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An alternative measure of sleep fragmentation in clinical practice: the sleep fragmentation index

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Abstract

Background and purpose: Micro-arousals (MA) are commonly considered as sleep components reflecting sleep fragmentation. However, their elucidation is time-consuming, with considerable inter-observer variability. The aim of our study was to investigate the usefulness of a sleep fragmentation index (SFI) to detect sleep disruption in a large sample of patients.

Patients and methods: Five-hundred ninety-eight polysomnographic studies made in controls and patients were examined. The SFI was calculated as the total number of awakenings and sleep stage shifts divided by total sleep time.

Results: In the whole group a significant correlation was found between the SFI and the MA index (MAI) ($P<0.001$) with good agreement across a wide range of values. When patients were stratified according to final diagnosis a significant relation was noted for patients with insomnia ($P<0.001$), parasomnia ($P<0.001$), circadian schedule disorders ($P<0.001$) and sleep related breathing disorders ($P<0.001$). Lower values were found in controls ($P<0.01$) and in patients with periodic limb movement disorder and/or restless legs syndrome ($P<0.05$). In 111 patients having two consecutive recording nights, a good reproducibility was present with no differences between nights ($P=$ns) and with significant correlation ($P<0.001$).

Conclusions: The SFI seems to be an accurate, reproducible and easy method to detect sleep fragmentation in patients with sleep disorders. Further studies are needed to validate the usefulness of this tool in clinical practice.

Keywords: Microarousals; Sleep fragmentation; Sleep disorders; Polysomnography

1. Introduction

It is generally accepted that conventional sleep parameters obtained as a result of visual sleep stage scoring poorly reflect the sleep disruption caused by pathological events, such as apnoeas or periodic leg movements, or occurring without any identifiable triggering cause, as in insomnia, and it is agreed that they are weakly related to subjective complaints of fatigue or sleepiness. Therefore, earlier reports have proposed shifts to stage 1 [1] or a combination of different levels of arousals and stage shifts [2] as predictors of daytime sleepiness. Recently, micro-arousals (MA) [3] have been introduced as the 'gold standard' to detect sleep fragmentation, a factor contributing to impaired daytime function and sleepiness as assessed by the Multiple Sleep Latency Test [4]. Although these measures of sleep fragmentation are related to sleepiness, they explain only part of the variance in subjective and objective daytime sleepiness [5,6]. Furthermore, the MA scoring is a time-consuming method, requiring a trained observer and manual editing, and, therefore, showing a high inter-scorer variability [7–9] and a lower specificity. Recently [10], the sleep fragmentation index (SFI) has been introduced as a crude estimate of sleep disruption in patients evaluated for sleep-disordered breathing (SDB), showing a good correlation with MA scoring, a high inter-night reliability and an association with age and the degree of respiratory disturbance. The primary objective of this study was to estimate the use of the SFI in the detection of sleep fragmentation in a large sample of patients with several sleep disorders. A second objective was

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to assess in which patients this measure might reliably detect sleep fragmentation. Finally we tested for an association between SFI and subjective sleepiness and, in a subgroup of patients, objective daytime sleepiness.

2. Patients and methods

The study included four hundred fifty-one patients recorded during one or more consecutive nights, allowing analysis of five hundred ninety-eight sleep studies. Patients were stratified according to final diagnosis in six groups, including controls (*n*:24), patients with insomnia (*n*:69, psychophysiological or primary insomnia as well as insomnia secondary to mood disorders), parasomnia (*n*:13), patients with circadian schedule disorders (*n*:16), patients with SDB (*n*:243), and patients having restless legs syndrome (RLS, *n*:30) or periodic limb movement disorder (PLMD, *n*:15).

Nocturnal polysomnography included seven electroencephalograms (EEG), right and left electrooculograms, submental electromyogram (EMG), and electrocardiogram. Respiratory airflow was monitored with a nasal cannula connected to a pressure transducer, thoracic and abdominal respiratory movements with piezoelectric strain gauges, tracheal sound by microphone and arterial oxygen saturation by a finger oxymeter. Tibialis EMG activity was monitored using surface electrodes placed on right and left legs.

Sleep was scored according to the standard criteria using 20-s epochs [11]. Awakening was defined as a shift in EEG frequency to alpha or faster frequencies, lasting 10-s or longer [11].

