Sleep disturbances complaints in stroke: implications for sleep medicine

ABSTRACT

Objectives: The aim of this study was to evaluate stroke patients’ sleep quality and its relationship with sleep disturbances complaints. Methods: A total of 70 subjects, 40 patients (57 ± 7 years) and 30 healthy controls (52 ± 6 years), assessed by the Pittsburg Sleep Quality Index (PSQI) took part in the study. Data analysis was realized by ANCOVA and multiple linear regression. Results: Significant differences in average PSQI were found between the groups (patients: 6.3 ± 3.5; healthy: 3.9 ± 2.2; p = 0.002). Regression analysis showed that the strongest predictor of sleep quality was compromised sleep efficiency (R² adjusted = 0.78) which may indicate less deep sleep can be compensated with increased daytime dysfunction, latency and sleep duration. Conclusions: We suggest that complaints of poor sleep quality be priority during clinical diagnosis.

Keywords: homeostasis, nervous system diseases, sleep disorders, stroke.

INTRODUCTION

Stroke is defined as an acute neurological deficit lasting for more than 24 hours. It is caused by a cerebral blood flow anomaly resulting in signs and symptoms associated with compromised focal brain areas. The clinical picture can include sensory-motor dysfunctions, tonus alterations, posture control and equilibrium disturbances as well as cognitive dysfunctions.

Sleep disturbances bring about cognitive deficits, diminishing certain capabilities such as attention span, spatial and temporal orientation, and memory efficiency. They also compromise social and psychological function. Thus, the acknowledgement of the possible occurrence of sleep related problems, directed toward stroke patient reports and complaints, seems to be an important component of the therapeutic, diagnostic and clinical approach adopted. For example, the rehabilitation process initiated at the onset of the disease can be continuous and prolonged in many cases. Poor sleep quality can compromise this process.

Quality of sleep is a difficult variable to define and measure in an objective manner. Alternatively, self-report methods such as sleep questionnaires provide a measurement of sleep quality experienced by the patient, while considering both the quantitative and qualitative aspects. These subjective methods are easily managed, inexpensive and can be widely applied in both research and clinical practice. The Pittsburgh Sleep Quality Index (PSQI) is a questionnaire that has been widely used to measure sleep quality and components from pattern areas generally focused on by clinics when patients report sleeping problems.
The greater prevalence of patients with sleep disturbances after stroke suggests an association between this pathology and sleeping problems. Many studies in the literature have given more attention to objective evaluation of sleep through polysomnographic patterns, considering mainly the acute phase of recovery\textsuperscript{[7,8]}. In these studies the relationship between sleeping problem complaints and quality of sleep was not considered relevant, nor the question of which sleep regulation mechanisms could be affected.

Foley et al.\textsuperscript{[5]} evaluated the association between sleeping problems and chronic illnesses in the elderly. They concluded that stroke is associated with the presence of one or more sleeping problems such as difficulty falling and staying asleep as well as daytime sleepiness. Müller et al.\textsuperscript{[10]} also found that stroke patients woke more often after falling asleep and had less sleep efficiency than those without the disorder. Vock et al.\textsuperscript{[8]}, who evaluated post ischemic stroke patients, also established a greater frequency of post-stroke sleep anomalies.

Thus, the aim of this study was to evaluate subjective quality of nocturnal sleep in hemispheric stroke patients and its relationship with sleep disturbances complaints.

**MATERIAL AND METHODS**

**Subjects**
The sample was composed of 70 subjects, including a group of 40 patients with diagnosis of unilateral stroke enrolled at physical therapy services in the city of Natal/RN who were compared to a group of 30 healthy employees of the Federal University of Rio Grande do Norte. The group of patients was composed of 27 men and 13 women, aged between 45 and 65 years (57 ± 7 years), lesion time between 1 and 36 months (11 ± 9 months), with 24 and 16 patients presenting with impaired right and left cerebral hemisphere, respectively. The group of healthy individuals was composed of 15 men and 15 women, aged between 45 and 64 years (52 ± 6 years). Schooling level varied between grade 6 and grade 11.

