Examining the Inter-relations of Depression, Physical Function, and Cognition with Subjective Sleep Parameters among Stroke Survivors: A Cross-sectional Analysis

Jennifer C. Davis, PhD,*,†,‡ Ryan S. Falck, MSc,†,‡,§,‖ John R. Best, PhD,†,‡,§,‖ Patrick Chan,‡,§ Stephanie Doherty,‡,§ and Teresa Liu-Ambrose, PhD†,‡,§,‖

Goal: Stroke survivors commonly experience depression as well as deficits in physical and cognition function. Emerging evidence also suggests sleep quality is compromised poststroke. Our primary objective was to examine the association of subjective sleep parameters (ie, total PSQI score) with depression, health related quality of life, physical function, and cognition among stroke survivors. *Materials and Methods:* Cross-sectional analysis of 72 older adults with chronic stroke (≥6 months postischemic stroke) enrolled in a randomized controlled trial of exercise or cognitive enrichment. Subjective sleep parameters were assessed using the Pittsburgh Sleep Quality Index (PSQI). We report total PSQI score and specific PSQI parameter scores (ie, PSQI-subjective sleep quality, PSQI-sleep latency, PSQI-sleep duration, PSQI-habitual sleep efficiency, PSQI-sleep disturbances, PSQI-use of sleep medication, and PSQI-daytime dysfunction). Bivariate correlations and multivariate linear regression assessed associations between subjective sleep parameters and depression/health related quality of life, physical function, and cognition. *Findings:* For bivariate correlations, depression was significantly associated with global PSQI, PSQI-subjective sleep quality, PSQI-habitual sleep efficiency, and PSQI-daytime dysfunction. Health related quality of life was significantly associated with PSQI-sleep medication. Physical function and health was significantly associated with PSQI-subjective sleep quality, PSQI-sleep latency, PSQI-sleep duration, and PSQI-daytime dysfunction. Multivariate linear regression demonstrated that PSQI-daytime dysfunction predicted depression and physical function; PSQI-subjective sleep quality predicted depression. No significant associations between global PSQI subjective sleep parameters with cognition were observed. *Conclusion:* Poor subjective sleep parameters and PSQI-subjective sleep quality among stroke survivors were associated with depression; PSQI-daytime dysfunction was associated with physical function. Thus, sleep should be considered in the management of those who have suffered a stroke to optimize poststroke rehabilitation outcomes.

Key Words: Chronic stroke—sleep quality—cognition

From the *Faculty of Management, University of British Columbia, Okanagan, Kelowna, British Columbia, Canada; †Aging, Mobility, and Cognitive Neuroscience Lab, Department of Physical Therapy, University of British Columbia, Vancouver, British Columbia, Canada; ‡Center for Hip Health and Mobility, Vancouver Coastal Health Research Institute, Vancouver, British Columbia, Canada; §Djavad Mowafaghian Centre for Brain Health, Vancouver, British Columbia; and ‖Department of Physical Therapy, University of British Columbia, Vancouver, British Columbia, Canada.

Received December 19, 2018; revision received April 3, 2019; accepted April 5, 2019.

Funding: This study is jointly funded by CIHR MOP-126130. TLA is a Canada Research Chair in Physical Activity, Mobility, and Cognitive Neuroscience, a Michael Smith Foundation for Health Research (MSFHR) Scholar, a Canadian Institutes of Health Research (CIHR) New Investigator, and a Heart and Stroke Foundation of Canada's Henry JM Barnett's Scholarship recipient. These funding agencies did not play a role in study design.

Ethics and dissemination: Ethical approval was obtained from the Vancouver Coastal Health Research Institute and the University of British Columbia's Clinical Research Ethics Board (H13-00715, July 26, 2013). Outcomes of this randomized controlled trial will be disseminated through publication in peer-reviewed journals as well as conference presentations.

Registration details: ClinicalTrials.gov Protocol Registration System: NCT01916486; registered July 23, 2013.

