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Longitudinal Polysomnographic Assessment from Acute to Subacute Phase in Infratentorial versus Supratentorial Stroke

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Key Words
Sleep-related breathing disorders · Infratentorial stroke · Supratentorial stroke · Polysomnography · Polygraphy · Acute phase · Subacute phase

Abstract
Background: Regulation of sleep and sleep-related breathing resides in different brain structures. Vascular lesions can be expected to differ in their consequences on sleep depending on stroke topography. However, studies addressing the differences in sleep and sleep-related breathing depending on stroke topography are scarce. The aim of the present investigation was to compare the sleep and sleep-related breathing of patients with supratentorial versus infratentorial stroke. ***Methods:*** This study was part of the prospective multicenter study SAS-CARE-1 (Sleep-Disordered Breathing in Transient Ischemic Attack (TIA)/Ischemic Stroke and Continuous Positive Airway Pressure (CPAP) Treatment Efficacy (SAS-CARE); NCT01097967). We prospectively included 14 patients (13 male, age 66 ± 6 years) with infratentorial lesions and 14 patients (14 male, age 64 ± 7 years) with supratentorial lesions, matched for age and stroke severity. Polysomnography was recorded in all during the acute phase within 9 days after stroke onset and 3 months later. ***Results:*** During the acute phase after stroke, patients with infratentorial lesions had significantly more sleep-related breathing disorders than patients with supratentorial lesions with an apnea-hypopnea index >20 observed in 8 (57%) patients with infratentorial stroke and in only 2 (14%) patients with supratentorial stroke. Sleep-related breathing improved from the acute to the subacute phase (3 months), albeit remaining elevated in a significant proportion of subjects. Sleep parameters did not differ between the two patient groups but there was a general improvement of sleep from the acute to the subacute phase which was comparable for both patient groups. Although stroke severity was mild, recovery after 3 months was worse in patients with infratentorial stroke with 12 of 14 patients with supratentorial stroke being symptom free (NIHSS = 0), while this was the case for only 6 of 14 patients with infratentorial stroke. ***Conclusions:*** Patients with infratentorial lesions are at an increased risk for sleep-related breathing disorders, which are frequent in this group. Monitoring of sleep-related breathing is therefore especially recommended in patients with infratentorial stroke. Because of the absence of reliable differences in sleep parameters between the two patient groups, polygraphy, with reduced diagnostic costs, rather than polysomnography could be considered. The higher prevalence of sleep-related breathing disorders and the poorer recovery of patients with infratentorial lesions suggest that early treatment interventions should be considered.

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Introduction

During the past two decades there has been a growing interest in the link between stroke and sleep [1]. One question that has received only limited attention concerns the effects of different stroke topographies on sleep. As the encephalic structures implicated in the generation and regulation of sleep are mainly located in the brainstem, hypothalamus and thalamus, different consequences on sleep are expected depending on the site of the vascular lesion [1–3]. In this respect, infratentorial structures are particularly vital for the maintenance of a regular breathing pattern during sleep, while cerebral hemispheres mainly modulate volitional breathing during wakefulness [4]. Indeed, sleep-related breathing disorders are found in 40–70% of patients with acute stroke [5–7]. Experimental evidence has demonstrated that brainstem neurons regulate REM sleep [8] and slow wave sleep is assumed to be mainly controlled on the level of the posterior hypothalamus [9]. In accordance with this, some previous studies have reported prominent REM sleep reductions in patients with brainstem lesions [2, 10, 11] and reductions of NREM sleep in patients with hemispheric lesions [12].

