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# Medical Hypotheses



# Subjective and objective features of sleep disorders in patients with acute ischemic or haemorrhagic stroke: It is not only sleep apnoea which is important



Evelina Pajediene<sup>a,\*</sup>, Adomas Pajeda<sup>b</sup>, Gintare Urnieziute<sup>a</sup>, Erlandas Paulekas<sup>a</sup>, Vanda Liesiene<sup>c</sup>, Indre Bileviciute-Ljungar<sup>d,e,f</sup>, Giedre Jurkeviciene<sup>a</sup>, Daiva Rastenyte<sup>a</sup>, Kestutis Petrikonis<sup>a</sup>

<sup>a</sup> Department of Neurology, Kaunas Clinics, Hospital of Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>b</sup> Department of Ophthalmology, Kaunas Clinics, Hospital of Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>c</sup> Medicine Centre Neuromeda, Kaunas, Lithuania

<sup>d</sup> Department of Clinical Sciences, Karolinska Institutet, Sweden

<sup>e</sup> Department of Rehabilitation Medicine, Danderyd University Hospital, Stockholm, Sweden

<sup>f</sup> Department of Medical and Health Sciences, Faculty of Medicine and Health Sciences, Linköping University, Pain and Rehabilitation Centre, Anaesthetics, Operations and

Specialty Surgery Centre, Region Östergotland, Linköping, Sweden

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# ABSTRACT

*Background:* More than half of stroke patients present with a sleep-related breathing disorder including both central and obstructive forms of sleep apnoea. A cerebral infarction in different brain areas can disrupt sleep regulating pathways and cause insomnia, hypersomnia, circadian rhythm disturbances and other sleep disorders. Therefore, there is a need of objective data about various sleep disorders arising after ischemic or haemorrhagic stroke in order to implement practical recommendations how to suspect, diagnose and treat these conditions. Our medical hypothesis is that non-breathing sleep disorders are common among patients with acute ischemic or haemorrhagic stroke.

*Objective:* To investigate the subjective and objective sleep parameters in the patients with an acute ischemic or haemorrhagic stroke.

*Methods:* In the acute period (from 3 to 10 days after the first symptoms) of stroke all the patients completed questionnaires about sleep complaints and symptoms experienced before and after stroke, Epworth Sleepiness Scale (ESS), National Institute of Health Stroke Scale, Hospital Anxiety and Depression Scale and Modified Rankin Scale. Patients were included for further polysomnography (PSG) and sleep electroencephalography according to these criteria: (1) patients expressing severe sleep related complaints and/or symptoms that are new or have exacerbated after the stroke; and/or (2) patients having the ESS score equal or > 10.

*Results*: 66 patients were examined in the acute period of stroke. 33 (50%) patients had at least one or more new or exacerbated sleep complaints and/or symptoms, mostly related to obstructive sleep apnoea (OSA) and insomnia. Finally, 13 (19.7% of the whole sample) patients were selected for performing PSG. 12 of 13 patients were diagnosed with sleep disorder: 1 patient got the diagnosis of mild OSA, 1 – central sleep apnoea (CSA), 2 – combination of OSA and CSA, 1 – combination of mild OSA, periodic limb movement disorder (PLMD) and REM sleep behaviour disorder (RBD), 1 – combination of mild OSA and PLMD, 3 – combination of PLMD and insomnia, 3 – insomnia. There were no significant relations between type, location or treatment of stroke and various PSG measures, as well as type of a diagnosed sleep disorder.

*Conclusions:* Half of our acute stroke patients had at least one or more new or exacerbated sleep complaints and/ or symptoms, mainly related to OSA or insomnia. In the selected PSG group almost all patients were diagnosed with a sleep disorder, half of them having non-breathing sleep disorder, such as PLMD, RBD and insomnia.

E-mail address: evelinapajediene@lsmuni.lt (E. Pajediene).

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<sup>\*</sup> Corresponding author at: Department of Neurology, Kaunas Clinics, Hospital of Lithuanian University of Health Sciences, Eiveniu st 2, Kaunas LT-50009, Lithuania.

# Introduction

Sleep is recognized to be considerable for health and well-being in all persons, but increasingly so in those recovering from brain damage [1]. It is known that sleep disorders are a frequent complication in patients with acute ischemic or haemorrhagic stroke, approximately 20–40% of stroke patients experience various sleep-wake disorders, such as insomnia, hypersomnia, REM sleep behavior disorder (RBD), periodic limb movement disorder (PLMD).

Even more, about 50–70% stroke patients present with a sleep-related breathing disorder including both central and obstructive forms of sleep apnoea [2,3]. Despite that, the majority of physicians do not screen stroke patients for sleep-disordered breathing [4]. Patients with stroke and OSA have a higher risk for repeated stroke and significantly increased mortality in one year after the stroke in comparison with the patients without apnoea [5,6]. Studies showed a significant reduction in stroke recurrence and mortality as well as improved neurological recovery among the patients treated with continuous positive airway pressure therapy (CPAP), consequently, CPAP treatment may reduce the risk of stroke in patients with OSA [7].

A cerebral infarction in subcortex, thalamus or mesencephalon can fully disrupt sleep and wakefulness cycle, leading to insomnia and agitation during the night, and severe sleepiness during the day [8]. Insufficient sleep after stroke can be followed by chronic fatigue, cognitive and emotional dysfunction, worse neurological outcome and life quality. Therefore, there is a need of objective data about various sleep disorders arising after ischemic or haemorrhagic stroke in order to implement practical recommendations how to suspect, diagnose and treat these conditions. Our medical hypothesis is that non-breathing sleep disorders are common among patients with acute ischemic or haemorrhagic stroke. The aim of the study presented in this article was to investigate the subjective and objective sleep parameters in the patients with an acute ischemic or haemorrhagic stroke.

