 22.6 events/h (Table 1).

Variable	Value
Age (year)	51.5 ± 9.8
Gender (M:F)	17:00
BMI (kg/m^2)	30.3 ± 4.9
ESS (points)	9.8 ± 5.4
Sleep Study	
Total Sleep Time (min)	475.8 ± 47.6
Sleep efficiency (%)	80.7 ± 7.9
Sleep latency (min)	11.6 ± 8.6
%Stage N1 (%)	30.5 ± 10.7
%Stage N2 (%)	48.3 ± 9.6
%Stage N3 (%)	5.4 ± 4.6
%Stage R (%)	15.8 ± 5.7
Arousal index (events/h)	43.6 ± 16.5
Apnea/hypopnea events (events/h)	489.1 ± 179.9
Apnea/hypopnea index (events/h)	61.4 ± 22.6
Desaturation index (events/h)	55.6 ± 21.2
SpO$_2$ mean (%)	93.6 ± 2.0
SpO$_2$ minimum (%)	71.9 ± 10.8
Sleep Latency tests	
SL$_{EEG}$ (min)	25.7 ± 12.2
SL$_{OSLER}$ (min)	26.9 ± 11.6

Data are presented as the mean ± SD. BMI: Body mass index, ESS: Epworth Sleepiness Scale, SLEEG: Sleep Latency – Electroencephalogram, SLOSLER: Sleep Latency – OSLER test, % Stage N1: % non-stage

Table 1: Patient characteristics (n=17).

Patients were prohibited from taking hypnotics, consuming caffeinated and alcoholic beverages, and smoking cigarettes over a 2-week period.

Subjective and objective assessment of EDS

At the initial outpatient visit, all patients were evaluated using the ESS questionnaire for the subjective assessment of EDS. Patients with a total ESS score of ≥ 11 were considered to have EDS [14]. On the day following completion of the PSG (hospital day 2), the OSLER test was performed simultaneously during EEG recording for the objective assessment of EDS. On hospital day 2, patients ate breakfast at 7:30 a.m. and lunch at 12:00 p.m. During the in-hospital tests, patients were strictly prohibited from consuming caffeinated drinks, smoking cigarettes, or taking a nap. Moreover, patients were instructed to remain awake as long as possible without moving the body, vocalizing, or applying any stimulus to the body during each test.

Overnight PSG

PSG was performed using an Alice 6^{TM} system (Philips Respironics Inc.; Murrysville, PA), and data were electronically recorded. All sleep studies were performed in a dedicated examination room with air conditioning (room temperature is between 24 to 26) at Iwate Medical University Hospital. PSG was initiated at 20:00 and completed at 6:00. Test conditions were kept as consistent as possible, and PSG was performed according to the performance standards indicated in the American Association of Sleep Medicine (AASM) guidelines version 2 [15]. Test results were displayed on a dedicated display device and visually assessed by laboratory technicians and physicians to determine the sleep and respiratory status of each patient.

Measurement of SL$_{OSLER}$

The OSLER test was performed using an OSLER device (Stowood Scientific Instruments, United Kingdom). All windows in the examination room were shaded, and the luminance in the room was set to 0.13 Lux. Patients were instructed to assume a comfortable Fowler position. An LED unit was placed in front of patients at eye level. Patients were instructed to hold the switch box in the dominant hand and gently place the index finger on the switch. In response to a 1-s LED stimulus presented every 3 s, patients were instructed to remove the index finger from the switch while the LED was illuminated, and to place the finger on the switch again when the LED was turned off. Based on the methodology described by Bennett et al. [11], each OSLER test session lasted up to 40 minutes, and a total of four sessions were performed every 2 h (9:00, 11:00, 13:00, and 15:00).

The session was terminated (1) when the patient failed to perform the switching task correctly seven times in a row (sleep onset) or (2) when 40 minutes had passed without seven consecutive failures (absence of sleep onset). SL$_{OSLER}$ was defined as the time until termination of each OSLER test session. In case (2), SL$_{OSLER}$ was expressed as a sleep latency of ≥ 40 minutes.