MA was defined according to ASDA criteria, and lasting $>3<10$-s [3]. An MA index (MAI) was calculated as the total number of MA divided by the total sleep time (TST) in hours. The SFI was calculated according to previous data [10] modified to include any sleep stage shift and the total number of awakenings, divided by TST/h. The stage shifts were computed for all sleep stages and were calculated automatically after manual sleep scoring. In REM sleep the sleep stage transition was defined as a shift to stage 1. Breathing events were scored using standard criteria [12]. Apneas were defined as the absence of airflow on the nasal cannula lasting for >10 s. Hypopnoeas were defined as a 50% or greater reduction in airflow from the baseline value lasting at least 10-s. associated with either a 3% oxygen desaturation or an arousal. Periodic limb movements were scored according to Coleman's criteria (i.e. movements lasting 0.5–5-s with intermovement intervals of 4–90-s and occurring in a series of at least four consecutive movements) [13].

Pearson's correlation test was used to assess the reliability of SFI compared to MAI and to examine the relation of SFI with nocturnal variables and subjective daytime sleepiness as assessed by the Epworth sleepiness scale (ESS) [14]. In 109 patients diagnosed as SDB, objective sleepiness was measured by means of the maintenance wakefulness test (MWT) [15] and a Pearson's correlation test was used to examine the relation of the mean sleep latency at the MWT and the MAI and SFI. In 111 patients having two consecutive recording nights, the night-to-night variability and reliability of the MAI and SFI was assessed using a *t*-test to ascertain consistent changes, and the correlation coefficient was also calculated.

3. Results

Patients characteristics and polygraphic parameters are shown in Table 1.

Table 1
Clinical and polysomnographic parameters for the entire group and different diagnostic categories

	Total	Controls	Circadian	Insomnia	Parasomnia	RLS + PLMD	SDB
	PSG = 598	PSG = 32	PSG = 25	PSG = 154	PSG = 22	PSG = 78	PSG = 293
Male (%)	48.5	45.8	75	56.5	69.2	60	70.7
Age (yrs)	49 (14.4)	36.2 (16.7)	32.8 (13.6)	48.9 (12.4)	30.8 (10)	55.4 (12.4)	53 (12.3)
TTS (min)	422.1 (91.4)	484.8 (80.4)	455.9 (121.6)	424.34 (101.2)	456.6 (74.7)	385 (82.5)	413.5 (73.6)
SE (%)	78.1 (13.4)	86.5 (7.7)	79 (18.1)	77.5 (13.6)	83.7 (7.5)	74.6 (14.7)	77.9 (12.8)
WASO (min)	88.4 (60.6)	51.2 (32)	68.9 (73.4)	87.3 (68)	62.5 (36.6)	98.3 (53.6)	93.6 (60.5)
St.1 (min)	57.4 (26.1)	45 (16.6)	44.1 (23.3)	50.1 (22.9)	45.4 (15.2)	54.4 (22.8)	63.9 (28.1)
St. 2 (min)	208.9 (58.7)	240 (53)	195.1 (66.4)	200.6 (60.8)	222.5 (48.9)	197.3 (54.6)	209.7 (56.9)
St. 3–4 (min)	69.3 (38.6)	86.9 (33.3)	90 (37.7)	76.3 (37.8)	88.9 (28.5)	63.2 (37.6)	64 (39.3)
St.REM (min)	81 (35)	108.4 (29.5)	104.2 (44.7)	85 (33.8)	88.2 (21.6)	69.7 (32.4)	75.7 (32.3)
AHI (n/h)	15.3 (17.7)	1.9 (1.6)	4.7 (9.7)	7.4 (9.7)	4.8 (5.4)	7.6 (8.1)	20.3 (19.6)
PLM index (n/h)	12 (18.5)	2.5 (3.7)	5.4 (9.2)	4.6 (7.7)	3.4 (5.1)	37 (27.6)	11.5 (15.6)
ESS	8.9 (4.9)	7 (3.9)	8.5 (4.7)	8 (5.8)	7.6 (3.7)	7.9 (5)	9.5 (4.5)
MWT (min)	–	–	–	–	–	–	22.5 (11.9)[a]
MAI (n/h)	17.7 (10.2)	10.3 (4.1)	15.8 (8.1)	12.7 (5.2)	12.2 (4.3)	22.8 (11.5)	20.5 (11)
SFI (n/h)	49.7 (24.8)	32.1 (8.6)	35.5 (13.4)	41.3 (14.7)	33.5 (7.6)	49.7 (20.8)	57.9 (28.7)

Means (SD). PSG, Polysomnography; TTS, Total sleep time; SE, Sleep efficiency; WASO, awake after sleep onset; AHI, Apnea/hypopnea; PLM, Periodic limb movement; ESS, Epworth sleepiness scale; MWT, Maintenance wakefulness test; MAI, index of microarousals; SFI, sleep fragmentation index; AHI, apnea/hypopnea index.