#### Methods

# Participants

This prospective observational study took place in the Department of Neurology, Kaunas Clinics, Hospital of Lithuanian University of Health Sciences, in the year 2015–2016. The participants were patients hospitalized into this department with the diagnosis of an acute ischemic or haemorrhagic stroke. Patients fulfilling the inclusion criteria were interviewed no later than 12 days after the onset of the first stroke symptoms. Inclusion criteria were: (1) age from 18 to 75 years; (2) diagnosis of ischemic or haemorrhagic stroke confirmed by neurological examination and/or computer tomography and/or magnetic resonance imaging of the brain; (3) score of the National institutes of stroke severity scale on the inclusion day range (0-11] points; (4) conscious patients. Exclusion criteria were: (1) previous stroke or other brain lesion; (2) clinically severe and unstable health status; (3) commorbidities that might affect sleep (e.g., respiratory disorders, uncontrolled thyroid dysfunction, etc.); (4) aphasia and/or agnosia; (5) inability to make a solution or sign an informed consent; (6) inability to perform a polysomnography and/or all-night sleep electroencephalography because of individual or technical reasons (the criterion applied only in the instrumental part of the study).

All the participants filled in the self-made questionnaire about sleeprelated habits, complaints and symptoms related to the main sleep disorders and experienced before and after the stroke; the Epworth Sleepiness Scale (ESS) [9]; the Hospital Anxiety and Depression Scale (HADS) [10]. The severity of neurological status was evaluated using the National Institutes of Health Stroke Scale, or NIH Stroke Scale (NIHSS) [11], and degree of disability – by the Modified Rankin Scale (mRS) [12].

Patients were included for further polysomnography according to

these criteria: (1) patients expressing severe sleep related complaints and/or symptoms that are new or have exacerbated after the stroke; and/or (2) patients having the Epworth Sleepiness Scale score equal or > 10.

The study protocol was approved by Kaunas Regional Biomedical Research Ethics Committee (no. 2015-08-24-1). Written informed consent was obtained from all participants.

# Objective examination

The objective examination of every patient consisted of measuring the neck and waist circumferences; evaluating the Mallampati Score and measuring body weight in kilos and height in meters for body mass index (BMI) [13]. Pulse rate, arterial blood pressure and oxygen saturation were measured during three time points: when filling the questionnaires (around midday), in the evening before the recording of polysomnography (from 7 to 9 pm) and in the morning after the polysomnography (from 7 to 9 am). Arterial blood pressure and pulse measurement was done according to the American Heart Association guidelines [14].

The neurological examination of every patient was done according to the NIHSS scale steps, followed by additional testing of cranial nerves function, as well as deep tendon and pathological reflexes in upper and lower limbs.

#### Polysomnography (PSG)

In-hospital, full-night PSG was performed using the portable sleep diagnostic system Alice PDx (Alice PDx Diagnostic System, Philips Respironics, no. 1053948) in combination with the video recording. Sixteen channels were recorded: EEG (sensors M1-M2, F3-M1, C4-M1), EOG (left and right), EMG chin and tibialis (left and right), oronasal flowmetry, respiratory movements (abdomen and thorax), snoring, ECG, pulse and body position. Measurements were interpreted manually by a certified specialist in sleep medicine. Parameters were defined in accordance with American Academy of Sleep Medicine 2014 [15], using Rule 1A for the hypopnoea, i.e. at least a 30% flow reduction leading to either a 3% oxygen desaturation lasting at least 10 s or arousal. For mild OSA diagnose the AHI is equal or higher than five, for moderate OSA  $\geq$  15, and for severe OSA  $\geq$  30. The other used respiratory parameters were the Respiratory Disturbance Index (RDI), Respiratory Effort-related arousals (RERA), and the oxygen desaturation index (ODI) (of 3% or more). Central sleep apnoea was diagnosed if two criteria are satisfied: (1)  $\geq 5$  central apneas and/or central hypopneas per hour of sleep, and (2) the number of central respiratory events is > 50% of the total number of apneas and hypopneas. PSGs with < 4 h total sleep time were not interpreted for sleep apnoea diagnosis. Periodic limb movements (PLM) and those causing arousals (PLMAI) were also noted and periodic limb movement disorder (PLMD) was diagnosed if the PLMAI was equal or higher than five. REM sleep behaviour disorder (RBD) was diagnosed if these criteria were satisfied: (1) sleep-related vocalization and/or complex motor behaviours documented by video-PSG; (2) PSG recording demonstrates REM sleep without atonia; and (3) typical clinical symptoms of RBD expressed by patient and/or partner.

Medications regularly used by the patients were not withdrawn prior to the PSG or in the night when PSG was performed, however, new prescriptions of sleep affecting medications were avoided. The patients were woken at 6–8 am due to the clinical routine in the neurology unit.

#### Statistical analysis

The Kolmogorov–Smirnov test was used to test the normality of the sample when the hypothesis of normality is rejected. Descriptive statistics are represented by percentages for qualitative variables and by means and standard deviations for parametric quantitative variables, and by median and minimal, maximal values for nonparametric quantitative variables.