Surprisingly, so far, few studies have directly compared sleep and sleep-related breathing patterns between patients with supratentorial (STS) and infratentorial (ITS) stroke (online suppl. table S1; for all online suppl. material, see www.karger.com/doi/10.1159/000356323). Bassetti et al. [13] compared results from polysomnographic recordings 1–49 days after stroke in 11 patients with ITS with those of 28 patients with STS and found no difference in sleep and sleep-breathing patterns. Likewise, Terzoudi et al. [14] found no difference in sleep patterns 6–10 days after stroke between patients with brainstem lesions and patients with hemispheric lesions. However, patients with cerebellar lesions showed less REM sleep than all other patients. Finally, two studies by Gasanov [15] and Gasanov et al. [16] found that patients with brainstem lesions had reduced REM sleep and reduced intrasleep wakefulness than patients with hemispheric lesions. Concerning sleep-related breathing, polysomnographic and polygraphic studies in the very acute [17–21], acute [13, 22–25] or subacute phase [26] after stroke found no differences between patients with ITS and STS (online suppl. table S1). Thus, despite prominent sleep and sleep-related breathing alterations described in selected patient groups, a direct comparison between ITS and STS has not revealed major differences. Possible reasons for this include small and/or heterogeneous patient groups, especially with regard to age, comorbidities and stroke severity. In addition, variance of time after stroke onset could obscure between-group differences as sleep and sleep-related breathing undergo significant changes from the acute to the subacute phase after stroke [17, 27–30].

Therefore, the aim of the present study was to compare the polysomnographic poststroke evolution of sleep and sleep-related breathing between two selected homogeneous groups of patients, one with STS and one with ITS.

Methods

Patients

This study is part of the prospective multicenter study SAS-CARE-1 (Sleep-Disordered Breathing in Transient Ischemic Attack (TIA)/Ischemic Stroke and Continuous Positive Airway Pressure (CPAP) Treatment Efficacy (SAS-CARE); NCT01097967). Details regarding the design of the SAS-CARE study have been published previously [31]. Briefly, the SAS-CARE cohort includes 35- to 75-year-old patients with a clinical diagnosis of TIA or ischemic stroke, who were admitted to a stroke unit within 2 days from onset of symptoms. The selection criteria included the absence of the following: unstable clinical situation (cardiorespiratory or life-threatening medical conditions); current or CPAP treatment during the last 3 months before stroke; nonischemic events (intracerebral/subarachnoid hemorrhage); coma/stupor, and any condition that interferes with the acceptance of CPAP treatment. The relevant local ethics committees approved the protocol of the study and informed consent was obtained from all participants.

For the current study we considered only patients who underwent nocturnal polysomnography both during the acute phase and 3 months after stroke or TIA in our center (Civic Hospital of Lugano). Additional exclusion criteria were new nonfatal cardiovascular events and significant change of psychotropic medications in the period between the two polysomnographic recordings.

The following parameters from SAS-CARE database were considered: age; BMI; medical history (dyslipidemia, diabetes, hypertension, previous cerebrovascular events, smoking and snoring); etiology of stroke according to the criteria of the TOAST study [32]; stroke severity as assessed by the National Institute of Health Stroke Scale (NIHSS) [33] at admission and 3 months after stroke; topography of current cerebrovascular event (ITS or STS) according to MRI or CT scans, and Epworth Sleepiness Scale score assessed within the first week after admission.

Nocturnal Polysomnographic Studies

All polysomnographic recordings were registered with Embla titanium and included 6 channels of electroencephalogram, submental electromyogram, electrooculogram, nasal airflow, 2 channels of breathing effort and oximetry. Recordings within the first 9 days (1–8 days) after stroke were performed in the stroke unit from 8–10 p.m. to 7–8 a.m. Polysomnographies after 3 months were recorded in the sleep laboratory from 9–11 p.m. to 6–7.30 a.m. All recordings were scored manually according to standard criteria by experts [34]. Standard sleep parameters such as total

sleep time (TST), sleep latency (time in minutes from 'lights-off' until sleep onset), REM latency (time in minutes from sleep onset to first epoch of REM), sleep efficiency (percentage of TST in total recording time), percentages of stages from TST, wake after sleep onset (time of wake from lights-off to lights-on minus sleep latency, in minutes) as well as apnea-hypopnea index (AHI; total number of apnea plus hypopnea divided by TST), separate indexes for obstructive, mixed and central apnea and desaturation (number of desaturations ≥4%, divided by TST), arousal index (number of arousal per hour of sleep) and saturation parameters were derived from all recordings in acute and subacute phase.

