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Sleep electroencephalogram changes in acute hemispheric stroke

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Abstract

Background/objective: Since reports of the effects of cerebral hemispheric stroke on sleep architecture are rare and contradictory, we prospectively studied 24 patients with first acute supratentorial, extra-thalamic stroke.

Methods: We assessed stroke severity, topography, and volume (on brain MRI). Sleep electroencephalogram recordings were performed a mean of 12 days after stroke onset, and scored for sleep stages over the healthy hemisphere. Sleep spindles and sawtooth waves were analyzed over both hemispheres. Data were compared with those of 17 age and gender-matched patients with normal brain imaging.

Results: Compared to controls, stroke patients had lower total sleep time ($P < 0.01$), lower sleep efficiency ($P = 0.02$), and reduced amounts of NREM sleep stages 2–4 ($P = 0.02$). Sleep spindles and sawtooth waves were often bilaterally reduced in patients with stroke volumes >25 ml. Abnormalities of REM sleep were more common in sleep studies performed within 3 days after stroke onset. Compared to patients with poor outcome, those with good outcome had higher sleep efficiency ($P < 0.01$), more sleep time ($P = 0.02$), and more NREM sleep stage 2 ($P < 0.01$).

Conclusion: Acute hemispheric stroke is accompanied by sleep EEG changes over the healthy hemisphere that correlate with stroke severity. These findings support the hypothesis that the cerebral hemispheres participate in the control of sleep.

Keywords: Cerebral hemispheric stroke; Extra-thalamic stroke; Sleep; EEG; Spindles

1. Introduction

Since the first EEG recording in sleep, sleep is no longer considered a passive state but the result of an active brain process. For several decades sleep was thought to depend mainly on brainstem mechanisms and to occur homogeneously over the cerebral hemispheres. Several recent observations, however, suggest a role of the forebrain in sleep regulation and the existence of focal differences in the EEG correlates of sleep over the cerebral hemispheres. First, there are regional differences in sleep EEG spectra at the macro EEG level with state-related and frequency-specific differences [1,2]. Second, intracellular recordings indicate that discrete neuronal populations contribute to sleep generation [3]. The reticular nucleus of the thalamus is the pace-maker of sleep spindles, the cerebral cortex may be essential for generation of *K* complexes and <1 Hz delta activity [4], and thalamo-cortico-thalamic networks for that of >1 Hz delta activity [5]. On the other hand, the generation of rapid eye movements (REM) sleep depends upon the integrity of the medio-lateral, ponto-mesencephalic tegmentum [6,7]. Third, ablation of the frontal cortex in the cat leads to reduction of both REM and non-rapid eye

† This paper is dedicated to the memory of Dr Aldrich, who recently passed away.

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movements sleep (NREM) sleep [8]. Fourth, functional neuroimaging (e.g. positron emission tomography) (PET)) has shown topographic differences in the activity level of distinct hemispheric areas during NREM and REM sleep [9–11].

Until now most reports of the effects of brain injury on sleep have concentrated on sleep EEG changes following brainstem or thalamic lesions [12–15]. In hemispheric stroke, Cress and Gibbs observed in 1948 a reduction of sleep spindles over the affected hemisphere [16]. In the 1970s, Hachinski et al. [17] reported a reduction of both sleep spindles and slow wave sleep in patients with large strokes and poor clinical outcome. A reduction of REM sleep has been described in patients with severe hemispheric lesions [18]. However, the effects of side and topography of the lesion on sleep architecture have rarely been analyzed and when they have, the results have been contradictory [18,19].

Studies on sleep EEG changes following hemispheric stroke reported to date suffer important limitations. First, neither sleep apnea, present in at least 50% of stroke patients [20–22], nor periodic limb movements were assessed in most studies, although both may affect sleep architecture. Second, data on clinical severity and radiological extension of stroke were usually absent or limited. Third, control groups often consisted of non-hospitalized persons, and hospitalization for acute illness may induce profound sleep EEG changes [23]. Fourth, a systematic assessment of sleep microstructure has not been performed [17,24,25].