Pearson correlation test was used to analyse correlations between two parametric quantitative variables, while Spearman correlation was used to analyse correlations between qualitative variables, or if at least one of them was non-parametric. One-way ANOVA and Bonferroni criterion were used to compare means between two or more groups of parametric variables, and Kruskal Wallis test – for nonparametric variables. Ninety-five percent confidence intervals (95% CIs) for proportions were calculated. A p-value of < 0.05 was considered to be significant. The statistical package SPSS 17.0 and MS Excel were used for coding and analysing the data.

# Results

# Demographic and stroke-related characteristics

66 patients (44 men) with the mean age of 60.3 (10.6) years were examined in the acute period of stroke. The average time after the first stroke symptoms when entering the study was 5.87 (2.84) days. All data from medical history and objective examination is presented in Table 1.

56 patients (84.8%) were diagnosed with ischemic stroke, 7 (10.6%) – haemorrhagic stroke and 3 (4.5%) – ischemic stroke with haemorrhagic transformation. In 33 (50%) cases stroke evolved in middle cerebral artery basin, 19 (28.8%) – in vertebrobasilar basin, and 14 (11.2%) – in the other or a few basins. The mean NIHSS score in the beginning of stroke was 4.89 (3.69) [0–16]. All stroke-related characteristics are presented in Table 2.

#### Sleep-related questionnaires

The sleep duration at hospital was 0.5 (2.0) h shorter comparing to the duration of sleep at home before the stroke event, the median of sleep duration change was 0.5 h. 1 patient had been officially diagnosed with a sleep disorder (insomnia) before the stroke event.

33 (50%) patients had at least one or more new or exacerbated sleep complaints and/or symptoms. When summing up the total number of the sleep complaints and/or symptoms that were new or got more severe after the stroke, the median was 0.5, while the mean total number 1.4 (2.2) [0–9]. The most common sleep complaints, which appeared or exacerbated after stroke were frequent arousals (n = 17, 25.8%), onset insomnia (n = 15, 22.7%), middle insomnia (n = 12, 18.2%), nocturia (n = 10, 15.2%), dry mouth (n = 9, 13.6%), morning headache (n = 8, 12.1%) and daytime sleepiness (n = 6, 9.1%). All sleep-related complaints and/or symptoms before and after stroke event are grouped and presented in Table 3.

ESS score median was 5, mean – 5.8 (3.4) [0–15], when ESS  $\geq$  10 was found in 9 patients. Comparing ESS score among the groups divided by a stroke location and type, time of the first stroke symptoms and Mallampati score, no significant differences were observed. There was a positive relation between ESS score and HADS anxiety score (p = 0.004). Relation between total number of sleep complaints and/or symptoms and gender, NIHSS, MRS, HADS depression and anxiety score, BMI, stroke location and type, ESS was not found.

# Objective findings from polysomnography (PSG)

Even though 33 patients expressed new or exacerbated sleep complaints and/or symptoms, we did not perform further PSG for those who

#### Table 1

Demographic characteristics. Data presented as numbers and percentage or as median; mean (standard deviation) [minimal-maximal values].