Statistical Analysis

We compared sleep and sleep-related breathing between patients with STS and patients with ITS during the acute phase and after 3 months. In addition, we analyzed changes in sleep and nocturnal breathing from the acute phase to 3 months later and explored whether the change across time differed between the two groups of patients.

The distribution of all continuous variables was carefully checked (Lilliefors test) and for variables significantly deviating from a normal distribution a transformation across the ladder of powers was sought to achieve approximate normality. Approximate normality could be achieved with a $\log_{10}$ transformation (with or without adding a small constant) for sleep onset latency, REM latency, percentage of N1 sleep, the AHI, the obstructive apnea index, the hypopnea index, and the oxygen desaturation index. A power transformation (x^4) was used for sleep period time. For the central apnea index, the mixed apnea index and the time spent with oxygen saturation below 90%, no suitable transformation could be found.

Comparison between groups was undertaken with t tests, Mann-Whitney U test or Fisher's exact test, as appropriate. Comparison between time points (acute vs. 3 months) used the Wilcoxon test for non-normally distributed variables. In addition, we quantified differences between the two groups with Cohen's d, an effect size measure [35]. Conventionally, for Cohen's d, an effect size of 0.2–0.3 is considered a 'small' effect, around 0.5 a 'medium' effect, and 0.8 or larger a 'large' effect.

Results

A total of 45 patients underwent a polysomnography study during the acute phase and 3 months later; 12 patients were excluded for the following reasons: 3 patients because of the occurrence of a new vascular event in the period between the two recordings, 1 patient for technical reasons, 1 patient because the ischemic episode was localized only in the retina, and 7 patients because of significant change of psychopharmacological medication between the two polysomnographic recordings [new introduction of pramipexole (n = 1), sertraline (n = 3), fluoxetine (n = 1), levetiracetam (n = 1), cessation of amitriptyline (n = 1)]. From the remaining 33 patients, 14 had an ITS, including 2 patients with additional supratentorial lesions (13 male, age 54–76 years, NIHSS scores 0–6). Because our sample size was too low to statistically control for possible differences in age and stroke severity, we excluded patients with STS that were below the age range of patients with ITS (n = 4, age 30–52 years) and 1 patient with an NIHSS score of 14 (well outside the range of patients with ITS). The final group of patients with STS included 14 subjects, all male, aged between 54 and 75 years and with overall mild stroke severity (NIHSS 0–6) comparable to those of the ITS group.

The two groups are described in table 1 and were well matched regarding demographic parameters, daytime sleepiness, self-reported snoring, stroke features or risk factors; 4 patients had a TIA (for 3 the location was supratentorial, for 1 infratentorial; p = 0.596). A description of stroke/TIA location is given in table 2. Sleep and sleep-related breathing parameters in the two groups are described in table 3. During the acute phase, patients with ITS had a higher AHI and a higher obstructive apnea index than patients with STS. There was also a large effect (d approx. 0.8) and statistical trend ($p < 0.1$) for an increased central apnea index and a higher number of desaturations per hour of sleep in patients with ITS; 8 patients with ITS but only 2 patients with STS had an AHI above 20 (p = 0.0461). Although on average, patients with ITS had less REM sleep and a longer REM latency, the effect was of only moderate magnitude (d approx. 0.5) and did not reach statistical significance with our sample size.

Comparing sleep and breathing in both patient groups 3 months later, patients with ITS still had a higher obstructive apnea index than patients with STS, but did not differ anymore in the AHI, central apnea index or oxygen desaturation index. For the total group of patients, sleep improved from the acute phase to 3 months later (table 3). In particular, sleep efficiency and REM sleep increased while sleep onset latency, REM latency, N1 sleep, the number of arousals, and wake after sleep onset decreased (table 2). Most sleep-related breathing parameters such as the number of apneas and hypopneas, including obstructive, central and mixed apneas, decreased significantly (fig. 1). Despite this improvement, 5 patients with ITS and 3 patients with STS had an AHI >20 at 3 months after the stroke (p = 0.678). There was no indication that for sleep and sleep-related breathing the change over time was different for patients with ITS compared with patients with STS (time × group interaction; table 3).