Nonetheless, the evidence concerning the role of the forebrain in sleep regulation suggests that the study of changes in the macro and microstructure of sleep following focal brain damage (e.g. stroke) may contribute as experiments of nature to a better understanding of regional aspects of sleep EEG generation. To assess the relationship between sleep EEG and stroke severity, topography and outcome, we analysed the macro and microstructure of sleep in a consecutive series of 24 patients with acute hemispheric, extra-thalamic stroke.

2. Patients and methods

2.1. Patients

Over a period of 40 weeks we assessed by means of conventional polysomnography 24 consecutive patients (eight women, 16 men), with a mean age ± SE of 62.1 ± 2.2 years (range: 26–78) admitted to the Neurology Department of the University of Michigan Hospitals because of a first acute hemispheric stroke documented by brain CT or MRI. The study protocol was approved by the Institutional Review Board of the University of Michigan Medical Center.

2.2. Stroke assessment

Patients were assessed clinically by one of the authors (C.B.) within the first 2 days of hospitalization. The maximal stroke severity was estimated with the scandinavian stroke scale (SSS), in which a score <30 occurs with severe stroke [26]. Stroke evaluation included standard blood tests, 12-lead ECG, chest X-ray, precranial and transcranial doppler ultrasonography, and brain CT or brain MRI or both. Cerebral angiography was performed on 15 patients and echocardiography on 13 patients. Brain images were reviewed with a standard protocol of evaluation by a neuroradiologist (D.Q.) blind to the clinical context. The estimated stroke volume corresponded to the sum of areas of altered signal directly measured on the different T2-weighted brain MRI images. Etiology of stroke was determined according to the criteria of the TOAST-study (trial of acute stroke treatment [27]). Short-term outcome was classified at discharge from the hospital as good (no deficits, or deficits without restriction in everyday life activities, independent), or poor (dependent).

2.3. Polysomnography

Conventional overnight polysomnography (PSG) was performed at the patient's bedside using a 16 channel paper recording system at 10 mm/s paper-speed. Recordings were performed as soon as possible after stroke according to the availability of the portable EEG machine. None of the patients was recorded during his stay in the intensive care unit and sleep-modifying medications were avoided the night of the study. The recordings included eight electroencephalogram channels, two electrooculogram channels, one chin electromyogram channel, and channels for nasal/oral flow (thermistor), chest and abdominal wall excursion, heart rate, oxyhemoglobin saturation

(SaO_2), and two tibialis anterior EMG channels. Each hemisphere was recorded with an ipsilateral reference electrode (e.g. C3-A1 and C4-A2). Sleep stage scoring was done visually over the healthy hemisphere according to standard criteria [28]. Sleep spindles were counted visually over the healthy hemispheres by an experienced sleep technologist and expressed as number per hour of sleep. REM density was calculated as time in REM sleep with rapid eye movements divided by total REM sleep time. The presence of well formed sawtooth waves was noted. Respiratory events were scored as previously described [22]. The number of apneas and of apneas plus hypopneas per hour of sleep was expressed as apnea-hypopnea-index (AHI). The number of periodic leg movements per/hour of sleep was expressed as periodic leg movements in sleep index (PLMI).

2.4. Control group

Seventeen patients with first acute transient ischemic attack (TIA) admitted to the same hospital during the study period served as a control group. Patients with TIA were recorded >24 h after resolution of neurologic symptoms and after exclusion of vascular lesions on brain MRI. Hence, the possibility of a small stroke causing severe sleep-wake disturbances in these patients appears very unlikely on clinical and neuroradiological grounds. This control group was chosen for two main main reasons: (1) TIA and stroke patients have similar clinical characteristics except for brain damage, including demographics, cardiovascular risk factors, and associated medical disorders; and (2) PSG recordings could be performed in both patient groups during acute hospitalization.