The exclusion criteria adopted for the patients were: recurrent cerebral lesion, serious cognitive disorders, aphasia and the use of tranquilizers, antidepressants or neuroleptics. For the controls, individuals with cognitive disorders, night workers or those who had taken a recent transmeridian trip were excluded. The recruitment of the participants was carried through personal contact in the institutions where the research was executed and the participation of them was voluntary.

**Procedures**
This study was conducted in accordance with the Declaration of Helsinki and approved by Research Ethics Committee of the Federal University of Rio Grande do Norte. The participants were informed of the research procedure and asked to sign a voluntary consent form.

The patients were interviewed and provided the following information: identification, results of computerized tomography, history of the disease, risk factors present, medication used and lesion time. The Cumulative Illness Rating Scale (CIRS), an assessment scale of comorbidities, was used with the healthy individuals. This scale consists of a standardized clinical evaluation that investigates the overall health data of the individual in six organic systems, with scores ranging from 0 to 4, to ensure the current healthy status of the individual\textsuperscript{[9]}. To determine the degree of neurological impairment of the patients, we used the National Institute of Health Stroke Scale (NIHSS)\textsuperscript{[20]}. The scale is composed of 11 items that assess awareness level, eye movements, visual field, facial movements, motor function and upper and lower limb ataxia, as well as sensitivity, language, presence of disarthria and visual-spatial neglect. The total score, ranging from 0 to 42 points, is the sum of the points of each item, in which higher scores indicate greater neurological impairment. A score between 0-6 indicated little damage, between 7-16 moderate damage, and between 17-30 severe damage. The subjective sleep evaluation of the participants was determined by applying the PSQI. It consists of 19 questions related to the previous month’s sleeping habits, and is divided into 7 components: sleep quality, sleep latency (time needed to fall asleep), sleep duration (hours of sleep per night), sleep efficiency (total sleep time divided by time spent in bed), sleep disturbances (waking in the middle of the night or very early), use of sleeping medication and daytime dysfunction (difficulty staying awake). The sum of the 7 components varied between 0 and 21, a score equal and greater than 5 implying poor sleep quality\textsuperscript{[4]}. The individuals who reported sleep problems were questioned as to the time frame of the problem in order to compare it with post-lesion time. This comparison confirmed whether the problem occurred before or after the stroke.

**Statistical analysis**
The data was analyzed using the SPSS 14.0 program (Statistical Package for the Social Science) at a significance level of 5%. Prior to analysis, the data were checked for normality using the Kolmogorov-Smirnov test. The non-paired Student’s t-test was used to determine the difference between the patient group and the healthy group as to age and schooling. ANCOVA was used to determine the difference between groups on the global PSQI considering age and schooling as a co-variable. The chi-square test was used to compare the groups in terms of the frequency of sleep qualified as “good” or “bad”, as well as sex and the complaints of sleep problems before and after stroke.

The association between demographic variables (sex, age, and schooling), clinical variables (cerebral hemisphere affected, neurological degree and post-lesion time) and the PSQI components (latency, duration, efficiency and daytime dysfunction) was established, considering them all as independent variables. These variables were analyzed with the global PSQI (dependent variable) to establish the entry order of the variables. Next, explanatory models were constructed with linear regression analysis to identify the variables that predicted the subjective quality of patient sleep. Following univariate analysis, the variables with p value < 0.05 were selected and, using the regression model, added one by one in decreasing order of
the correlation coefficient and by significance (stepwise forward). The correlation matrix (Pearson correlation test) checked for the presence of confusion variables and of multicollinearity (correlation approaching +1 or -1), in order to avoid overlap between independent variables in the regression model.

RESULTS
The groups did not show any significant difference where the sex variable was concerned (p = 0.139). This was not the case when schooling (p = 0.016) or age (p = 0.002) were considered: the patient group had a higher mean age and a higher percentage of subjects with 6 years of schooling or less (72.5%). NIHSS scores varied from 4 to 19 (7.7 ± 3.5), and showed reduced muscular force and motor coordination of the upper and lower limbs as well as sensitivity deficits and muscular hypertonia. This indicated a moderate degree of neurological compromise.