Measurement of SL$_{EEG}$

During each OSLER test session, EEG electrodes were placed based on the performance standards for PSG to assess the state of wakefulness for each participant. During EEG recording, patients were asked to remain awake and perform the OSLER task for as long as possible. Each EEG session lasted up to 40 minutes, and a total of four EEG sessions were performed every 2 hours (9:00, 11:00. 13:00, and 15:00). Sleep onset was defined as the first epoch of greater than 15 sec of cumulative sleep in a 30 sec epoch, whereas the absence of sleep onset was determined when 40 minutes had passed without sleep onset. SL$_{EEG}$ was defined as the sleep latency measured via EEG during

the OSLER test session. EEG sessions were terminated based on the same criteria used for OSLER test sessions. Moreover, patients were prohibited from sleeping for any length of time prior to PSG and between OSLER test sessions.

Statistical analysis

Statistical analysis was performed using StatView 5.0^{TM} (Abacus Concepts, CA, and USA). The correlation between SL_{EEG} and SL_{OSLER} was analysed using Pearson's correlation coefficient, while the correlation between ESS scores and SL_{EEG} or SL_{OSLER} was analysed using Spearman's rank correlation coefficient. In addition, the consistency between SLEEG and SLOSLER was assessed using a Bland-Altman plot. A p value of <0.05 was considered to indicate a significant difference.

Results

Subjective and objective assessment of EDS

Patient characteristics and PSG data are presented in Table 1. The mean ESS score for all 17 patients was 9.8 ± 5.4. Six patients were considered to exhibit EDS, based on an ESS score ≥ 11. PSG yielded the following data: mean total sleep time (TST): 475.8 min ± 47.6 min; mean arousal index: 43.6 ± 16.5 events/h; mean AHI: 61.4 ± 22.6 events/h; mean desaturation index: 55.6 ± 21.2 events/h; mean peripheral artery oxygen saturation (SpO_2): 93.6% ± 2.0%; and minimum SpO_2: 71.9% ± 10.8%. The mean SL_{EEG} was 25.7 min ± 12.2 min, while the mean SL_{OSLER} was 26.9 min ± 11.6 min.

A significant positive correlation was observed between SL_{EEG} and SL_{OSLER}, which were obtained over four sessions per patient, for a total 68 sessions (r=0.941, p<0.0001) (Figure 1A).
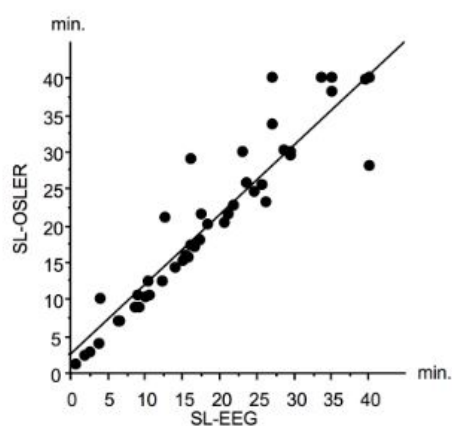

Figure 1A: Association between sleep latency as determined via the Oxford Sleep Resistance test (SL_{OSLER}) and electroencephalography (SL_{EEG}). A significant positive correlation was observed between SL_{OSLER} and SL_{EEG} across the 68 total sessions ([*]: r=0.941, p<0.0001). The correlation between SL_{OSLER} and SL_{EEG} was analysed using Pearson's correlation coefficient. A p value of <0.05 was considered to indicate a significant difference.