DemographiesSet: male44 (66.7%)9 (69.2%)35 (66%)0.828Age61; 60.3 (10.6) [33-75]61; 57.2 (12.7) [34-73]62; 61.3 (10) [33-75]0.349BMI (kg/m <sup>2</sup> )28.3; 29.3 (5.4) [19.3-48.4]27.8; 29.3 (8.4) [21.6-48.4]28.5; 29.3 (4.5) [19.3-40.7]0.441Education30 (45.5%)4 (30.8%)26 (49.1%)0.349Professional18 (27.3%)4 (30.8%)13 (24.5%)0.349University18 [27.3%)4 (30.8%)13 (24.5%)0.349Working status9 (69.2%)23 (43.4%)0.349Working is altifs now5 (7.6%)9 (69.2%)23 (43.4%)0.349Retired34 (51.5%)4 (30.8%)30 (56.6%)14Shift work99 (69.2%)29 (54.7%)0.346HabitsFrequent tobacco intake5 (7.6%)2 (15.4%)12 (22.6%)0.762Frequent tobacco intake5 (7.6%)2 (15.4%)18 (33.9%)0.182Habits14 (21.2%)6 (46.2%)18 (33.9%)0.089Medical historyI01 (1.9%)0.62Diabets mellitus14 (21.2%)2 (15.4%)12 (22.6%)0.569Hypertension44 (66.7%)7 (33.8%)7 (33.2%)0.278Arrial fubrillation10 (15.2%)2 (15.4%)12 (22.6%)0.62Diabets mellitus14 (21.2%)2 (15.4%)12 (22.6%)0.62Diabets mellitus14 (21.2%)2 (15.4%)3 (23.1%)0.278Arrial fibrillat	Variables	All respondents ( $n = 66$ )	PSG group (n = 13)	Non PSG group ( $n = 53$ )	PSG vs. non PSG group (p value)
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Had worked on shifts before      36 (57.6%)      9 (69.2%)      29 (54.7%)      0.346        Habits           Frequent tobacco intake      16 (24.2%)      4 (30.8%)      12 (22.6%)      0.123        Frequent alcohol intake      5 (7.6%)      2 (15.4%)      3 (5.7%)      0.123        Frequent affeine intake      2 4 (36.4%)      6 (46.2%)      18 (33.9%)      0.089        Medical history        56.7%      0.62        Diabetes mellitus      14 (21.2%)      2 (15.4%)      37 (69.8%)      0.559        Hypertension      44 (66.7%)      7 (53.8%)      37 (69.8%)      0.377        Heart failure      2 (3%)      3 (23.1%)      7 (13.2%)      0.377        Heart failure      2 (3%)      2 (3.8%)      0.48      96        Malampati Score        103 (10.3 (12.9) [83-131]      0.89        Malampati Score      12 (18.2%)      0      12 (22.6%)      0.89        Class II      12 (18.2%)      0      12 (22.6%)      0.89        Malampati Score      2 (33.8%)      3 (23.1%)	Shift work				
Habits    Image: Constraint of the state	Working on shifts now	5 (7.6%)	0	5	0.253
Frequent tobacco intake16 (24.2%)4 (30.8%)12 (22.6%)0.762Frequent caffeine intake5 (7.6%)2 (15.4%)3 (5.7%)0.123Frequent caffeine intake24 (36.4%)6 (46.2%)18 (33.9%)0.089Medical history1 (1.9%)0.62Epilepsy1 (1.5%)*01 (1.9%)0.62Diabetes mellitus14 (21.2%)2 (15.4%)12 (22.6%)0.569Hypertension44 (66.7%)7 (53.8%)37 (69.8%)0.377Atrial fibrillation10 (15.2%)3 (23.1%)7 (13.2%)0.48Heart failure2 (3%)02 (3.8%)0.48Objective examinationNeck circumference (cm)40; 40.5 (1.2] (31-49]42; 40.5 (5.6) [31-48]40; 40.5 (3.8) [33-49]0.99Mallampati Scoreclass I12 (18.2%)012 (22.6%)0.768class II23 (34.8%)8 (61.5%)15 (28.3%)0.768class IV10 (15.2%)3 (23.1%)163 (3.9%)-class IV10 (15.2%)2 (15.4%)8 (15.1%)-elot testsBlood tests	Had worked on shifts before	38 (57.6%)	9 (69.2%)	29 (54.7%)	0.346
Frequent alcohol intake5 (7.6%)2 (15.4%)3 (5.7%)0.123Frequent caffeine intake24 (36.4%)6 (46.2%)18 (33.9%)0.089Medical history $I$ $I$ $I$ $I$ $I$ Epilepsy1 (1.5%)*01 (1.9%)0.62Diabetes mellitus14 (21.2%)012 (22.6%)0.569Hypertension44 (66.7%)7 (53.8%)37 (69.8%)0.278Atrial fibrillation10 (15.2%)3 (23.1%)7 (13.2%)0.377Heart failure2 (3%)02 (3.8%)0.48Objective examination $I$ $I$ $I$ $I$ $I$ Neck circumference (cm)40; 40.5 (4.2) [31-49]42; 40.5 (5.6) [31-48]40; 40.5 (3.8) [33-49]0.99Waits circumference (cm)103.5; 104.0 (14.2) [80-145]104; 104.5 (19.1) [80-145]103; 103.9 (12.9) [83-131]0.89Mallampati Score $I$ $I$ $I$ $I$ $I$ $I$ $I$ $I$ $I$ class I12 (18.2%)012 (22.6%)0.768 $I$ <	Habits				
Frequent caffeine intake Medical history24 (36.4%)6 (46.2%)18 (33.9%)0.089Medical history $I$	Frequent tobacco intake	16 (24.2%)	4 (30.8%)	12 (22.6%)	0.762
Medical historyEpilepsy1 (1.5%)*01 (1.9%)0.62Diabetes mellitus14 (21.2%)2 (15.4%)12 (22.6%)0.569Hypertension44 (66.7%)7 (53.8%)37 (69.8%)0.278Atrial fibrillation10 (15.2%)3 (23.1%)7 (13.2%)0.377Heart failure2 (3%)02 (3.8%)0.48Objective examination $V$ $V$ $V$ $V$ Neck circumference (cm)40; 40.5 (4.2) [31-49]42; 40.5 (5.6) [31-48]40; 40.5 (3.8) [33-49]0.99Waist circumference (cm)103.5; 104.0 (14.2) [80-145]104; 104.5 (19.1) [80-145]103; 103.9 (12.9) [83-131]0.89Mallampati Score $V$ $V$ $V$ $V$ $V$ $V$ $V$ $V$ $V$ class I12 (18.2%)012 (22.6%)0.768 $V$ $V$ class III23 (34.8%)8 (61.5%)15 (28.3%)0.768class IV10 (15.2%)2 (15.4%)18 (33.9%) $V$ class IV10 (15.2%)2 (15.4%)8 (15.1%) $V$ Blood tests $V$ $V$ $V$ $V$ $V$ $V$	Frequent alcohol intake	5 (7.6%)	2 (15.4%)	3 (5.7%)	0.123