Address correspondence to Jennifer C. Davis, PhD, 4123 EME Building, 1137 Alumni Ave, Kelowna, British Columbia, Canada. E-mail: jennifer.davis@ubc.ca.

1052-3057/$ - see front matter

https://doi.org/10.1016/j.jstrokecerebrovasdis.2019.04.010

Introduction

Worldwide, 1 in 6 older adults suffers a stroke.[1] Common consequences of stroke include: depression, physical function restrictions, and impaired cognition.[2-4] One-third of all stroke survivors report depression poststroke.[5] Left untreated, poststroke cognitive deficits can lead to progressive restrictions in activities of daily living, and in social and leisure activities. Most stroke survivors adopt or return to sedentary lifestyles postrehabilitation.[6] Poststroke physical deficits (eg, poor balance) are associated with reduced activity participation[7,8] and depression.[5] Importantly, individuals with significant physical and cognitive deficits poststroke are twice as likely to have an early death or suffer a second catastrophic stroke.

One strategy of increasing interest is improving sleep quality among adults with stroke, given that sleep is a modifiable factor. Sleep disturbances are common in older adults with stroke,[9] and there is mounting evidence that stroke and sleep are interconnected.[10] Because stroke damages the central nervous system, it often leads to both changes in brain activity, brain function, and sleep architecture.[11] Sleep architecture is regulated by a complex interaction of multiple mechanisms located in the brainstem, hypothalamus, preoptic area, and thalamus.[12] This may explain why 20%-40% of stroke survivors have a sleep disorder and 50%-70% have a sleep-related breathing disorder,[10] which may significantly interfere with poststroke outcomes and recovery.[11]

Mounting evidence also links sleep with cognition,[13] depression, and physical function. For example, reduced paradoxical sleep (ie, Rapid Eye Movement sleep) can profoundly affect memory and learning.[12] Sleep disturbances also play a role in the development of cognitive impairment, and poor sleep is a risk factor for dementia.[14] Moderate sleep disturbances in older adults are frequently linked with elevated fatigue and mood disturbances including depressive symptoms and lower quality of life.[15-17] Alterations in sleep architecture—such as those found in restricted sleep—can also impair physiological function and increase depressive like symptoms. Further, research suggests sleep acts as an antiinflammatory mechanism which may help maintain physical function in later life.[18]

Stroke survivors commonly experience deficits in depression, health related quality of life, physical function, and cognition. It is therefore reasonable to hypothesize that stroke associated damages in sleep architecture may negatively impact depression, health related quality of life, physical function, and cognition. Yet, the specific associations that depression, health related quality of life, physical function, and cognition have with sleep quality among stroke survivors remains unknown. Hence, our primary objective was to examine the association of subjective sleep quality with depression, health related quality of life, physical function, and cognition among stroke survivors.

Methods and Analysis

Study Design

This is a cross-sectional analysis of variables at baseline of a 6-month proof-of-concept randomized controlled trial. The randomized controlled trial protocol is published.[19]

Participants

The sample consisted of 72 community dwelling women and men who have had an ischemic or hemorrhagic stroke (confirmed by previous MRI or computed tomography scan). In addition, individuals were required to meet the following inclusion criteria: (1) aged 55 years and over; (2) history of a single stroke of at least 1 year prior to study enrolment; (3) Mini-Mental State Examination (MMSE)[20] score of greater than or equal to 20/30 at screening; (4) community-dwelling; (5) living in Greater Vancouver area; (6) able to comply with scheduled visits, treatment plan, and other trial procedures; (7) read, write, and speak English with acceptable visual and auditory acuity; (8) not expected to start or are stable on a fixed dose of cognitive medications (eg, donepezil, galantamine, etc.) during the 12-month study period; (9) able to walk for a minimum of 6 meters with rest intervals with or without assistive devices; (10) based on interview, have an activity tolerance of 60 minutes with rest intervals; (11) not currently participating in any regular therapy or progressive exercise; and (12) provide a personally signed and dated informed consent document indicating that the individual (or a legally acceptable representative) has been informed of all pertinent aspects of the trial.