[a] In 109 patients.

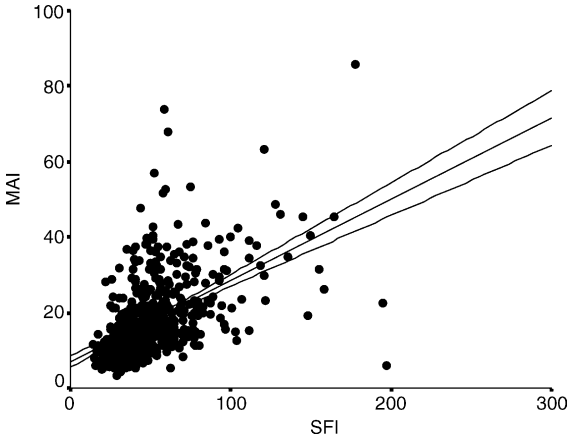

Fig. 1. Scatterplot showing the significant correlation between the SFI and the MAI in the whole group of patients.

In the group of patients as a whole, a statistically significant correlation ($r=0.52$; $P<0.001$) (Fig. 1) was found between the SFI and the MAI, even though SFI substantially overestimated the number of MA with a mean index difference of 31.2 ± 20.8/h.

The MAI and the SFI were highly reproducible in patients having two nocturnal recordings. The mean MAI and SFI in the first night were, respectively, 12.8 ± 0.5 and 44.3 ± 1.7 and $17.6\pm$and 47.6 ± 1.8 in the second night, with no significant differences between nights. The correlation coefficient between nights was 0.77 for the SFI ($P<0.001$) and 0.78 for the MAI ($P<0.001$) (Fig. 2).

When considering patient groups on the basis of the final diagnosis, there was a significant correlation between the SFI and the MAI with the lowest correlation in controls and patients with RLS/PLMD. The relation of sleep fragmentation indices with polygraphic parameters showed that while in insomniac patients the SFI was highly correlated with the amount of wake after sleep onset ($r=0.41$; $P<0.001$), in patients with SDB the SFI was highly correlated with the apnea/hyponea index (AHI) ($r=0.6$; $P<0.001$) and the oxygen desaturation index (ODI) ($r=0.56$; $P<0.001$) similar to that found when MAI was considered (AHI $r=0.66$; $P<0.001$, ODI: $r=0.61$; $P<0.001$). When patients with RLS/PLMD were considered, while the MAI was significantly related to the periodic limb movements index (PLM index) ($r=0.46$; $P<0.001$), no significant correlation was found between the SFI and the PLM index ($r=0.06$; $P=0.58$).

To assess the relation between measures of sleep fragmentation and subjective and objective sleepiness, a correlation analysis was done between MAI and SFI and the ESS score and mean sleep latency at the MWT. Despite a weak relation between ESS and MWT ($r=-0.36$, $P<0.01$) neither the SFI nor the MAI showed a significant correlation with the ESS ($r=-0.03$ and -0.09, respectively, $P=$ns) or with the mean latency at the MWT ($r=-0.03$ and $r=-0.02$, p=ns).