Finally, despite overall low stroke severity and no differences at admission, after 3 months patients with ITS had higher NIHSS scores than patients with STS (p = 0.022; fig. 2). While 12 of 14 patients with STS were symp-

Table 1. Description of participants

	Total group (n = 28)	Patient groups		Test statistic, p value
		STS (n = 14)	ITS (n = 14)	
Males, n	27 (96%)	14 (100%)	13 (93%)	
Age, years	64.89±6.52	63.86±6.65	65.93±6.49	t = –0.8, p = 0.411
BMI, kg/m^2	27.51±4.93	28.39±4.6	26.63±5.27	t = 0.94, p = 0.354
Epworth sleepiness scale	6.71±3.60	7.07±3.99	6.36±3.27	t = 0.52, p = 0.609
Self-reported snoring	17 (61%)	8 (57%)	9 (64%)	p = 1.0
NIHSS at admission	2.54±1.72	2.29±2.46	2.79±1.72	W = 83, p = 0.497
TOAST, n				p = 0.368
Large-artery atherosclerosis	2 (7%)	0 (0%)	2 (14%)	
Cardioembolism	9 (32%)	6 (43%)	3 (21%)	
Small-vessel occlusion	7 (25%)	2 (14%)	5 (36%)	
Other etiology	2 (7%)	1 (7%)	1 (7%)	
Undetermined	8 (29%)	5 (36%)	3 (21%)	
Thrombolysis	5 (18%)	3 (21%)	2 (14%)	p = 1.0
Dyslipidemia				p = 1.0
No dyslipidemia	9 (32%)	4 (29%)	5 (36%)	
Treated	6 (21%)	3 (21%)	3 (21%)	
Untreated	13 (46%)	7 (50%)	6 (43%)	
Diabetes	2 (7%)	2 (14%)	0 (0%)	p = 0.482
Hypertension				p = 1.0
No hypertension	11 (39%)	5 (36%)	6 (43%)	
Treated	15 (54%)	8 (57%)	7 (50%)	
Untreated	2 (7%)	1 (7%)	1 (7%)	
Smoking (current or past 10 years)	10 (36%)	6 (43%)	4 (29%)	p = 0.695
ESSEN risk score	1.75±1.14	1.93±1.21	1.57±1.09	W = 114, p = 0.447

tom free (NIHSS = 0) 3 months after the stroke, this was the case for only 6 of 14 patients with ITS (p = 0.046). Neither the AHI nor the proportion of patients with AHI >20 differed between ITS patients who had an NIHSS score of 0 after 3 months and those who did not.

Discussion

We prospectively assessed sleep and sleep-related breathing parameters in the acute and subacute phase after stroke and compared sleep patterns and their time course between 14 patients with STS and 14 with ITS, who were well matched in terms of demographic parameters and stroke severity. We found that ITS patients had significantly more sleep-related breathing disorders than STS patients during the acute phase. Our study is therefore the first that found marked differences in sleep-related breathing between ITS and STS. Sleep-related breathing improved from the acute to the subacute phase, albeit remaining elevated in a significant proportion of subjects. In addition, there was a general improvement of

Table 2. Stroke location

ITS/TIA	*STS/TIA*
M, 58 y C medulla	M, 75 y L occipital Co
M, 77 y L medulla	M, 55 y L parietal SC
M, 62 y R medulla	M, 70 y R frontoparietal Co + SC
M, 56 y R medulla	M, 55 y L basal ganglia SC
M, 63 y R pons	M, 75 y L parietal SC
M, 70 y R pons	M, 70 y L parietal Co
M, 66 y C pons	M, 68 y R frontotemporal/ parietal Co + SC
M, 71 y C pons	M, 60 y R frontal (insular) Co
M, 70 y C pons, R midbrain	M, 72 y L parietal Co
M, 70 y R cerebellum	M, 65 y R frontal Co
M, 54 y R cerebellum	M, 64 y L frontoparietal Co + SC
M, 64 y L cerebellum	M, 62 y L parietal Co
M, 62 y L cerebellum	M, 65 y R frontal SC
ITS + STS/TIA	
M, 59 y L midbrain + L thalamus	
F, 67 y L medulla + pons + thalamus	

M = Male; F = female; y = years; C = central; R = right; L = left; Co = mainly cortical; SC = mainly subcortical.