Individuals were excluded who were: (1) diagnosed with dementia of any type; (2) diagnosed with another type of neurodegenerative or neurological condition (eg, Parkinson's disease) that affects cognitive function and mobility; (2) at high risk for cardiac complications during exercise and/or unable to self-regulate activity or to understand recommended activity level (ie, Class C of the American Heart Risk Stratification Criteria); (3) have clinically significant peripheral neuropathy or severe musculoskeletal or joint disease that impairs mobility, as determined by his/her family physician; (4) taking medications that may negatively affect cognitive function, such as anticholinergics, including agents with pronounced anticholinergic properties (eg, amitriptyline), major tranquilizers (ie, typical and atypical antipsychotics), and anticonvulsants (eg, gabapentin, valproic acid, etc.); or (5) aphasia as judged by an inability to communicate by phone.

Ethical approval was obtained from the Vancouver Coastal Health Research Institute and the University of British Columbia's Clinical Research Ethics Board (H13-00715, July 26, 2013). All participants provided written informed consent.

Measures

We report measures relating to sleep quality, depression, cognition, and physical function that were collected at baseline. We also report general health, demographics, socioeconomic status, and education ascertained by questionnaires.

Measures—Dependent Variables

Depression and Health Related Quality of Life

Depression is a prevalent clinical entity in stroke survivors—it has been reported to be as high as 38%[21]—and is negatively associated with cognitive function.[22] We used the CES-D.[23] The CES-D is a 10-item scale where a score of 4 or greater has strong specificity and sensitivity to assess for major depression in older adults.[24] We used the EQ-5D-3L[25] to assess health-related quality of life. The reliability and validity of the EQ-5D-3L in the stroke population have been established.[26]

Physical Function

Mobility and balance were assessed using the Short Physical Performance Battery (SPPB)[27] and the Timed-Up-and-Go Test (TUG).[28] For the SPPB, participants were assessed on performances of standing balance, walking, and sit-to-stand. Each component is rated out of 4 points, for a maximum of 12 points; a score less than 9/12 predicts subsequent disability.[29] For the TUG, participants were instructed to rise from a standard chair, walk a distance of 3 meters, turn, walk back to the chair, and sit down. A TUG performance time of greater than or equal to 13.5 seconds correctly classified persons as fallers in 90% of cases.[28] We used the Six-Minute Walk Test[30] to assess mobility—a component of physical function. Total distance walked (in meters) in 6 minutes was recorded. To assess physical health, we measured systolic blood pressure, diastolic blood pressure, heart rate, and comorbidities using the Functional Comorbidities Index. Resting systolic blood pressure and diastolic blood pressure were recorded in duplicate, using a voscillometric sphygmomanometer, the Omron HEM-775. Values were presented as an average of 2 recordings that were taken 1 minute apart.

Cognition

We assessed global cognitive function using (1) MMSE[31]; (2) Montreal Cognitive Assessment (MoCA)[32]; and (3) 11-item Alzheimer's Disease Assessment Scale (ADAS-Cog). Briefly, the MMSE and MoCA are scored on a 30-point scale; ADAS-COG is scored on a 70 point scale with higher scores indicating greater severity of cognitive impairment.[33] To capture 3 important and distinct executive function processes,[34] we used: (1) the Trail Making Tests (Part A and B) to assess processing speed (Trail Making Test Part A) and set shifting (ie, Trail Making Part B – Trail Making Part A),[35]; and (2) the Digits Forward minus Backwards to assess working memory.

Primary Outcome Measure: Sleep Quality (PSQI Global score)—Independent Variable

The Pittsburgh Sleep Quality Index (PSQI) is a subjective measure of sleep quality consisting of 19 self-rated questions.[36] The 19 self-rated questions are utilized in scoring. A global score is obtained by adding the 7 components (see below) to yield a global score on a 0 to 21-point scale. Lower scores indicate healthier overall sleep quality. Individuals with depressive symptoms generally score greater than 5 on the PSQI global score.[36] The PSQI is deemed a suitable instrument among adults (aged 18-80 years) to assess sleep quality.[37]

Exploratory Outcome Measures–Independent Variables

The 19 items combine to form 7 components: (1) subjective sleep quality, (2) sleep latency, (3) sleep duration, (4) habitual sleep efficiency, (5) sleep disturbances, (6) use of sleeping medication, and (7) daytime dysfunction.[36] Each of the 7 components have a range of 0-3 points where "0" indicated no difficulty and "3" indicates severe difficulty. The Cronbach's alpha for the intercomponent scores was .83.[38]

Statistical Analyses

We report baseline demographics using mean and standard deviation or frequency (%) where relevant.

