Sleep-wake disorders and stroke

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Summary

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Sleep-disordered breathing and sleep-wake disturbances are frequent in stroke patients. They deserve attention because they may influence rehabilitation process and functional outcome. In addition, sleep-disordered breathing may increase the risk of stroke recurrence. 50–70% of stroke patients are found to have sleep-disordered breathing, mostly obstructive sleep apnoea. In some patients stroke recovery is accompanied by an improvement of sleep-disordered breathing. The treatment of choice for obstructive sleep apnoea is continuous positive airway pressure (CPAP). Oxygen, theophyllin and other forms of ventilation may be helpful in patients with other forms of sleep-disordered breathing (e.g. Cheyne-Stokes breathing). In at least 20–40% of stroke patients sleep-wake disturbances are present, mainly in form of increased sleep needs (hypersomnia), excessive daytime sleepiness or insomnia. Depression, anxiety, sleep-disordered breathing, complications (e.g. nycturia, dysphagia, urinary/respiratory infections) and drugs may contribute to sleep-wake disturbances and should be addressed first. In patients with sleep-wake disturbances of primary neurogenic origin treatment with stimulants/dopaminergic drugs and hypnotics/sedating antidepressants respectively can be tried.

Keywords: stroke; sleep; apnoea; sleep-disordered breathing; hypersomnia; insomnia

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Introduction

In 1818, Cheyne first described periodic breathing in a patient with cardiac disease and "apoplexy" [1]. Jackson later recognised that this breathing pattern frequently accompanies bilateral hemispheric stroke (quoted in reference [2]). In 1877, Broadbent reported features consistent with obstructive sleep apnoea in a patient with intracerebral haemorrhage [3]. In the 19th century, it was also already known that stroke may cause profound changes of the sleep-wake cycle. Post-stroke hypersomnia was recognised by MacNish as early as in 1830 (quoted in [4]). At the beginning of the 20th century thalamic and mesencephalic strokes were recognised as more commonly associated with severe, post-stroke hypersomnia [5]. Neurogenic insomnia (agrypnia) related to thalamo-mesencephalic stroke was first described by Lhermitte in 1922 and van Bogaert in 1926, respectively (quoted in reference [6]). Asymmetries of the electroencephalogram (EEG) during sleep, with a reduction of spindle activity over the affected hemisphere, were first described by Cress in 1948 [7]. Over the last few decades, abnormalities of sleep macro- and micro-architecture – including changes of non-rapid eye movement (NREM) and rapid eye movement (REM) sleep – following supra- and infratentorial strokes have been characterised (quoted in reference [6]). More recently, the link between sleep-disordered breathing and vascular disorders including stroke has been recognised and discussed in detail. This article gives an overview of post-stroke sleep-disordered breathing and sleep-wake disturbances.

Sleep-disordered breathing in ischaemic stroke

Prevalence of sleep-disordered breathing in stroke patients

About 50–70% of all stroke patients have a sleep-disordered breathing, as defined by an apnoea-hypopnoea-index (AHI) ≥10/h [8–11]. As many as

42% of patients have an AHI ≥25/h [11]. Although sleep-disordered breathing mostly improves after the acute phase of stroke, up to 61% of patients still exhibit an AHI ≥10/h 3 months after the acute event [10]. Since sleep-disordered breathing is associated with transient hypoxaemic episodes, significant changes in blood pressure and cerebral haemodynamics, sleep-disordered breathing may contribute to stroke onset, stroke progression and influence stroke outcome (fig. 1).

Sleep-disordered breathing and its impact on vascular disorders/stroke

An increasing number of studies indicate that abnormal sleep breathing may contribute to vascular disease. The data on snoring and sleep-disordered breathing as independent risk factors of stroke remain controversial. Recent epidemiological studies have confirmed previous data mainly from Scandinavian countries (see for a summary of these data reference [6]) that self-reported habitual snoring increases the risk of evolution of hypertension [12] and stroke [13]. In a recent study, however, snorers have not shown any independent increase in the risk of stroke when such covariant risk factors as age, smoking and body mass index (BMI) were controlled [13]. On the other hand, in a large study on 6424 subjects, Shahar et al. [14] found that sleep-disordered breathing – as assessed by overnight polysomnography at home – was more strongly associated with self-reported heart failure and stroke than self-reported coronary heart disease.