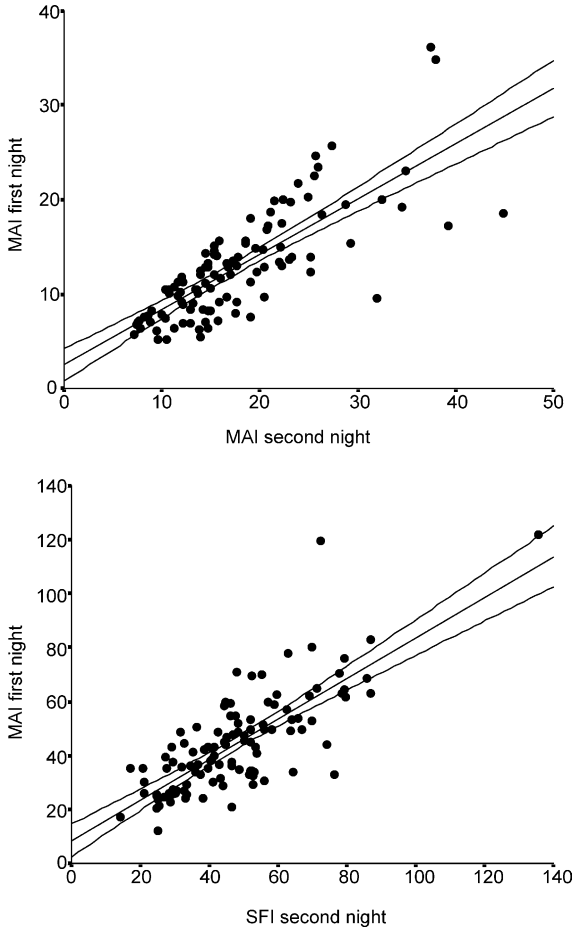

Fig. 2. Scatterplots showing the reproducibility of the MAI (upper panel) and the SFI (bottom panel) in patients undergoing two consecutives nights.

4. Discussion

This study shows that the SFI is a simple, accurate and reliable method to detect sleep fragmentation in clinical practice, the SFI significantly correlated to the MAI. Moreover, it appears to reflect easily the degree of sleep alterations, the SFI being significantly related to indices of sleep discontinuity, i.e. wake after sleep onset, AHI and ODI, and with a relation similar to that found for MAI. These findings replicated in larger samples could give clinicians an easier means to estimate sleep fragmentation in sleep disorders.

The growing interest in sleep fragmentation consequences has stressed the need to quantify MA, the ‘gold standard’ commonly used to define and measure sleep fragmentation. Even if progress has been made in automatic analysis of MA [16], the analysis of MA is still manual, time consuming, associated with high inter-scorer variability [7–9] and, consequently, difficult to perform routinely in clinical practice. Besides, there is a lack of agreement in what constitutes a MA, shorter EEG changes [17–19] and autonomic arousals [20] being proposed as more sensitive markers of sleep fragmentation. However, even with

the inclusion of these indices the relation between sleep fragmentation and daytime sleepiness still remains unclear [21,22]. The first finding of our study is that although SFI overestimated the number of MA, it seems to be an easy, quick and reproducible method to assess sleep fragmentation. In studying a larger sample than formerly reported, we were able to find a good correlation between the two variables, similar to that previously described [10], with a good test–retest reproducibility, the SFI being similar in two consecutive nights. Although our SFI was slightly different from that previously described because we included in its definition all sleep stage shifts, our results replicate those previously published, with a reliability present not only in SDB patients but also in other sleep disorders. In insomniac patients the SFI reflects the degree of sleep discontinuity, commonly indicated by time awake during sleep, while in patients with SDB the SFI was significantly related to MAI, AHI and ODI, suggesting that in these two sleep disorders SFI may easily detect the sleep feature defining the disease. Interestingly, we found a lower relation in patients with RLS/PLMD, suggesting that in these patients the SFI may underestimate the real sleep fragmentation. The lack of strong correlation in these patients may be explained by the fact that PLMs are only rarely associated with full awakening or stage shifts (2%), in only 34% cases associated with MA, 64% of PLM not inducing any change in the EEG activity [19]. If so, it could be predicted that in these patients the SFI would show a lower reliability in detecting sleep fragmentation. Alternatively it can be suggested that PLMs are not specific and pathological phenomena arising from sleep [23], but simply the translation at motor level of the cyclic sleep instability of NREM sleep [24].

Although the aim of this study was not to predict sleepiness by the use of this measure of sleep fragmentation, we analyzed whether SFI and MAI might contribute to subjective and objective sleepiness. In our patients, neither the SFI nor the MAI contributed to the ESS and MWT mean latencies. This lack could be explained by two factors. First, our sample was a heterogeneous unselected clinical population in whom factors others than sleep fragmentation, for example sleep deprivation [25], narcolepsy [26] and drug intake [27], could have interfered with the sleepiness evaluations. Second, although some studies in selected populations have found significant correlations with several nocturnal sleep parameters [1,2,4,28] others found poor [29] or not association at all [30–32]. This would stress that factors outside sleep fragmentation may contribute to daytime sleepiness.

In summary, the SFI may be a practical and easy tool in clinical practice and may be an accurate instrument for routine estimation of sleep fragmentation. Since SFI underestimates sleep fragmentation in RLS/PLMD and does not predict daytime impairment in our patients, further studies in larger samples, including patients weakly represented in our sample, are needed to validate the clinical usefulness of this measure.

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