Bivariate Correlations

We conducted bivariate correlations with depression/health related quality of life (ie, CES-D, EQ-5D-3L, respectively), physical function (fatigue severity, meters walked in 6 minutes, TUG, and SPPB total score), and cognition (global cognition and executive function). First, we tabulated the PSQI global score as a continuous measure (21 points max; comprised of 7 components) to examine the association of subjective sleep parameters (ie, global PSQI score) as a continuous measure) with depression, physical function, and cognition with sleep among stroke survivors. Second, we examined the association of the 7 component scores of the PSQI with depression, physical function, and cognition with sleep among stroke survivors. The 7 components that comprise the PSQI include: (1) PSQI-subjective sleep quality, (2) PSQI-sleep latency, (3) PSQI-sleep duration, (4) PSQI-habitual sleep efficiency, (5) PSQI-sleep disturbances, (6) PSQI-use of sleeping medication, and (7) PSQI-daytime dysfunction.

Multivariate Analysis

For all multivariate analyses, independent sleep parameter variables that demonstrated significant bivariate correlations with the dependent variables of interest (ie, measures of depression and physical function) were incorporated into each multivariate model. Forward stepwise selection was used to confirm final multivariate models. Collinearity was determined by calculating the correlation coefficients and estimating the variance inflation factors of moderately correlated variables. In cases of collinearity, variables demonstrating the strongest association with the dependent variable were entered into the model. Age and FCI were entered first into all multivariate models followed by the relevant PSQI-global (primary analysis) or component (exploratory analyses) variable based on the bivariate analyses.

Results

Participants

Baseline characteristics of the 72 participants are presented in Table 1. The mean ± SD age was 68 ± 8 years. The mean ± SD PSQI score (max 21 points) was 5.1 ± 3.0 suggestive of sleep quality problems. Fifty of the 72 (68%) participants included in this study had a CES-D score of 4 or greater indicating the presences of depressive symptoms (Table 2). Thirty-four of the 72 (47%) individuals in this study had a PSQI global score of 5 or greater indicative of poorer sleep quality (Table 2). Table 3 reports the distribution of subjective sleep quality components (ie, subcomponents of the PSQI). The mean ADAS-Cog was 16.9 ± 7.7. The mean baseline MoCA score of 22 ± 4 (range: 10-30) indicated that on average, participants had mild cognitive impairment.[32] The mean baseline TUG score 18 ± 15 (range: 6-107) and a mean baseline SPPB score of 8.2 ± 2.8 (range: 1-12) confirmed that participants had mobility impairments.

Bivariate Correlations

Global PSQI

Global PSQI (β = .17 (.04); P= .000; r^2 = .21) was associated with depression. Global PSQI was not significantly associated with physical function or cognition.

Exploratory Bivariate Correlations—7 Components of the PSQI

Subjective Sleep Quality

Subjective sleep quality (β = .02 (.01); P= .038; r^2 = .06) was associated with depression (ie, CES-D).

Sleep Latency

Sleep latency (β = .03 (.01); P= .007; r^2 = .10) predicted depression (ie, CES-D).