Iranzo et al. observed in a population of 50 patients that obstructive sleep apnoea was associated with early neurological worsening, but not with neurological deficits or functional outcome 6 months after stroke [11]. These data suggest a negative impact of sleep-disordered breathing on stroke evolution, although it remains unclear in that study why obstructive sleep apnoea worsened short-term but not long-term outcome. In fact, single studies in the literature suggest the possibility that sleep-disordered breathing may also have an impact on long-term outcome (functional status, mortality) after stroke [15].

Diagnosis of sleep-disordered breathing in stroke patients

Sleep-disordered breathing in the acute stroke setting is best diagnosed by respiratory polygraphy, by which nasal airflow, thoracic and abdominal respiratory movements in addition to oxymetry (capillary oxygen saturation) are assessed. Conventional polysomnography offers additional information (sleep architecture, motor activity, etc.) but is expensive and cumbersome, and should therefore be reserved to unclear/complex situations. Based on nasal airflow, respiratory movements and oxygen desaturation recordings, various forms of sleep-disordered breathing can be defined, such as obstructive and central sleep apnoea as well as Cheyne-Stokes breathing. In stroke patients the coexistence of different breathing disturbances may be observed [16]. The number of apnoeic and hypopnoeic events per hour of sleep (AHI) and the number/severity of desaturations are indicators of the severity of sleep-disordered breathing.

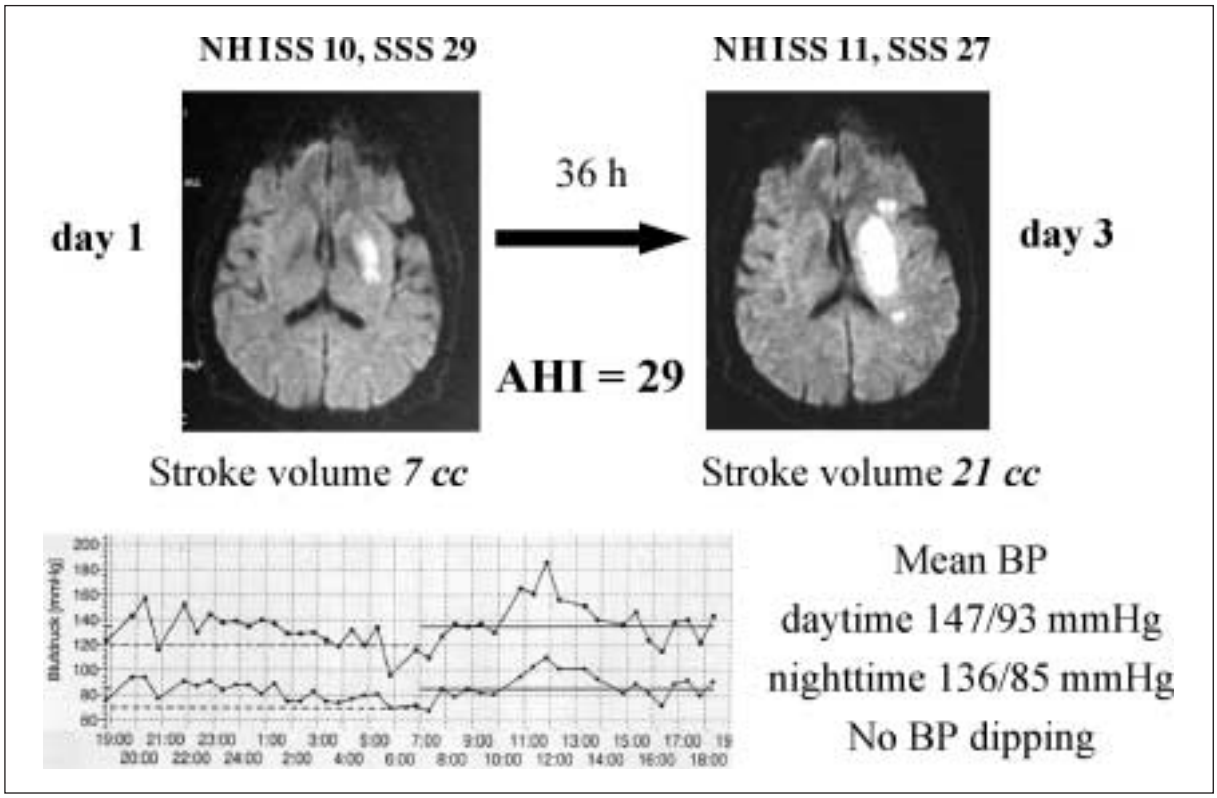
Treatment of sleep-disordered breathing in stroke patients