When the mean measurements obtained over the four sessions of each patient were analyzed, a significant positive correlation was again observed between SL_{EEG} and SL_{OSLER} (r=0.963, p<0.0001) (Figure 1B).
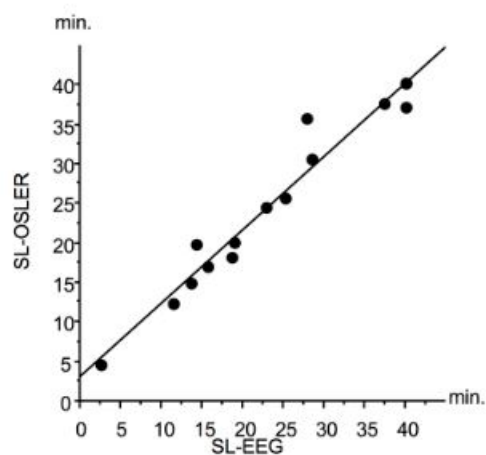

Figure 1B: When the mean measurements obtained over the four sessions of each patient were analyzed, a significant positive correlation was again observed between SLEEG and SLOSLER ([#]: r=0.963, p<0.0001).

However, SL_{EEG} and SL_{OSLER} tended to decrease as ESS scores increased, though no significant correlations were observed.

Bland-Altman plots revealed that the majority of SL_{EEG} and SL_{OSLER} measurements from all 68 sessions (94%) converged within a range of mean ± 1.96 SD (mean: 1.18; SD: 3.29; mean+1.96 SD: 7.62; mean −1.96 SD:−5.26) (Figure 2A).
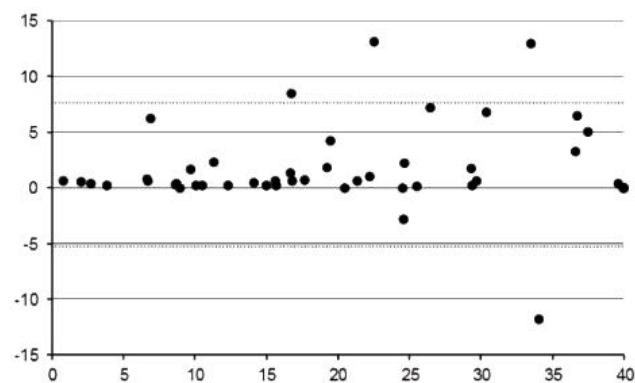

Figure 2A: Bland-Altman plots. Bland-Altman plot depicting the association between sleep latency as measured via the Oxford Sleep Resistance Test (SL_{OSLER}) and electroencephalography (SL_{EEG}) over all sessions (n=68; mean: 1.18; SD: 3.29; mean+1.96 SD: 7.62; mean−1.96 SD: −5.26).

Similarly, 94% of the plotted mean measurements for each of the 17 patients also converged within a range of mean ± 1.96 SD (Figure 2B).
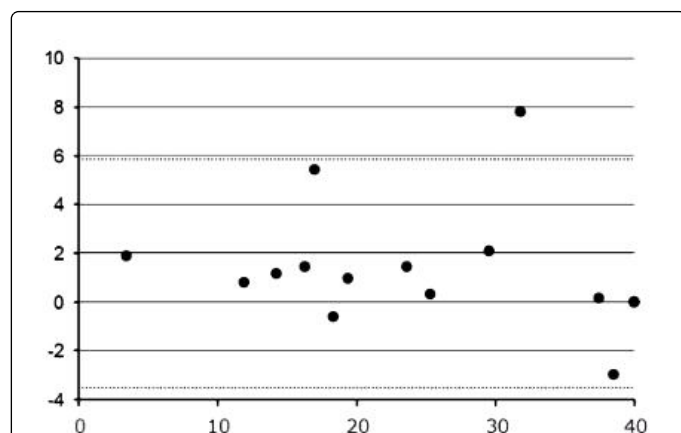
Figure 2B: Bland-Altman plots. Bland-Altman plot depicting the association between SL_{EEG} and SL_{OSLER} for each patient (n=17; mean: 1.18; SD: 2.39; mean+1.96 SD: 5.87; mean−1.96 SD: −3.51).