2.5. Statistical analysis

All values are expressed as mean ± standard error. To compare values between patient groups we used the chi-square test or Fisher's exact test for nominal (categorical) variables; the Mann–Whitney-*U* test for ordinal variables and non-normally distributed continuous variables; and the unpaired *t*-test for two independent samples for continous variables. All tests of significance were two-tailed. Statistical significance was set at $P < 0.05$.

3. Results

There were 13 left-sided and 11 right-sided strokes. The mean ± SE score of the scandinavian stroke scale (SSS) was 36.7 ± 3.4 (range 12–56). Eight patients had a severe stroke (SSS < 30). Stroke volume ranged from 0.3 to 122 ml (mean ± SE = 20.2 ± 6.5 ml). A presumed stroke etiology was identified in 17 (71%) of 24 patients.

Outcome at hospital discharge was good (independent) in 16 (66%) of 24 patients. As expected, there was a significant difference in SSS ($P < 0.001$) between patients with good and bad short-term outcome. PSG were performed a mean ± SE of 11.7 ± 2.8 days after stroke (range: 1–49 days). In 12 (50%) of 24 patients recordings were performed within 7 days from onset of symptoms. In five patients PSG was recorded more than 2 weeks after onset of symptoms. Patients with poor short-term outcome were recorded later than patients with good short-term outcome ($P = 0.01$). All patients had a normal baseline oxygen saturation (>90%). Sleep disordered breathing (AHI >10) was found in 13 (54%) of 24 patients and periodic limb movement in sleep disorder (PLMI >10) in ten (42%) of 24 patients.

3.1. Sleep architecture in patients with acute hemispheric stroke vs. controls (Table 1)

When compared to controls, patients with acute hemispheric stroke had less total sleep time ($P < 0.01$), lower sleep efficiency ($P = 0.02$), less NREM stage 2 sleep ($P = 0.02$), and less NREM stage 3–4 sleep ($P = 0.03$). No significant differences were found between stroke patients and controls in REM sleep measures, AHI and PLMI. Controls had, as expected, lower sleep efficiency, and reduced amounts of NREM and REM sleep than published norms for non-hospitalized persons.

3.2. Sleep spindles and sawtooth waves in patients with acute hemispheric stroke vs. controls

The mean number of sleep spindles per/hour of sleep was lower in stroke patients, but this difference was not statistically significant. In six (35%) of 17 controls, sleep spindle counts were low (<35/h of sleep) over both hemispheres. In stroke patients sleep spindles and sawtooth waves were usually

Table 1
Sleep EEG changes in acute hemispheric stroke: patients vs. controls[a]

	Stroke patients	Controls	*P*-value[b]
Number of subjects	24	17	
Age (range)	62.1 ± 2.2 (26–78)	58.6 ± 3.2 (26–69)	
Male:female	16:8	13:4	
General sleep parameters			
Total sleep time (min)	246.2 ± 14.6	304 ± 10.9	< 0.01
Sleep efficiency	69.1 ± 2.7	78.4 ± 2.5	0.02
Apnea-hypopnea index	25.0 ± 7.2	16.7 ± 3.3	
PLMI[c]	15.2 ± 4.5	9.0 ± 3.0	
NREM sleep parameters			
Sleep latency (min)	37.7 ± 11.1	29.5 ± 6.4	
NREM 1 (% SPT)	23.2 ± 2.7	18.7 ± 2.0	
NREM 2	25.1 ± 3.2	34.9 ± 9.2	0.02
NREM 3–4	1.6 ± 0.5	5.2 ± 1.8	0.03
Sleep spindles /h of sleep	68.9 ± 21.6	95.2 ± 30.2	
REM sleep parameters			
REM latency (min)	91.2 ± 13.5	72.0 ± 8.3	
REM periods	2.7 ± 0.3	2.9 ± 0.3	
REM (%SPT)	9.9 ± 1.4	13.2 ± 1.6	
REM density	0.09 ± 0.01	0.09 ± 0.03	
Sawtooth waves[d]	16/23	13/16	

[a] Scoring performed over the healthy hemisphere, values expressed as mean ± SE.
[b] Unpaired *t*-test.
[c] PLMI, periodic limb movements in sleep-index; SPT, sleep period time.
[d] Well developed wave forms.

more reduced over the affected hemisphere. No obvious relationship was evident between sleep spindle counts and amounts of slow wave sleep (SWS).