Epilepsy1 (1.5%)*01 (1.9%)0.62Diabetes mellitus14 (21.2%)2 (15.4%)12 (22.6%)0.569Hypertension44 (66.7%)7 (53.8%)37 (69.8%)0.278Atrial fibrillation10 (15.2%)3 (23.1%)7 (13.2%)0.377Heart failure2 (3%)02 (38%)0.99Objective examinationunder state of the state	Frequent caffeine intake	24 (36.4%)	6 (46.2%)	18 (33.9%)	0.089
Diabetes mellitus    14 (21.2%)    2 (15.4%)    12 (22.6%)    0.569      Hypertension    44 (66.7%)    7 (53.8%)    37 (69.8%)    0.278      Atrial fibrillation    10 (15.2%)    3 (23.1%)    7 (13.2%)    0.377      Heart failure    2 (3%)    0    2 (3.8%)    0.48      Objective examination    V    40; 40.5 (4.2) [31-49]    42; 40.5 (5.6) [31-48]    40; 40.5 (3.8) [33-49]    0.99      Waist circumference (cm)    103.5; 104.0 (14.2) [80-145]    104; 104.5 (19.1) [80-145]    103; 103.9 (12.9) [83-131]    0.89      Mallampati Score	Medical history				
Hypertension    44 (66.7%)    7 (53.8%)    37 (69.8%)    0.278      Atrial fibrillation    10 (15.2%)    3 (23.1%)    7 (13.2%)    0.377      Heart failure    2 (3%)    0    2 (3.8%)    0.48      Objective examination	Epilepsy	1 (1.5%)*	0	1 (1.9%)	0.62
Arial fibrillation    10 (15.2%)    3 (23.1%)    7 (13.2%)    0.377      Heart failure    2 (3%)    0    2 (3.8%)    0.48      Objective examination	Diabetes mellitus	14 (21.2%)	2 (15.4%)	12 (22.6%)	0.569
Heart failure    2 (3%)    0    2 (3.8%)    0.48      Objective examination    2 (3.8%)    0.48      Neck circumference (cm)    40; 40.5 (4.2) [31–49]    42; 40.5 (5.6) [31–48]    40; 40.5 (3.8) [33–49]    0.99      Waist circumference (cm)    103; 104.0 (14.2) [80–145]    104; 104.5 (19.1) [80–145]    103; 103.9 (12.9) [83–131]    0.89      Mallampati Score    2    2    2    2    2    2    2    2    2    2    2    2    2    2    3    3    3    3    3    3    3    3    3    40; 40.5 (3.8) [33–49]    0.99    3 <td>Hypertension</td> <td>44 (66.7%)</td> <td>7 (53.8%)</td> <td>37 (69.8%)</td> <td>0.278</td>	Hypertension	44 (66.7%)	7 (53.8%)	37 (69.8%)	0.278
Objective examination      Neck circumference (cm)      40; 40.5 (4.2) [31–49]      42; 40.5 (5.6) [31–48]      40; 40.5 (3.8) [33–49]      0.99        Waist circumference (cm)      103.5; 104.0 (14.2) [80–145]      104; 104.5 (19.1) [80–145]      103; 103.9 (12.9) [83–131]      0.89        Mallampati Score	Atrial fibrillation	10 (15.2%)	3 (23.1%)	7 (13.2%)	0.377
Neck circumference (cm)      40; 40.5 (4.2) [31–49]      42; 40.5 (5.6) [31–48]      40; 40.5 (3.8) [33–49]      0.99        Waist circumference (cm)      103; 104.0 (14.2) [80–145]      104; 104.5 (19.1) [80–145]      103; 103.9 (12.9) [83–131]      0.89        Mallampati Score        12 (18.2%)      0      12 (22.6%)        class I      23 (34.8%)      8 (61.5%)      15 (28.3%)      0.768        class III      21 (31.8%)      3 (23.1%)      18 (33.9%)      .        class IV      10 (15.2%)      2 (15.4%)      8 (15.1%)      .	Heart failure	2 (3%)	0	2 (3.8%)	0.48
Waist circumference (cm)    103.5; 104.0 (14.2) [80–145]    104; 104.5 (19.1) [80–145]    103; 103.9 (12.9) [83–131]    0.89      Mallampati Score	Objective examination				
Mallampati Score    12 (18.2%)    0    12 (22.6%)      class I    23 (34.8%)    8 (61.5%)    15 (28.3%)    0.768      class III    21 (31.8%)    3 (23.1%)    18 (33.9%)    class IV    10 (15.2%)    2 (15.4%)    8 (15.1%)      Blood tests    5    5    5    5    5    5    5	Neck circumference (cm)	40; 40.5 (4.2) [31-49]	42; 40.5 (5.6) [31-48]	40; 40.5 (3.8) [33–49]	0.99
class I  12 (18.2%)  0  12 (22.6%)    class II  23 (34.8%)  8 (61.5%)  15 (28.3%)  0.768    class III  21 (31.8%)  3 (23.1%)  18 (33.9%)    class IV  10 (15.2%)  2 (15.4%)  8 (15.1%)	Waist circumference (cm)	103.5; 104.0 (14.2) [80-145]	104; 104.5 (19.1) [80–145]	103; 103.9 (12.9) [83–131]	0.89
class II  23 (34.8%)  8 (61.5%)  15 (28.3%)  0.768    class III  21 (31.8%)  3 (23.1%)  18 (33.9%)    class IV  10 (15.2%)  2 (15.4%)  8 (15.1%)	Mallampati Score				
class III  21 (31.8%)  3 (23.1%)  18 (33.9%)    class IV  10 (15.2%)  2 (15.4%)  8 (15.1%)    Blood tests	class I	12 (18.2%)	0	12 (22.6%)	
class IV 10 (15.2%) 2 (15.4%) 8 (15.1%) Blood tests	class II	23 (34.8%)	8 (61.5%)	15 (28.3%)	0.768
class IV 10 (15.2%) 2 (15.4%) 8 (15.1%) Blood tests	class III	21 (31.8%)	3 (23.1%)	18 (33.9%)	
	class IV		· ·	. ,	
Iron-deficiency anaemia 3 (5.4%) 1 (7.7%) 2 (3.8%) 0.543	Blood tests		-		
	Iron-deficiency anaemia	3 (5.4%)	1 (7.7%)	2 (3.8%)	0.543