When a sleep latency of 20 minutes was set as the cut-off value for the "presence of sleepiness" based on the findings of a previous study by Sagaspe et al. [4], SL_{OSLER} was <20 minutes in seven patients (ESS=11.7 ± 5.5; three patients with ESS<11 [range, 3-10], four patients with ESS ≥ 11 [range, 12-18]) and ≥ 20 minutes in 10 patients (ESS=8.5 ± 5.1; eight patients with ESS<11 [range, 3-10], two patients with ESS ≥ 11 [range, 17-18]). Furthermore, an SL_{OSLER} cut-off of 20 minutes resulted in sensitivity and specificity values of 1.0, while an ESS cut-off of 11 resulted in a sensitivity of 0.57 and specificity of 0.8.

Discussion

The present study aimed to determine whether SL_{EEG} could be sufficiently estimated from SL_{OSLER} in Japanese patients with OSA. Our findings indicated that the duration of sustained wakefulness as determined by EEG could also be estimated using the results of the OSLER test when performed during EEG recording, consistent with the findings of Krieger et al. [12]. Thus, the present study is the first to demonstrate that assessment of EDS via the OSLER test is comparable to that via EEG in a Japanese population.

Although EDS is not inevitable in patients with OSA, it is nonetheless a clinically significant symptom. The ESS was developed by Johns et al. [6] for the evaluation of subjective sleepiness in soporific circumstances of daily life. Based on the findings of a previous study, which demonstrated that the ESS exhibits higher sensitivity and specificity for the diagnosis of narcolepsy than MSLT, a total ESS score of ≥ 11 is considered to indicate the presence of EDS [14]. While the mean ESS score of patients in the present study was 9.8 ± 5.4 (range: 3-18), six of the 17 patients had an ESS score ≥ 11. This result suggests that our study included patients without subjective EDS despite the presence of OSA, consistent with the findings of Mediano et al. [16]. As the ESS is subjective in nature, participants may provide inaccurate information regarding sleepiness and wakefulness [17]. Although we did not investigate the relative impact of under- or over-estimation in the present study, both factors may have influenced our findings.

Although objective methods for the assessment of EDS include the MSLT and MWT, AASM guidelines indicate that the MWT is more useful for determining therapeutic effects in patients with disorders associated with EDS [18]. In the present study, analysis of Bland-Altman plots revealed that 94% of SL_{OSLER} and SL_{EEG} measurements converged within a range of mean ± 2 SD. Bennett et al. [11] reported that sleep latency measured via the OSLER test correlated with that measured via the MWT. In the present study, we performed EEG recording and the OSLER test simultaneously to eliminate differences associated with performing the procedures in separate conditions. Our findings indicated that SL_{OSLER} was nearly identical to SL_{EEG}, demonstrating that the findings of Bennett et al. are applicable to Japanese patients as well.

Sangal et al. [10] performed Spearman's correlation analysis of sleepiness as assessed using the ESS and MWT in patients with OSA, reporting a weak correlation between the two techniques. Although comparison between SL_{EEG} and SL_{OSLER} in the present study revealed that sleep latency tended to decrease as ESS score increased, no statistically significant correlations were observed. Taken together, the findings of these studies suggest that the subjective results of the ESS are not as reliable as the objective results of the MWT or OSLER test.

Plante et al. [19] further reported that odds ratios for depression were higher in patients with high ESS scores, in contrast to findings obtained for MSLT scores, suggesting that subjective scale scores may be affected by events other than sleepiness. Moreover, Leclerc et al. [20] reported that pre-intervention ESS scores were significantly lower when measured prior to therapeutic interventions for OSA syndrome than when measured via recall following CPAP therapy. These findings suggest that, when OSA remains untreated for a long period of time, the ESS may underestimate EDS. Thus, it is likely that these subjective factors contributed to the lack of correlation between ESS scores and sleep latency in the present study.