A reduction of sleep spindle counts of >50% over the stroke side, as compared to counts obtained over the healthy side, was found in eight of 24 patients. In these eight patients stroke was located in territories of the middle cerebral artery (MCA, $n = 4$); anterior cerebral artery (ACA, $n = 1$); posterior cerebral artery (PCA, $n = 1$); MCA and ACA ($n = 1$); MCA and old ipsilateral strokes in the territory of ACA and PCA ($n = 1$).

Sleep spindle counts were reduced to <30 /h in six of eight patients with large strokes (stroke volume >25 ml) over both hemispheres. One patient with a small (9 ml) right subcortical stroke had a severe reduction of sleep spindles to 58 /h of sleep over the affected side as compared to 220 /h of sleep over the healthy hemisphere.

There was a trend towards a more frequent reduction of sawtooth waves in right-sided strokes. Large strokes (stroke volume = 26–122 ml) were accompanied by a bilateral reduction of sawtooth waves in all four patients with right-sided lesions but in none of

Fig. 1. Fifty nine year-old man with moderate to severe left hemispheric stroke in the deep territory of the middle cerebral artery (Scandinavian stroke score = 33/58). Sleep studies were performed 9 days after stroke. There was mild sleep-disordered breathing (AHI = 16, minimal SaO_2 = 89%); no periodic limb movements in sleep; a reduction of sleep efficiency (72%) and of NREM sleep stages 2–4 (42% of total sleep time = TST); and increased amounts of REM sleep (30% of TST). Sleep spindle counts were reduced over the left hemisphere (6 /h of sleep) but were normal over the right hemisphere (345 /h of sleep, Fig. 1a). Well-formed, symmetric sawtooth waves were seen over both hemispheres (Fig. 1b). At hospital discharge 2 weeks later the patient was still dependent in everyday life activites, his Barthel index was 64.