Table 1. *Participant characteristics (N = 72)*

Variables	Minimum	Maximum	Mean	Std. deviation
Age (years)	55	87	68.4	7.6
FCI	1	9	3.2	1.9
Mini-mental state examination (max 30)	21	30	27.7	2.3
Montreal cognitive assessment (max 30)	10	30	21.9	4.0
Instrumental activities of daily living	2	8	6.6	1.7
Resting heart rate (beats/min)	48	110	69	13
Resting systolic blood pressure (mmHg)	93	171	131	16
Resting diastolic blood pressure (mmHg)	60	111	80	10
Sleep (primary outcome measure)				
Global PSQI score (max 19 points)	1	13	5.1	3.0
Depression				
CES-D	0	43	9.0	8.3
Health related quality of life				
EQ-5D-3L (max 1.0)	0	1	.763	.220
Executive functions				
Trails B-A (s)	16.7	621.9	107.5	120.3
Digit backward (s)	1	11	5.4	2.1
Physical function and health				
SPPB	1	12	8.2	2.8
Mean TUG (s)	6.1	107.3	18.1	14.8
Meters walked (in 6 min)	61	600	327	138
Fatigue severity	9	60	31.6	12.4

Abbreviations: CES-D, Centre for Epidemiologic Studies Depression Scale; EQ-5D-3L, EuroQol-5Domain-3Level; FCI, Functional Comorbidity Index; PPA, physiological profile assessment; SPPB, short performance physical battery; TUG, timed up and go.

Table 2. *Distribution of the CES-D and the PSQI (n = 72)*

Score	CES-D	PSQI global score
0	7 (9.7%)	N/A
1	4 (5.6%)	6 (8.3%)
2	6 (8.3%)	5 (6.9%)
3	5 (6.9%)	15 (20.8%)
4	6 (8.3%)	12 (16.7%)
>4	44 (61%)	34 (47.2%)

Abbreviations: CES-D, Centre for Epidemiologic Studies Depression Scale; PSQI, Pittsburgh Sleep Quality Index.

Sleep Duration

Sleep duration (β = .0014 (.0007); *P*= .054); r^2 = .05) was associated with physical function (ie meters walked in 6 minutes).

Habitual Sleep Efficiency

Habitual sleep efficiency (β = .04 (.01); *P*= .002; r^2 = .13) was associated with physical function (ie meters walked in 6 minutes).

Sleep Disturbances

The sleep disturbances component did not predict depression, physical function, or cognition.

Use of Sleeping Medication

Use of sleeping medication (β = −1.1 (.6); *P*= .051; r^2 = .05) was associated with health related quality of life (ie, EQ-5D-3L).

Daytime Dysfunction

Daytime dysfunction (β = .0034 (.009), *P*< .000, r^2 = .18; β = .023 (.006), *P*= .000, r^2 = .19; β = −.0016 (.0005), *P* −= .004, r^2 = .11), for depression, fatigue severity, and meters walked in 6 minutes, respectively) were associated with depression and physical function (ie, fatigue severity and meters walked in 6 minutes).

Multivariate Linear Regression

Table 4 reports the multivariate linear regression models for depression and physical function (meters walked

Table 3. *Distribution of the 7 sleep quality components (n = 72)*

Component	No difficulty "0"	Mild difficulty "1"	Moderate difficulty "2"	Severe difficulty "3"
Subjective sleep quality	49 (68%)	14 (19%)	9 (13%)	0 (0%)
Sleep latency	22 (31%)	37 (51%)	6 (8%)	7 (10%)
Sleep duration	38 (53%)	24 (33%)	6 (8%)	4 (6%)
Habitual sleep efficiency	49 (68%)	8 (11%)	9 (13%)	6 (8%)
Sleep disturbances	2 (3%)	50 (69%)	20 (28%)	0 (0%)
Use of sleeping medication	56 (78%)	4 (6%)	3 (4%)	9 (13%)
Daytime dysfunction	32 (44%)	32 (44%)	8 (11%)	0 (0%)