Table 3. Sleep and sleep-related breathing parameters in patients with STS (n = 14) and ITS (n = 14) during the acute phase and 3 months later

	Total group		Time	Groups				Between-group comparison				Time × group
				STS		ITS		STS vs. ITS				
	acute phase	3 months	acute phase vs. 3 months p value	acute phase	3 months	acute phase	3 months	effect sizes		p values		p value
								acute phase	3 months	acute phase	3 months	
TST, min	386.46±93.5	388.45±60.7	0.914	392.86±81.8	369.82±35.3	380.07±106.6	407.07±75.2	–0.14	0.14	0.725	0.110	0.180
SE, %	64.58±13.6	76.3±9.9	*<0.001*	63.19±11.5	75.42±9.1	65.97±15.69	77.18±10.9	0.20	0.18	0.598	0.648	0.844
SOL, min	24.25 (10–51)	6.5 (3–11)	*<0.001*	16.5 (11.2–30)	7.5 (3.2–10)	36.25 (10.2–73)	6 (3.62–12)	0.47	–0.01	0.236	0.990	0.192
REM latency[a], min	148.5 (115–245)	69 (55.9–100)	*<0.001*	152.75 (118.2–256)	76 (51.5–111)	128 (111.5–198)	69 (62.2–86)	–0.42	0.15	0.295	0.704	0.269
N1 (%TST)	11.36 (4.8–17)	6.06 (3.5–10)	*0.002*	10.18 (4.3–13)	5.73 (4.7–8)	12.04 (5.9–22)	7.63 (2.8–11)	0.48	0.09	0.223	0.809	0.373
N2 (%TST)	46.26±15.2	48.59±11.9	0.361	48.53±15.2	48.57±13.1	43.99±15.4	48.61±11.0	–0.30	0.00	0.441	0.992	0.370
N3 (%TST)	23.87±11.7	24.33±10.5	0.861	24.41±11.7	23.03±12.1	23.33±12.1	25.62±8.9	–0.09	0.25	0.813	0.524	0.487
REM (%TST)	14.21±6.1	19.75±5.6	*<0.001*	15.71±6.4	21.28±5.3	12.71±5.6	18.21±5.7	–0.50	–0.56	0.201	0.153	0.980
Arousal index	30.42±15.5	23.05±12.9	*0.025*	28.38±16.8	24.63±13.4	32.46±14.3	21.48±12.6	0.26	–0.24	0.496	0.528	0.253
WASO, min	232.96±92.4	136.79±51.1	*<0.001*	242.96±77.9	141.32±50.1	222.96±106.9	132.25±53.5	–0.22	–0.18	0.577	0.647	0.772
AHI	15.51 (8.9–43)	15.33 (5.3–23)	*0.039*	11.41 (8.2–16)	13.16 (4.7–19)	39.16 (15.2–46)	16.83 (6.5–24)	*0.89*	0.21	*0.028*	0.590	0.142
OAI	3.96 (2.0–8)	3.69 (1.2–5)	*0.081*	2.45 (0.8–6)	3.12 (0.4–4)	6.27 (3.8–14)	4.48 (3.5–8)	*0.85*	*0.91*	*0.036*	*0.032*	0.687
CAI	0.4 (0–3)	0 (0–0.5)	*0.006*[b]	0.05 (0–1)	0 (0–1)	1.36 (0.1–4)	0.1 (0–0.4)			0.068[b]	0.861[b]	
MAI	0 (0–1)	0 (0–0)	*0.019*[b]	0 (0–1)	0 (0–0)	0.23 (0–1)	0 (0–0)			0.252[b]	0.840[b]	
HI	8.76 (6.3–16)	8.62 (3.6–14)	0.466	7 (3.7–12)	10.1 (3.7–14)	12.92 (6.6–23)	6.72 (3.6–17)	0.61	0.03	0.117	0.930	0.161
ODI	6.65 (2.6–21)	8.31 (4.6–17)	0.666	4.47 (1.2–9)	7.15 (4.3–14)	14.29 (5.6–26)	10.24 (5.8–19)	*0.79*	0.41	0.052	0.293	0.197
Mean O^2	92.95±1.7	92.94±1.7	0.983	92.69±1.5	92.82±1.8	93.21±1.9	93.06±1.8	0.31	0.13	0.429	0.727	0.679
Minimum O^2	85.57±5.3	84±5.2	0.986	87.14±3.8	84.86±5.3	84.00±6.1	83.14±5.2	0.63	–0.35	0.119	0.366	0.646
Time <90% O^2	2.55 (0–14)	5.1 (0.9–16)	0.466[b]	1.95 (0–19)	6.8 (0.8–16)	2.55 (0.2–10)	4.3 (1.5–14)			0.742[b]	0.927[b]	