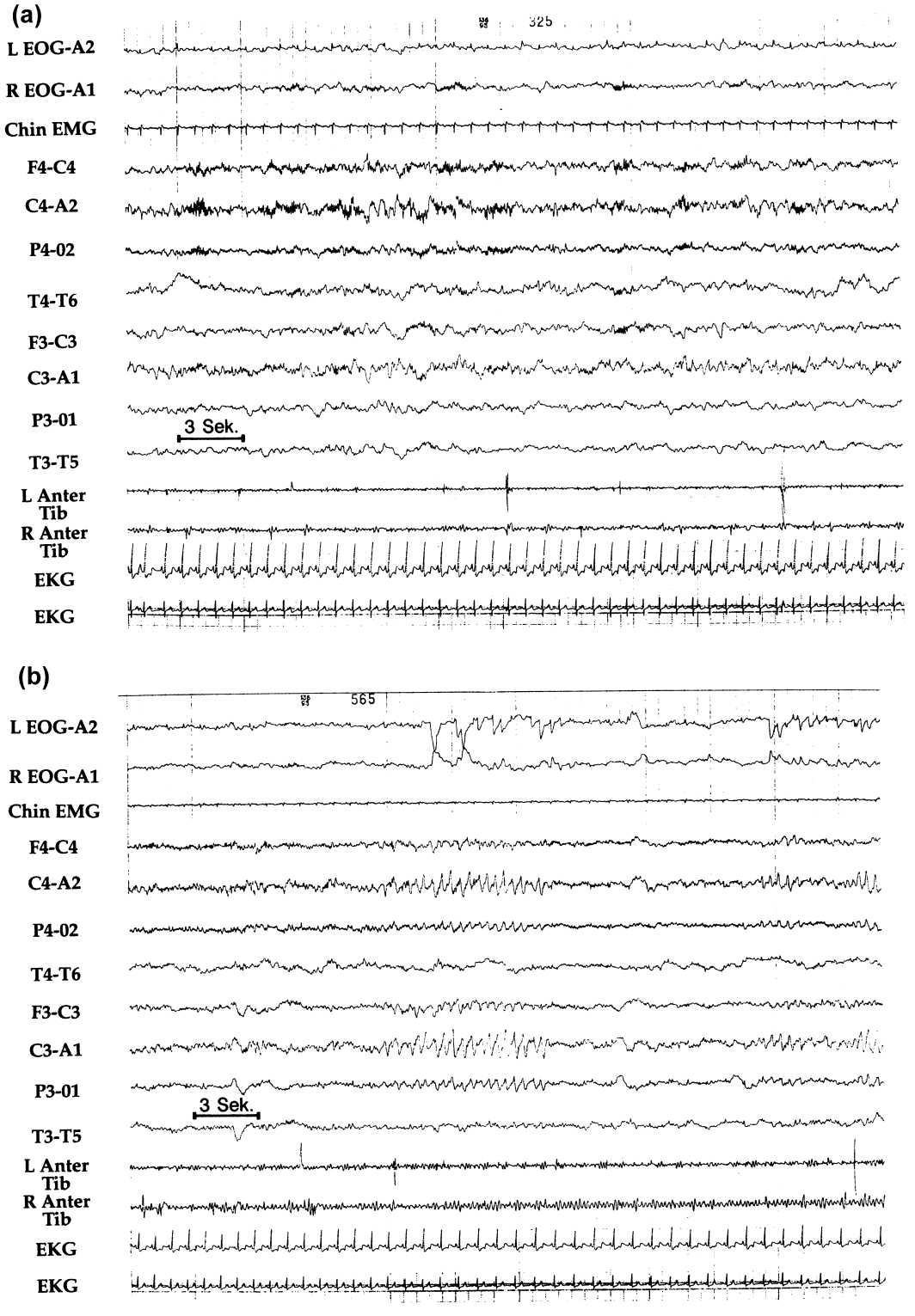
(a)
325
L EOG-A2
R EOG-A1
Chin EMG
F4-C4
C4-A2
P4-02
T4-T6
F3-C3
C3-A1
P3-01
3 Sek.
T3-T5
L Anter Tib
R Anter Tib
EKG
EKG
(b)
565
L EOG-A2
R EOG-A1
Chin EMG
F4-C4
C4-A2
P4-02
T4-T6
F3-C3
C3-A1
P3-01
3 Sek.
T3-T5
L Anter Tib
R Anter Tib
EKG
EKG

Table 2
Sleep EEG changes in acute hemispheric stroke: right vs. left-sided strokes[a]

	R-hemispheric stroke	L-hemispheric stroke	*P*-value[b]
Number of subjects	11	13	
Age (range)	57.2 ± 3.5 (26–69)	66.2 ± 2.5 (48–78)	
Male:female	8:3	8:5	
Scandinavian stroke scale	35.4 ± 5.0	37.6 ± 4.8	
General sleep parameters			
Interval to PSG (days)	10.9 ± 4.6	12.4 ± 3.6	
Total sleep time (min)	243.0 ± 23.7	249.0 ± 18.9	
Sleep efficiency	70.2 ± 3.5	68.3 ± 4.1	
Apnea-hypopnea-index	19.1 ± 9.1	30.8 ± 11.2	
PLMI[c]	14.3 ± 5.4	16.2 ± 7.5	
NREM sleep parameters			
Sleep latency (min)	54.0 ± 21.9	25.2 ± 10.0	
NREM 1 (%SPT)	18.3 ± 3.4	25.9 ± 2.8	
NREM 2	28.3 ± 5.1	24.7 ± 3.2	
NREM 3–4	1.3 ± 0.6	1.5 ± 0.6	
Sleep spindles /h of sleep	92.3 ± 36.6	65.6 ± 24.1	
REM sleep parameters			
REM latency (min)	66.7 ± 14.4	113.7 ± 20.7	0.08
REM periods	3.4 ± 0.3	2.3 ± 0.3	0.05
REM (% SPT)	9.5 ± 1.9	10.0 ± 1.8	
REM density	0.10 ± 0.02	0.08 ± 0.01	
Sawtooth waves[d]	5/10	11/13	0.07