PSG - polysomnography; BMI - body mass index.

\* Secondary epilepsy caused by stroke.

# Table 2

Stroke-related characteristics. Data presented as numbers and percentage or as median, mean, standard deviation, minimal and maximal values.

Variables	All respondents ( $n = 66$ )	PSG group (n = $13$ )	Non PSG group ( $n = 53$ )	PSG vs. non PSG group (p value)
Stroke type				
Ischemic	56 (84.8%)	11 (84.6%)	45 (80.4%)	0.836
Haemorrhagic	7 (10.6%)	0	7 (13.2%)	
Ischemic with haemorrhagic transformation	3 (4.5%)	2 (15.4%)	1 (1.9%)	
Stroke location				
Left middle cerebral artery basin	18 (27.3%)	2 (15.4%)	16 (30.2%)	0.635
Right middle cerebral artery basin	15 (22.7%)	5 (38.5%)	10 (18.9%)	
Vertebrobasilar basin	19 (28.8%)	6 (46.2%)	13 (24.5%)	
Left anterior cerebral artery basin	1 (1.5%)	0	1 (1.9%)	
Other	13 (19.7%)	0	13 (24.5%)	
Time of the first stroke symptoms				
Night	5 (7.6%)	1 (7.7%)	4 (7.6%)	0.13
Morning	16 (24.2%)	2 (15.4%)	14 (26.4%)	
Daytime	19 (28.8%)	4 (30.8%)	15 (28.3%)	
Evening	16 (24.3%)	6 (46.2%)	10 (18.9%)	
Time is unknown	10 (15.2%)	0	10 (18.9%)	
Stroke severity				
NIHSS in the beginning	4; 4.9 (3.7) [0–16]	6; 6.9 (4.3) [2–16]	4; 4.6 (3.4) [0–15]	0.036*
NIHSS before performing PSG	_	4; 3.9 (2) [1–7]	_	
NIHSS at discharge time	2; 2.0 (1.8) [0-8]	3; 2.7 (1.9) [0-6]	1; 1.9 (1.8) [0-8]	0.168
mRS				0.288
0 no symptoms	26 (39.4%)	3 (23.1%)	23 (43.4%)	
1 no significant disability	34 (51.5%)	9 (69.2%)	25 (43.4%)	
2 slight disability	4 (6.1%)	1 (7.7%)	3 (5.7%)	
3 moderate disability	1 (1.5%)	0	1 (1.9%)	
4 moderately severe disability	1 (1.5%)	0	1 (1.9%)	
Stroke treatment				
Thrombolysis	19 (28.8%)	9 (69.2%)	10 (18.9%)	< 0.001*

PSG - polysomnography; NIHSS - the National Institutes of Health Stroke Scale; mRS - the Modified Rankin Scale. \* p value < 0.05 is considered to be significant.

# Table 3

Sleep related complaints and/or symptoms before and after the stroke event. Data presented in total numbers and percentage.

Complaints and symptoms related to the main sleep disorders (n = $66$ )	Experienced before the stroke event	Appeared after the stroke event	Exacerbated after the stroke event	New or exacerbated symptoms after the stroke event
Insomnia-like symptoms	59 (89.4%)	12 (18.2%)	18 (27.3%)	30 (45.5%)
Onset insomnia	32 (48.5%)	7 (10.6%)	8 (12.1%)	15 (22.7%)
Frequent arousals	54 (81.8%)	4 (6.1%)	13 (19.7%)	17 (25.8%)
Middle insomnia	26 (39.4%)	6 (9.1%)	6 (9.1%)	12 (18.2%)
Periodic limb movements disorder-like symptoms	44 (66.7%)	7 (10.6%)	1 (1.5%)	8 (12.1%)
Restless legs	17 (25.8%)	2 (3%)	0 (0%)	2 (3%)
Periodic limb movements during sleep	23 (34.8%)	1 (1.5%)	1 (1.5%)	2 (3%)
Untidy bed sheets in the morning	33 (50%)	4 (6.1%)	0 (0%)	4 (6.1%)
Limb movements reported by a sleep partner	7 (10.6%)	0 (0%)	0 (0%)	0
Parasomnias-like symptoms	42 (63.6%)	2 (3%)	2 (3%)	4 (6.1%)
Nightmares	17 (25.8%)	0 (0%)	2 (3%)	2 (3%)
Bruxism/excessive teeth grinding	9 (13.6%)	1 (1.5%)	0 (0%)	1 (1.5%)
Sleep enuresis	4 (6.1%)	0 (0%)	0 (0%)	0
Sleep talking	26 (39.4%)	0 (0%)	0 (0%)	0
Sleepwalking	1 (1.5%)	0 (0%)	0 (0%)	0
Abnormal movements during sleep	1 (1.5%)	1 (1.5%)	0 (0%)	1 (1.5%)
Narcolepsy-like symptoms	14 (21.2%)	0	0	0
Cataplexy	2 (3%)	0 (0%)	0 (0%)	0
Sleep paralysis	3 (4.5%)	0 (0%)	0 (0%)	0
Hypnagogic/hypnopompic hallucinations	11 (16.7%)	0 (0%)	0 (0%)	0
Sleep apnoea syndrome-like symptoms	63 (95.5%)	12 (18.2%)	13 (19.7%)	25 (37.9%)
Snoring:				
on back	49 (74.2)	0 (0%)	1 (1.5%)	1 (1.5%)
on the right side	29 (43.9%)	0 (0%)	0 (0%)	0
on the left side	27 (40.9%)	0 (0%)	0 (0%)	0
on the abdomen	13 (19.7%)	0 (0%)	0 (0%)	0
Sleep apnoea	12 (18.2%)	0 (0%)	1 (1.5%)	1 (1.5%)
Nocturia	53 (80.3%)	5 (7.6%)	5 (7.6%)	10 (15.2%)
Excessive sweating during sleep	39 (59.1%)	1 (1.5%)	4 (6.1%)	5 (7.6%)
Morning headache	26 (39.4%)	4 (6.1%)	4 (6.1%)	8 (12.1%)
Dry mouth	41 (62.1%)	2 (3%)	7 (10.6%)	9 (13.6%)
Daytime sleepiness	39 (59.1%)	3 (4.5%)	3 (4.5%)	6 (9.1%)