In agreement with the PSQI analysis, 57.5% of patients suffered poor sleep quality, whereas only 26.7% of the healthy individuals showed the same result (p = 0.01). A significant difference between groups was found for mean global age and schooling adjusted PSQI values (mean ± standard deviation; patients: 6.3 ± 3.5; healthy: 3.9 ± 2.2; p = 0.002). Patients also confirmed an increased prevalence of post-stroke sleep problems: difficulty falling sleep (before: 30.8%; after: 69.2%), and fragmented sleep (before: 35%; after: 65%).

A significant correlation between the global PSQI and the sex variable was determined (r = 0.33; p = 0.037) but no correlation was found with age (r = 0.19; p = 0.228) and schooling (r = -0.227; p = 0.159), or with the clinical variables (affected cerebral hemisphere: r = 0.083; p = 0.612; neurological degree: r = 0.008; p = 0.963; lesion time: r = -0.081; p = 0.621). However, the PSQI components showed significant correlations when compared with sleep latency (r = 0.667; p = 0.001), duration (r = 0.448; p = 0.004) and efficiency (r = 0.728; p = 0.001) as well as daytime dysfunction (r = 0.623; p = 0.001). Owing to this, these variables and the sex variable were selected for inclusion in the multiple linear regression model, in order to evaluate the predictor value of each variable in sleep quality.

The variables were added one by one, and the behavior of the model was observed as each variable was introduced. After regression analysis, it was found that sleep efficiency, latency, duration and daytime dysfunction contributed significantly to the global PSQI value. Thus, model 4 was chosen since it best explains sleep quality variation (R² adjusted = 0.78) (Table 1). According to this relationship, each increase in the efficiency score represents a decrease of 2.057 in sleep quality, in addition to an increase of 1.476 for daytime dysfunction, 1.221 for sleep latency, and 0.784 for sleep duration.

DISCUSSION
This study shows that stroke patients suffer from lower sleep quality than that of healthy individuals. This is supported by a higher global age and schooling adjusted PSQI average for the patient group. Campos et al.(11) found the same results when studying sleep quality in the chronic stage of stroke recovery.

They also observed an increase in sleep duration and more daytime napping. According to the authors, these alterations seem to compensate for worsened sleep quality in patients, suggesting that they suffer behavioral changes that compensate for the effects of a stroke.

In this study, no relation was found between the global PSQI and age or schooling, even though studies have reported a correlation between alterations in sleep quality and advanced age(12) as well as a relationship between poor sleep quality and low social class(13). This can be explained by the fact that no elderly individuals were included in the study sample and that the schooling did not vary greatly among the patients.

The clinical variables were not found to be associated with sleep quality evaluated by the PSQI. Bassetti & Aldrich(14), who studied the effects of acute hemispherical stroke on sleep, did not find significant differences between stroke patients affected in the right or left hemisphere. As in our study, they found that aspects of sleep were not affected by the hemisphere in which the lesion was located. These authors also report that acute left or right hemisphere stroke is accompanied by alterations in electroencephalographic recordings during sleep that are correlated with stroke severity. In addition to the studies using different methodologies (objective measurement versus subjective measurement), the divergence associated with lesion severity can be explained by the fact that the patients of the present study showed little difference in the amount of neurological damage. Furthermore, since most of the patients were in the chronic post-stroke stage, this might have favored the
non-association between post-lesion time and sleep quality. This shows the importance of long term studies that evaluate fluctuations in sleep quality throughout the patient’s clinical evolution. The greater prevalence of patients with sleep disturbances after stroke suggests an association between this pathology and sleeping problems.

The specific way in which stroke compromises sleep quality by interfering in the sleep mechanism has not been greatly debated. Sleep regulation involves two basic processes: the homeostatic (process S) and the circadian (process C). The homeostatic process is responsible for the increased propensity toward sleep during wake times and a decrease during sleep times. The circadian process promotes the temporal organization of the sleep-wake cycle and through alert mechanisms maintains wakefulness during the day, thus facilitating sleep consolidation at night. Several brain neurotransmitter or neuromodulator systems have been strongly implicated in such processes(19).