Values are expressed as mean ± SD or as median and interquartile range where variables deviated significantly from a normal distribution. CAI = Central apnea index; HI = hypopnea index; MAI = mixed apnea index; OAI = obstructive apnea index; SE = sleep efficiency; SOL = sleep onset latency; TST = total sleep time; WASO = wake after sleep onset; ODI = oxygen desaturation index.

[a] 1 subject had no REM sleep and consequently no REM latency. [b] Nonparametric test.

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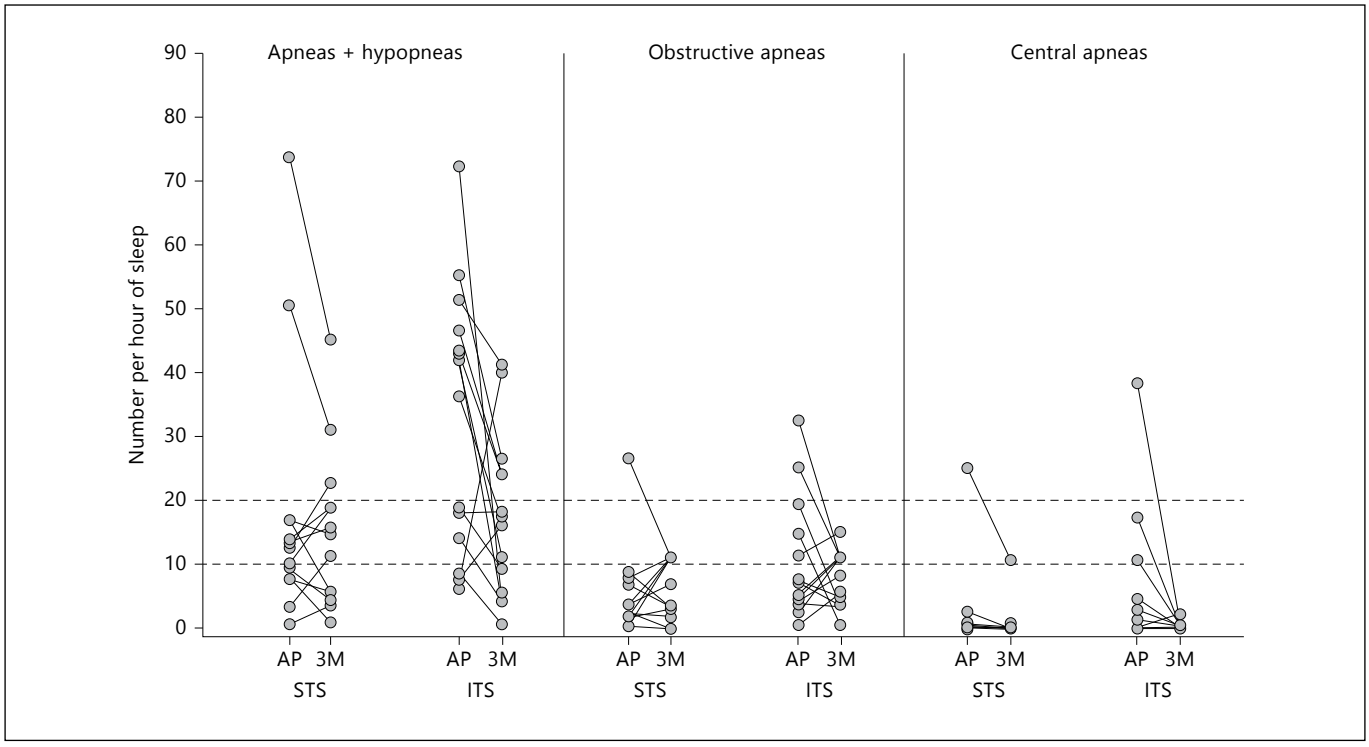