There are only very few systematic studies on treatment of sleep-disordered breathing (mainly obstructive sleep apnoea) in stroke patients. Treatment of sleep-disordered breathing in stroke patients represents a major clinical, technical, and logistic challenge. Treatment strategies should always include prevention and early treatment of secondary complications (e.g. aspiration, respiratory infections, pain) and a cautious use/avoidance of alcohol and sedative-hypnotic drugs, which all may negatively affect breathing control during sleep.

Body position may influence sleep-disordered breathing. Central and particularly obstructive events may be aggravated by the supine position. On the other hand, lying on the hemiparetic side can aggravate hypoxaemia [17].

Treatment with continuous positive airway pressure (CPAP) is the treatment of choice for obstructive sleep apnoea. CPAP treatment prevents the collapse of the upper airway, acting as a pneumatic splint (for review see [18]). Two types of CPAP devices are available, i.e. classical and automatic CPAP (the latter also being called "intelligent" or auto-CPAP). Auto-CPAP systems can be used for simultaneous detection of upper airway obstructions and treatment, which is made possible by automatic titration of CPAP pressure. A detailed discussion of ventilatory options and strategies in patients with obstructive sleep apnoea is beyond the scope of this review. CPAP can be highly beneficial in stroke patients with obstructive sleep apnoea with treatment success in up to 70% of well-selected patients [19]. Compliance to CPAP

Figure 1 65-year-old man with acute ischaemic stroke, clinical (NIHSS = NIH Stroke Scale, SSS = Scandinavian Stroke Scale) and radiological (MRI, Diffusion-Weighted Imaging) progression, moderate–severe sleep apnoea (AHI = Apnoea Hypopnoea Index) and non-blood pressure (BP)-dipping status (36-hour blood pressure monitoring).



may be reduced by such problems as dementia, delirium, aphasia, anosognosia, facial and pseudobulbar/bulbar palsy. In a substantial subgroup of stroke patients sleep-disordered breathing improves within the first weeks after the acute stage of stroke [10, 20]. Reassessment of sleep-disordered breathing in the subacute phase of stroke (after 1–3 months) is therefore advisable and may improve the overall compliance to treatment.

Improvement of Ceyne-Stokes breathing (CSB) can be obtained in stroke patients with oxygen. A novel method of ventilatory support called adaptive servo-ventilation was shown to suppress central apnoea and/or CSB in patients with heart failure more than CPAP. Oxygen may be effective in stroke patients, as well [21]. Theophyllin, sedatives and opiates have anecdotically been reported to improve CSB and neurogenic hyperventilation [22], but should only be used with caution. Overall, most drugs have been shown to have little or no effect on sleep-disordered breathing (for review see [23]). Tracheostomy and mechanical ventilation may be needed in patients with central hypoventilation.

Recent studies have demonstrated an effect of CPAP treatment on vascular disorders. A small to moderate effect of CPAP on arterial blood pressure was found [24, 25] when CPAP-treated patients were compared with a CPAP sham-exposure group. Favourable effects were detected both for diastolic and systolic blood pressure, during both sleep and wakefulness. Along this line, a recent study on 16 stroke patients has reported a significant reduction in mean nocturnal blood pressure after a 10-day treatment with CPAP [19]. Hence, treatment of patients with stroke (and TIA) may have an impact not only on stroke outcome but also on their overall risk profile.