[a] Scoring performed over the healthy hemisphere, values expressed as mean ± SE.
[b] Unpaired *t*-test, chi-square test.
[c] PLMI, periodic limb movements in sleep-index; SPT, sleep period time.
[d] Well developed wave forms.

three patients with left-sided lesions. In a few patients with large strokes we observed a reduction of sleep spindles but not of sawtooth waves over the affected hemisphere (Fig. 1).

3.3. Sleep electroencephologram and topography of stroke (Table 2)

There were no statistically significant differences in sleep EEG parameters, AHI or PLMI between patients with right-sided and left-sided strokes. Trends towards a higher REM latency and a lower number of REM periods in left-hemispheric strokes may have been in part determined by the higher AHI in the latter patient group. The lack of significant difference in sleep EEG findings persisted also when comparing patients with large right-sided ($n = 4$) and left-sided ($n = 4$) stroke.

3.4. Sleep electroencephalogram and outcome of stroke (Table 3)

Patients with poor short-term outcome had lower sleep efficiency ($P < 0.01$), less total sleep time ($P = 0.02$), less NREM stage 2 (<0.01), fewer sleep spindles (n.s.), and less NREM stage 3–4 sleep (n.s.) when compared with patients with good short-term outcome. Most REM sleep measures were also more severely altered in patients with poor short-term outcome but only the reduction in sawtooth waves ($P = 0.01$) was statistically significant. These differences in sleep EEG changes may have been somewhat underestimated considering the longer interval

Table 3
Sleep EEG changes in acute hemispheric stroke: good vs. bad short-term clinical outcome[a]

	Good outcome	Bad outcome	*P*-value[b]
Number of subjects	16	8	
Age (range)	60.6 ± 3.1 (26–78)	65.1 ± 2.4 (55–76)	
Male:female	8:3	8:5	
Scandinavian stroke scale	46.2 ± 2.8	21.3 ± 3.1	<0.001*
General sleep parameters			
Interval to PSG (days)	6.8 ± 1.4	21.0 ± 6.8	0.01**
Total sleep time (min)	269.1 ± 15.4	200.1 ± 25.1	0.02**
Sleep efficiency	70.2 ± 3.5	68.3 ± 4.1	<0.01**
Apnea-hypopnea-index	15.2 ± 4.1	42.1 ± 17.3	0.07[c]*
PLMI[c]	19.9 ± 6.6	7.2 ± 3.1	
NREM sleep parameters			
Sleep latency (min)	29.1 ± 8.1	59.8 ± 31.9	
NREM 1 (% SPT)	19.6 ± 2.1	28.2 ± 5.1	0.07**
NREM 2	32.5 ± 3.0	14.0 ± 3.5	<0.01**
NREM 3—4	1.7 ± 0.5	0.8 ± 0.7	
Sleep spindles per/h of sleep	94.0 ± 26.2	49.5 ± 32.7	
REM sleep parameters			
REM latency (min)	104.2 ± 15.4	61.5 ± 24.8	
REM periods	2.9 ± 0.3	2.3 ± 0.5	
REM (%SPT)	11.0 ± 1.6	7.3 ± 1.8	
REM density	0.10 ± 0.02	0.07 ± 0.02	
Sawtooth waves[d]	13/15	3/8	0.01***

[a] Scoring performed over the healthy hemisphere, values expressed as mean ± SE.
[b] *Mann–Whitney-U-test, **unpaired *t*-test, ***chi-square test.
[c] PLMI, periodic limb movements in sleep-index; SPT, sleep period time.
[d] Well developed wave forms.

between PSG recordings and stroke onset ($P = 0.01$) in patients with poor outcome. There was a trend towards higher AHI in patients with poor short-term outcome and higher PLMI in patients with good short-term outcome.