In the present study, Bland-Altman plots were used to analyse SL_{EEG} and SL_{OSLER}. Although 94% of the plotted measurements converged within a range of mean ± 2 SD (1.96 SD), some patients exhibited longer SL_{OSLER} than SL_{EEG}. During EEG evaluation for the MSLT and MWT, sleep onset is determined by the appearance of sleep EEG patterns lasting for ≥ 50% of a 30-second epoch. In contrast, sleep EEG patterns must be observed for at least 21 seconds during the OSLER test, as sleep onset is determined when the examinee fails to correctly perform the switching task seven times in a row. Thus, when sleep EEG patterns appear for a total of ≥ 15 seconds in an EEG epoch, instead of 21 seconds, the examinee is determined to have fallen asleep, though he or she may continue to perform the OSLER task, which may explain the longer SL_{OSLER} than SL_{EEG} duration for some patients in the present study (3/68 sessions; 4.4%). Moreover, EEG may be unable to determine sleep onset when sleep EEG patterns appear for ≥ 21 seconds over two epochs but total <15 seconds in each epoch, resulting in a shorter SL_{OSLER} than SL_{EEG}. In addition, Priest et al. [21] examined the number of OSLER test failures and micro sleep patterns on EEG, reporting some cases with <7 failures in OSLER test despite sleep patterns lasting ≥ 15 to ≤ 23 seconds on EEG. These authors reported a sensitivity of 85% and specificity of 94% for the detection of micro sleep using the OSLER test.

The discrepancy between SL_{OSLER} and SL_{EEG} may also be attributable to variations in the manner in which examinees perform the task. For example, if an examinee moves only the tip of the thumb and keeps a part of it attached to the switch during the OSLER test, a failure may be recorded. Such failures can be avoided to some extent through careful monitoring by laboratory technicians.

In the present study, Bland-Altman analysis revealed that 94% of the plotted measurements converged within a range of mean ± 2 SD,

indicating that SL_{OSLER} and SL_{EEG} were sufficiently consistent. When the presence of sleepiness was determined using an SL_{OSLER} cut-off of <20 minutes, the sensitivity and specificity were 1.0, suggesting that sleep latency measurements were comparable between the OSERL test and EEG recording.

The present study has some limitations. First, it is possible that the OSLER task itself may be a stimulus for wakefulness on EEG. Thus, it is difficult to strictly compare the test results with those of the MWT, during which no tasks are assigned. However, Krieger et al. [12] reported that the duration of sustained wakefulness measured by the OSLER test (referred to as SL_{OSLER} in the present study) was significantly correlated with the duration measured by simultaneously performed EEG recording (referred to as SL_{EEG} in the present study), as well as the duration measured by standard MWT performed on a separate day. Second, the sample size of the present study was relatively small (n=17). Future studies should evaluate the usefulness of the OSLER test using larger sample sizes in patients with various clinical presentations.

Conclusion

The findings of the present study demonstrated that SL_{OSLER} is consistent with SL_{EEG} in Japanese patients with OSA. Moreover, because a significant positive correlation was observed between SL_{OSLER} and SL_{EEG}, SL_{OSLER} may also be correlated with sleep latency measured by MWT. In order to determine whether the OSLER test is an appropriate substitute for the MWT, future studies should analyse the association between the duration of sustained wakefulness determined by each test. Overall, our findings indicate that the OSLER test may represent a simple method for the objective assessment of EDS and duration of sustained wakefulness on EEG.

Acknowledgment and Disclosures

Conflicts of interest

Author contributions

Keisuke Hosokawa had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Keisuke Hosokawa, Tetsuya Kizawa, and Tsuguo Nishijima prepared the application to the ethics committee and performed data management. Tsuguo Nishijima contributed to the study design and revision of the manuscript, and Shigeru Sakurai contributed to the study concept and design, acquisition of funding, study supervision, and writing of the manuscript.

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