Disruption of wake- or sleep-promoting pathways results in behavioral state instability. There is evidence that the homeostatic and circadian process may be affected separately. In this sense, compromised sleep regulation may depend on the location of the stroke. The study of patients with subcortical stroke and compromised hypothalamus suggests a functional interruption of the suprachiasmatic nucleus, which affects the promotion of wakefulness in the circadian process, causing alterations in alertness, expressed mainly by diurnal somnolence in the patients(16). On the other hand, Beloosesky et al.(17) studied melatonin rhythms in post hemispheric stroke patients. The authors detected persistent rhythmicity of melatonin production, indicating that the circadian process and the neural connection for the pineal gland were not affected.

In the present study, multiple linear regression analysis showed that the strongest predictor of poor sleep quality was compromised sleep efficiency, which may indicate less deep or intense sleep. We can associate this result with the high prevalence of difficulty in falling asleep and fragmented sleep. Müller et al.(18) found that stroke patients woke more often after falling asleep and had less sleep efficiency than the control group. Considering that insomnia is defined as a difficulty to fall or stay asleep, or as non-restorative sleep that compromises daytime functioning, the complaints of difficulty in falling asleep and of fragmented sleep suggest the occurrence of insomnia in this study sample. This conclusion was also reached in a study by Leppävuori et al.(19), who found that insomnia was a common complaint after ischemic stroke. Daytime dysfunction, latency and sleep duration were also considered predictors of patient sleep quality. Foley et al.(19) who evaluated the association between sleep problems and chronic illnesses, concluded that stroke is associated with the presence of one or more sleeping problems.

Likely a hemispheric stroke does not reach the subcortical structures or the neural pathways of the hypothalamus related to the circadian system, but the cortical injuries mainly in the sensory motor cortical areas can result in a reduction of inputs involved in the feedback mechanism of homeostatic sleep regulation, resulting in a difficulty to fall and stay asleep, thus compromising sleep quality, expressed first by decreased sleep efficiency and second by increased daytime dysfunction, latency and sleep duration (Figure 1). The electroencephalographic data of the Vock et al.(19) showed changes in NREM sleep, sleep efficiency and alertness after sleep onset, which could also support the idea of compromised process S of sleep regulation. This interpretation is based on the fact that process S derives from a physiological variable EEG slow wave activity (SWA). When sleep episodes are shortened, SWA increases in NREM sleep, expressing a greater need for deep sleep, and decreases immediately after the first night of sleep recovery(19).

The aim of the hypothesis raised in the present study is to stimulate a discussion about how sleep regulating mechanisms are affected after a hemispheric stroke, leading to compromised sleep quality. We are carrying through studies with actigraphy and polysomnography to confirm this hypothesis. Moreover, the findings are not sufficient to definitively affirm that the homeostatic process is affected isolatedly in hemispheric stroke cases, because we cannot rule out the possibility of changes in the interaction with the circadian process.

This study had certain limitations. The patients did not have the different degrees of neurological compromise needed to evaluate the fluctuations in sleep quality clinically associated with this affliction. Nor did this study examine the relationship between sleeping problems and the location of specific cerebral lesions. This was because the neuroimaging examinations were carried out at different hospitals, making the standardization of the medical reports impossible. The lack of sleep apnea screening should be included as a study limitation. Furthermore, it would be important to analyze the influence of the circadian system on the sleep regulation of these patients.
CONCLUSION
This study confirmed that stroke patients have compromised subjective sleep quality mainly associated with alterations in sleep efficiency. This was compensated with increased daytime dysfunction, latency and sleep duration. From a therapeutic point of view, the results of this study point to the need for investigating stroke patient sleep patterns in more detail. We suggest that complaints of poor sleep quality be given priority assessment during clinical diagnosis. Treatment strategies of sleep medicine should be taken, since sleep alterations can compromise the cognitive and motor rehabilitation process of these patients.

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