Fig. 1. Number of apneas or hypopneas per hour of sleep during the acute phase and 3 months later in patients with STS or ITS. AP = Acute phase; 3M = after 3 months.

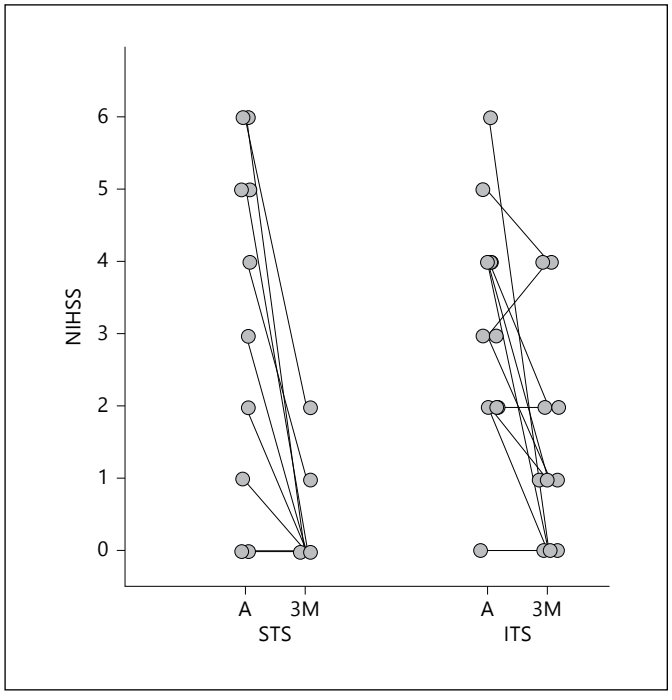

Fig. 2. NIHSS scores at admission and after 3 months in patients with STS or ITS. A = At admission; 3M = after 3 months.

sleep from the acute to the subacute phase which was comparable for both ITS and STS patients.

Concerning the general improvement of sleep, two interesting implications have to be underlined. Firstly, independent of the location and size of the lesion, stroke per se induced sleep disruption, suggesting that systemic changes such as inflammatory or hemodynamic ones, more than single nuclei impairment, may explain sleep abnormalities during the acute phase. Secondly, from the acute to the subacute phase, neither total sleep time nor slow wave sleep increased, suggesting that sleep improvement mainly consisted of a better reorganization with a reduction of sleep fragmentation (arousal index) and improved REM regulation. In other words, in an emergency, the brain sacrifices sleep continuity and REM sleep first rather than slow wave sleep or the total amount of sleep.

We did not observe significant differences in sleep parameters between patients with ITS and STS. In particular, no differences in REM sleep were found, which has been reported in some [15, 16] but not all [13, 36] previous studies. In fact, REM sleep and slow wave sleep were comparable between the two groups and effect sizes for these comparisons were only moderate, so that

low statistical power cannot fully explain the absence of differences.