#### Table 4

Sleep measures from the PSGs. Data presented as median, mean, standard deviation, minimal and maximal values (n = 13). The PSG results are compared with normal values according to the AASM Manual for the Scoring of Sleep and Associated Events (2014). The numbers of patients with abnormal values are presented as a total number and a percentage.

Polysomnography measure	Median; mean (SD) [min-max]	Abnormal values	Number of patients with abnormal values
Total sleep time (min)	242.5; 232.9 (113) [80-477]	< 7 h (420 min)	12
		> 9 h (540 min)	0
Sleep efficiency (SE) (%)	38.2; 40.5 (15) [20.3-75.5]	75-85% - decreased	1
		< 75% – very decreased	12
Sleep latency (min)	45.5; 74 (70.2) [13.1–254.5]	< 5 min	0
		> 20 min	10
REM stage latency (min)*	94.5; 114.6 (80) [5.5–279.5]	≤8 min	1
SWS1 duration (%)	16.3; 19.1 (9.2) [7.5–39.1]	< 5%	0
		> 10%	12
SWS2 duration (%)	46; 48.7 (13.9) [29.9-80]	< 45%	5
		> 55%	3
SWS3 duration (%)	9.8; 11.5 (9.6) [0-33.9]	< 5%	2
		> 25%	2
REM duration (%)	21.5; 20.7 (9) [0-34.5]	< 15%	2
		> 25%	3
AHI	8.6; 13.7 (12.9) [1-38.3]	≥5	6
Supine position-related AHI	15.4; 30 (32.1) [0-85.7]	≥5	6
RERA index	2.8; 5.3 (5.1) [0.4–14.6]	≥5	3
RDI	9.1; 13.9 (12.9) [1-38.4]	≥5	6
ODI	9.4; 12.4 (11.4) [2.8-36.9]	≥5	6
PLMI	20.2; 33.9 (35.1) [1-107.2]	> 5	10
PLMAI	2.8; 5.6 (6.2) [0.2–22.2]	≥5	6
Spontaneous AI	4.5; 8.1 (10.9) [1.4-42.6]	> 15	1
Leg movement related AI	10.3; 11.2 (8.4) [1–29]	> 5	8
Total AI	20.9; 26.2 (20.6) [9–84.7]	> 15	8

SD – standard deviation; REM – rapid eye movements; SWS1, SWS2, SWS3 – respectively slow waves sleep stage 1, 2, 3; RERA – respiratory effort related arousals; RDI – respiratory disturbance index; AI – arousal index; AHI – apnoea-hypopnoea index; ODI – oxygen desaturation index; PLMI – periodic limb movements index; PLMAI – periodic limb movements arousal index, NA – not applicable.

\* The cut-off of 8 min for REM stage latency is chosen according to the diagnostic criteria for narcolepsy.

had mild symptoms, refused this investigation or there were technical difficulties to perform it. Therefore, PSG group consisted of 13 (19.7% of the whole sample) patients (9 males). All demographic and stroke-related data from this group is presented in Tables 1 and 2.

According to objective findings from PSG and subjectively expressed sleep related complaints and symptoms, 12 of 13 patients were diagnosed with sleep disorder: 1 patient got the diagnosis of mild OSA, 1 – CSA, 2 – combination of OSA and CSA, 1 – combination of mild OSA, PLMD and RBD, 1 – combination of mild OSA and PLMD, 3 – combination of PLMD and insomnia, 3 – insomnia.

Sleep measures from PSGs are summarized in Table 4. Majority of patients had diminished total sleep time, inefficient sleep, prolonged sleep onset, increased amount of light (N1 sleep stage) sleep, and frequent arousals. These features reflecting worse sleep pattern were related to higher severity of neurological status, older age, and more depressed mood There were no significant relations between type, location or treatment (thrombolysis applied or not) of stroke and various PSG measures, as well as type of a diagnosed sleep disorder.