3.5. Sleep EEG early and late after stroke (Table 4)

In patients recorded <4 days after stroke, we found higher REM sleep latency ($P < 0.01$), reduced amounts of REM sleep ($P = 0.01$) and fewer REM periods (n.s.) compared with patients recorded later. These REM sleep changes may have been underestimated considering the higher AHI and SSS found in patients recorded >4 days after stroke (both differences, were, however, statistically n.s.). Measures of NREM sleep were similar in both patient groups.

4. Discussion

In this study, sleep macro and microstructure was assessed in 24 consecutive patients with, MRI-proven acute extra-thalamic hemispheric stroke. We found that acute hemispheric stroke is associated with a severe reduction in sleep efficiency, with reduced amounts of both NREM and REM sleep, compared to published norms [29]. However, the presence of sleep architecture changes in our control population indicates that the observed sleep EEG changes can be attributed only partially to brain damage. Such factors as acute change in sleep environment; biological and psychological stress; increased bed rest; drugs, fever, pain and other systemic complications may affect sleep. This assumption is supported by the observation of similar, profound sleep EEG changes in patients with acute myocardial infarction [23].

Table 4
Sleep EEG changes in acute hemispheric stroke: early and late polysomnographic recordings[a]

	Early PSG (<4 days)	Late PSG (≥4 days)	*P*-value[b]
Number of subjects	9	14	
Age (range)	63.6 ± 2.3 (26–78)	60.3 ± 3.5 (55–76)	
Male:female	8:3	8:5	
Scandinavian stroke scale	39.7 ± 5.5	35.1 ± 4.4	
General sleep parameters			
Interval to PSG (days)	2.9 ± 0.6	17.4 ± 4.0	< 0.01
Total sleep time (min)	231.1 ± 24.2	256.8 ± 19.5	
Sleep efficiency	70.0 ± 4.1	68.1 ± 3.8	
Apnea-hypopnea-index	16.4 ± 5.0	30.9 ± 11.5	
PLMI[c]	23.9 ± 10.1	9.2 ± 2.4	
NREM sleep parameters			
Sleep latency (min)	50.1 ± 21.0	30.5 ± 13.7	
NREM 1 (%SPT)	22.9 ± 4.1	22.3 ± 3.0	
NREM 2	26.6 ± 5.7	25.8 ± 3.5	
NREM 3–4	2.2 ± 0.9	1.1 ± 0.5	
Sleep spindles /h of sleep	77.9 ± 42.5	82.5 ± 24.6	
REM sleep parameters			
REM latency (min)	105.8 ± 14.4	73.2 ± 17.5	< 0.01
REM periods	2.2 ± 0.6	3.1 ± 0.3	
REM (%SPT)	5.8 ± 2.0	12.4 ± 1.4	0.01
REM-density	0.10 ± 0.03	0.09 ± 0.01	
Sawtooth waves[d]	5/8	10/14	

[a] Scoring performed over the healthy hemisphere, values expressed as mean ± SE.
[b] Unpaired t-test.
[c] PLMI, periodic limb movements in sleep-index; SPT,sleep period time.
[d] Well developed wave forms.