During the acute phase, patients with ITS had significantly more sleep-related breathing disorders, both central and obstructive, than patients with STS. This difference largely disappeared in the subacute phase, mainly due to a marked decrease of hypopneas in ITS. Even so, more patients in the ITS group (36%) remained at pathological levels (AHI >20/h) at 3 months compared with those with STS (21%). The most likely explanation for this is that by matching both groups with regard to age and stroke type/severity our study was able to unmask these differences which could have been obscured in previous studies by differences in patient characteristics. In addition, since differences were no longer apparent at 3 months, heterogeneity of time after stroke might have further contributed to the lack of findings in previous studies (see online suppl. table S1).

A further prominent finding was the significant improvement of sleep-related breathing from the acute to the subacute phase. For obstructive sleep apnea this is in agreement with previous studies [17, 29, 30, 37–39]. For central sleep apnea, some [17] but not all [30, 38] have observed a significant reduction over time. We found a reduction of both central and obstructive apneas. Despite a general significant tendency to decrease the number of apneas and hypopneas, however, this was not the case for every patient (fig. 1). During the acute phase, 8 patients with ITS but only 2 with STS had clinically significant sleep breathing disorders (AHI >20). While the AHI decreased in all these patients, AHI >20 was still observed in 5 ITS and 2 STS patients at 3 months. Importantly, 1 STS patient had new clinically significant sleep breathing disorder at 3 months. Indeed, also in previous studies a persistence of significant sleep-related breathing disorders [17, 37] or even a worsening [29] in a considerable number of patients has been observed. Together with our results, this suggests that monitoring of sleep-related breathing might be considered also in the subacute phase to identify patients with significant sleep-related breathing disorders. Because of the higher prevalence in ITS patients, monitoring of sleep-related breathing is especially recommended for this group. However, it should be taken into account that large STS, for mechanical or other reasons, might affect even brainstem activity. In addition, because of the absence of reliable differences in sleep parameters between the two groups, this would argue for assessment of sleep-related breathing in ITS by a simple polygraph rather than polysomnography during the acute phase, with reduced diagnostic costs.

The early identification of sleep breathing disorders is of importance, because treatment of sleep apnea in stroke patients has been associated with a better outcome [40–42]. Even though stroke severity was mild in our sample, we found that patients with ITS, which as a group had more sleep-related breathing disorders, also showed poorer recovery. This could suggest that early treatment in these patients may positively influence future outcomes. In fact, early treatment of obstructive sleep apnea by nasal CPAP has been reported to improve the neurological recovery in patients with ischemic stroke [40, 41]. Despite the fact that we only observed a limited number of central events, which almost universally disappeared by month 3, an automatic servo-ventilation device may be considered in acute phase of stroke instead of a simple CPAP or auto-CPAP treatment.

Our study has some limitations which have to be taken into consideration. For one, our sample size was relatively small which has resulted in low statistical power to detect significant group differences. Indeed, we were only able to identify large effects ($d > 0.8$). Future studies with larger samples may therefore reveal further differences between ITS and STS patients, especially in the area of REM sleep where effect sizes indicated a moderate effect. On the other hand, a strength of the present study is the homogeneity of the two groups in terms of demographic features, cardiovascular risk factors, or type and severity of stroke. Another limitation is the low stroke severity in our sample. This represented adequately our study population but may hinder generalization to more severely affected patients. Nevertheless, even in this sample of mildly affected patients we found a 29% prevalence of sleep-related breathing disorders with differences in sleep-related breathing and recovery from stroke according to stroke topography. A further caveat concerns the polysomnographic recordings: sleep was recorded in the stroke unit during the acute phase and in the sleep laboratory 3 months later. It remains, therefore, a possibility that this has contributed to the general, observed changes in sleep which we observed. On the other hand, it seems unlikely that this could account for the reduction in sleep-related breathing disorders.

In summary, we found that patients with ITS lesions are at an increased risk for sleep-related breathing disorders, which is frequent in this group. Although sleep-related breathing improved over time, the slow and incomplete improvement and the poorer recovery of ITS patients suggest that early treatment interventions should be considered in these patients.

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