# Discussion

Our study of 66 patients with acute ischemic or haemorrhagic stroke revealed that half of them had at least one or more newly expressed or exacerbated sleep complaints and/or symptoms, mostly related to sleep-breathing disorders and insomnia, that is comparable with the previous studies, also showing them as a remarkable prognostic factor after cerebral infarction [16,17]. Excessive daytime sleepiness was detected in 13.6% of patients and was not significantly associated with total number of sleep complaints and/or symptoms, as well as with objective PSG measures, that reveals the lack of sensitivity of the commonly used Epworth Sleepiness Scale. However, the higher scores of this scale were related to higher anxiety levels and more severe neurological status in the beginning of stroke. In order to suspect and diagnose sleep disorders among stroke patients, clinical practitioners should use the combination of a few different and more disorder specific questionnaires evaluating the risk of wide range of sleep disorders (e.g., Insomnia Severity Index [18], Berlin Sleep Apnea Questionnaire [19], etc.).

The majority of respondents were experiencing symptoms related to sleep apnoea syndrome (95.5%), insomnia (89.4%), periodic limb movement disorder (66.7%) and parasomnias (63.6%) before the stroke event, but only 1 patient was officially diagnosed and treated for his sleep disorder. That distinguishes the people complaining about their sleep as a group with a higher stroke-related risk that must be adequately diagnosed and treated.

PSG analysis of our patients revealed diminished total sleep time, prolonged sleep onset, inefficient and fragmented sleep, increased amount of light sleep. Meta-analysis of 9 PSG-based studies among acute stroke patients done by Baglioni and colleagues showed similar results [1]. In our study the worse quality of sleep, objectively measured in PSG, was also related to higher severity of neurological status, older age, and more depressed mood. The latter finding should draw more sleep-oriented attention to the group of elderly patients with severe stroke and depression.

Almost all patients that underwent PSG were diagnosed with a sleep disorder. What is expected and compatible with other studies, the most common were sleep breathing disorders – obstructive and/or central sleep apnoea [1,2,4]. However, half of the PSG group were diagnosed with other sleep disorders, such as periodic limb movement disorder, REM sleep behaviour disorder and insomnia, what should not be missed when treating acute stroke patients. Insomnia prevalence rates in the acute period of stroke have been reported as 50–68% [20] and was mostly related to subcortical thalamic, thalamo-mesencephalic or pontine lesions, disturbing the regulation of sleep-wake cycle [21]. In our study insomnia was equally diagnosed in both supratentorial and infratentorial stroke cases.

Regarding elevated arousal index, caused by periodic limb movements, PLMD was diagnosed for 46% of PSG group, when PLMS index > 5/h was detected in approximately 77%, that is comparable with other studies [22]. 3 from 5 of our patients diagnosed with PLMD were also expressing RLS related complaints. According to the literature, PLMD with or without RLS symptoms have been reported in approximately 12.4% of acute stroke cases, mainly observed in subcortical structures [23].

RBD is the only type of parasomnia reported only in few cases of ischemic pontine stroke. A recent study of 119 ischemic stroke patients showed RBD prevalence of 11%, however, RBD assessment was only questionnaire-based [24]. REM sleep without atonia, one of the main symptoms of RBD, is explained by the damage of the pathways responsible for atonia, that are related to the structures near locus coeruleus and reticular formation. Interestingly, our RBD case was detected in the ischemic stroke of medial cerebral artery basin, however, detected only by computer tomography.

The strict inclusion criteria for performing PSG is the strength, and at the same time a weak point of our study. In order to define only newly established sleep disorders that could be caused by stroke, PSG was not done for patients experiencing sleep problems already before the cerebrovascular event, which allows at least partly understand the sleep changes after stroke. However, we could have missed some new or exacerbated sleep disturbances when symptoms were not described by the patients. The high prevalence of sleep-disordered breathing has been detected in several studies of stroke and transient ischemic attack patients [1,25], showing them as a preexisting condition. These findings also direct to look for CSA, PLMD, RBD, insomnia and hypersomnia – sleep disorders that could more likely establish exclusively after stroke event.

The other disadvantage of this study is relatively small sample of quite mild stroke patients (the average NIHSS score in the beginning of stroke was 4.9), as higher neurological disability should result in more disturbed sleep. However, as almost all PSGs performed revealed sleep pathology it raises the awareness for all stroke patients irrespective of their neurological status.

# Conclusions

In this retrospective–prospective observational study half of our acute stroke patients had at least one or more new or exacerbated sleep complaints and/or symptoms, mainly related to OSA or insomnia. In the selected PSG group almost all patients were diagnosed with a sleep disorder, half of them having non-breathing sleep disorder, such as periodic limb movement disorder, REM sleep behaviour disorder and insomnia. Purposeful interview and questionnaires targeting various sleep disorders should be the routine screening instruments applied for stroke patients, independent of type, location or severity of stroke, helping to decide for further investigation with polysomnography and adequate treatment and follow-up.

# Declarations

#### Consent for publication

Not applicable.

# Availability of data and materials

The dataset generated and analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request. Funding

No funding.

#### CRediT authorship contribution statement

**Evelina Pajediene:** Conceptualization, Methodology, Software, Investigation, Data curation, Writing - original draft. **Adomas Pajeda:** Software, Investigation, Data curation. **Gintare Urnieziute:** Software, Investigation, Data curation. **Erlandas Paulekas:** Software, Investigation, Data curation. **Vanda Liesiene:** Conceptualization, Methodology. **Indre Bileviciute-Ljungar:** Supervision, Resources. : . **Giedre Jurkeviciene:** Conceptualization, Methodology, Supervision. **Daiva Rastenyte:** Conceptualization, Methodology, Supervision. **Kestutis Petrikonis:** Conceptualization, Methodology, Supervision.

# **Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

# Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.mehy.2019.109512.

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