Nevertheless, our data supports the hypothesis that focal hemispheric lesions disrupt sleep architecture. While a reduction of total sleep time and lower sleep efficiency are almost universally found after strokes, reports in the literature of changes in NREM sleep and REM sleep differ. Amounts of NREM sleep stages 2 and SWS were significantly reduced in this study and other studies [17,30]. Other authors, however, reported an increase of SWS was found following hemispheric stroke [18,19,31]. Differences in recording and scoring strategies (bipolar vs. monopolar electrodes, affected vs non affected hemisphere), patients age, and stroke extension may partially account for these differences. Indeed, large strokes may occasionally increase slow wave activity during wakefulness and sleep over both the affected and the non-affected hemisphere [31,32]. A reduction of NREM sleep was observed also in experimental hemispheric lesions [33,34] in cats without neocortex and striatum ('diencephalic cats'). This impaired capacity to consolidate NREM sleep in the presence of hemispheric lesions may be due to the disruption of cortico-thalamo-cortical and intracortical mechanisms essential for spindling and SWS [3,5].

While reports of changes of NREM sleep after acute hemispheric stroke differ, most studies agree in suggesting a reduction of REM sleep in stroke patients. REM sleep appears to be particularly affected in the first few days after stroke [18]. The mean latency of 12 days between stroke onset and sleep studies in our series may explain why we did not find significant differences in REM sleep between stroke patients and controls. Furthermore, the observation of similar REM sleep changes in patients with mild and severe stroke suggests that REM sleep

abnormalities are more likely to reflect, in most cases, acute illness than brain damage [18].

In our study, sleep spindles and sawtooth waves were often reduced over the affected hemisphere [16,25]. The absence of a statistical difference between patients and controls in spindle counts in our series is possibly due to the inclusion of small strokes and to the low, probably age-related number of sleep spindles in one third of our controls [35]. Ipsilateral depression of phasic sleep events can occur even in the absence of abnormalities in the waking EEG [16] and, as shown in our study, without a direct correlation with changes in SWS. Similar observations in patients with isolated thalamic stroke and in decorticated cats [15,33] fit with the experimental evidence suggesting differences in the underlying mechanisms of these EEG activities [5]. Although large cortico-subcortical lesions or thalamic lesions are more effective in reducing sleep spindles [15] we confirm that smaller and even subcortical lesions may have similar effects [36,37]. Among cortical lesions we could not test whether parietal lesions may be particularly associated with a reduction of sleep spindles, as suggested before [38]. More studies are evidently needed to elucidate the role of topography and volume of cerebral hemispheric lesions on spindle activity.

Of particular interest is our observation of a bilateral reduction of sleep spindles and sawtooth waves phasic following unilateral strokes. This finding demonstrates a functional involvement of the unaffected side in unilateral hemispheric stroke as documented, before by wake EEG or PET [39,40].

Our observations do not suggest a major influence of stroke side on sleep EEG changes. Körner et al. [19] reported previously that right-sided strokes can decrease preferentially REM sleep, and that left-sided strokes can selectively reduce stage 4 NREM sleep. Based on our experience we believe that these sleep EEG changes may be related to differences in stroke extension and interval of recording from stroke onset (see above) rather than to stroke side. Our observation that right-sided hemispheric strokes may affect sawtooth waves more often than left-sided strokes is possibly fortuitous.

This research has several potential limitations. First, the high frequency of sleep apnea and PLMS in patients and controls influenced sleep macro and microstructure. Second, heterogeneity in timing of the study, stroke topography and extension, and age of patients probably affected our results. Third, in the absence of a continuous activity monitoring in our patients, the observed reduction in sleep efficiency and NREM sleep at night may in part be related to sleep episodes ('dozing off') during the day. Fourth, sleep EEG was scored over only one electrode using a visual rather than a spectral analysis of the signal. This technique may have precluded the recognition of subtle (topographic or frequency specific) changes in electrogenesis. Finally, a type 2 statistical error can not be excluded considering the small numbers of patients studied.

In conclusion, our report supports the hypothesis that the cerebral cortex has a role in the modulation of sleep-wake functions. Further studies are needed to elucidate the relationship between stroke topography and stroke extension with changes of sleep macro and microstructure.

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