Sleep-wake disorders in ischaemic stroke

Prevalence of sleep-wake disturbances in stroke patients

In stroke patients, at least 20–40% of patients present with sleep-wake disturbances, mostly with increased sleep needs (hypersomnia), excessive daytime sleepiness or insomnia [26, 27]. Often sleep-wake disturbances are mild and/or transient. Persistent, severe sleep-wake disturbances are suggestive of bilateral paramedian thalamic, mesencephalic or brainstem infarcts, but can also be seen following large hemispheric strokes (for further

discussion see [6]). Patients with post-stroke sleep-wake disturbances often have associated complaints such as fatigue, depression and attention/memory problems. Environmental factors including noise, light and intensive medical monitoring may contribute to post-stroke sleep-wake disturbances. Furthermore, sleep-disordered breathing, cardio-respiratory disorders, seizures, infections, fever and drugs may contribute to sleep fragmentation and result in sleep-wake disturbances. The importance of these factors is well illustrated by the high occurrence rate of sleep-wake disturbances among intensive care unit patients without brain damage [28].

Parasomnias are less common forms of sleep-wake disturbances following stroke. Strokes in the pontine tegmentum, for example, may result in REM sleep behaviour disorder, in which patients act out their dreams because of a loss of physiological REM atonia. Patients with dorsal pontine/mesencephalic or paramedian thalamic strokes may experience Lhermitte's peduncular hallucinosis, characterised by complex, often colourful, dream-like visual hallucinations, particularly in the evenings and at sleep onset (see [6] for further discussion on parasomnias after stroke).

Diagnosis of sleep-wake disturbances in stroke patients

Associated neurological deficits usually point towards the topography of the underlying lesion. The correlation of post-stroke sleep-wake disturbances and sleep EEG is poor [27]. Sleep EEG may reveal a reduction, less commonly an increase in NREM and/or REM sleep. A reduction in sleep spindle activity is characteristic for thalamic [29], but can also be seen in hemispheric [30] infarcts. Interestingly, reduction in spindle activity can be found ipsi- but also contralaterally to the lesion [30]. Since sleep spindles participate in the generation and consolidation of NREM sleep, it has been suggested that changes in spindling activity may reflect a basic mechanism responsible for sleep-wake disturbances [30]. Multiple sleep latency tests may be inadequate for assessment of post-stroke hypersomnia and excessive daytime sleepiness [29]. Actigraphy can conversely be helpful to estimate changes in the sleep-wake cycle and sleep/rest needs following stroke.

Treatment of sleep-wake disturbances in stroke patients

There are almost no systematic studies on treatment of sleep-wake disturbances in stroke patients. Treatment of post-stroke hypersomnia / excessive daytime sleepiness is often ineffective. In single patients some improvement was seen in thalamic and mesencephalic stroke with amphetamines, modafinil, methylphenidate and dopaminergic agents (for details see [6]). Catsman-Berrevoets and Harskamp for example reported improvement of apathy and pre-sleep behaviour in patients with paramedian thalamic stroke with 20–40 mg of bromocriptine [31]. Autret et al. described a dramatic improvement of alertness with 200 mg of modafinil in a patient with bilateral meso-diencephalic paramedian infarct [32]. Treatment of an associated depression with stimulating antidepressants may also improve post-stroke excessive daytime sleepiness and hypersomnia. It is noteworthy that a favourable influence on early post-stroke rehabilitation was reported both for methylphenidate (5–30 mg/d, 3-week trial) and levodopa (100 mg/d, 3-week trial), an effect that may at least in parts be related to improved alertness in these patients [33, 34].

Treatment of post-stroke insomnia should include placement of patients in private rooms at night; protection from nocturnal light, noise and unnecessary arousals; increased mobilisation with exposure to light during the day; and, when unavoidable, temporary use of hypnotics that are relatively free of cognitive side effects, such as zolpidem and benzodiazepines. It should be kept in mind, however, that in stroke patients benzodiazepines may not only enhance sedation and neuropsychological deficits but also lead to the reemergence of other neurological deficits [35]. Treatment of an associated depression with sedating antidepressants may also improve post-stroke insomnia. In a recent study of 51 stroke patients 60 mg/d mianserin led to an improvement of insomnia complaints compared to placebo, even in patients without associated depression [36]. Antidepressants may be preferable for long-term management of post-stroke insomnia.

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