Table 4. *Multivariate linear regression results*

	Model and dependent variable	
Independent variables	Unstandardized (standard error)	*P* value
Primary analysis		
Depression (dependent variable) (n = 71)	**R^2 25%**	**.0002****
Global PSQI	1.2 (.3)	**.001****
Age	−.2 (.1)	.102
FCI	.5 (.5)	.328
Exploratory analyses		
Depression (dependent variable) (n = 71)	**R^2 31%**	**.0001****
Daytime dysfunction	5.3 (1.3)	**.001****
Sleep quality	3.6 (1.2)	.005*
Age	−.1 (.1)	.375
FCI	.6 (.5)	.184
Physical function (dependent variable) (n = 71)	**R^2 15%**	**.009****
Daytime dysfunction	−77 (22)	**.004****
Age	−3.6 (2.0)	.088
FCI	−2.7 (8.1)	.748

*$P < .05$.
**$P < .001$.

in 6 minutes). There were no significant predictors of cognition identified from the bivariate analyses; therefore, multivariate analyses predicting cognition were not conducted.

Primary Analyses—Multivariate linear regression

Depression—Dependent Variable

The PSQI global score was associated with depression. Specifically, daytime dysfunction ($\beta = 1.2$ (.3); $P = .001$, $R^2 = .28$) was associated with depression after adjusting for age and FCI.

Exploratory Analyses—Multivariate linear regression

Depression—Dependent Variable

Two components of the PSQI was associated with depression ($R_{total}^2 = .31$). Specifically, daytime dysfunction ($\beta = 5.3$ (1.3); $P = .001$) was associated with depression after adjusting for age and FCI. Sleep quality ($\beta = 3.6$ (1.2); $P = .005$) was associated with depression after adjusting for age.

Physical Function—Dependent Variable

One component, daytime dysfunction, of the PSQI was associated with physical function (meters walked in 6 minutes) ($\beta = -66.6$ (22.4); $P = .004$, $R^2 = .15$) after adjusting for age, sex, FCI, and MoCA.

Discussion

Poor subjective sleep parameters (ie, PSQI global scores and PSQI sub parameters) among stroke survivors were associated with depression; PSQI-daytime dysfunction was associated with physical function. These findings highlight modifiable factors that may be intervened upon in poststroke rehabilitation. Thus, sleep should be considered in the management of those who have suffered a stroke to optimize poststroke rehabilitation outcomes.

There is an emerging area of research examining the benefit of sleep in regulating emotional brain reactivity.[39] In this study, we found that depression was significantly associated with sleep quality, sleep latency, habitual sleep efficiency, and daytime dysfunction. Further, depression was predicted by 4 of the 7 components of the PSQI. Previous research has demonstrated that sleep deprivation is associated with subjective reports of irritability.[40,41] Interestingly, specific changes in activation within the brain and functional connectivity have been noted for individuals who are sleep deprived compared with those who are not.[42] Specifically, sleep deprivation resulted in a 60% greater magnitude or amygdala reactivity and a significant loss of functional connectivity between the amygdala and the medial prefrontal cortex.[43] At this point, it is unclear how the sleep deprived chronic stroke brain responds. Our cross-sectional data provide insight that indeed depression is significantly associated with 4 modifiable sleep factors. Thus, targeting these 4 modifiable sleep factors may be an important intervention strategy to test in improving depressive symptoms among individuals with chronic stroke.

Stroke survivors commonly experience impaired physical function. Poor sleep may impede recovery from stroke and thus be related to reduce physical function following stroke. Data suggest sleep restriction is associated with lower energy expenditure.[44] It is plausible that this decreased energy expenditure may in turn negatively impact physical function. Animal based studies provide some initial support for this claim. Specifically, 1 rat study demonstrated that sleep disturbances have detrimental effect on functional outcomes after stroke thereby suggesting a role for sleep in the recovery processes and neuroplasticity among those with chronic stroke.[45]

Regular physical activity is also essential for maintaining physical function throughout life,[46] however decreased physical activity is a common consequence of poststroke patients.[40] Studies have demonstrated that poststroke, people spend a median of 20 out of 24 hours in sedentary behaviour.[47] Individuals with chronic stroke have greater sedentary time and lower rates of physical activity. People with stroke sleep longer than their nonstroke controls, spend 75% of their awake hours in sedentary behavior, and engage in minimal physical activity such as walking poststroke.[40] Evidence indicates that poor sleep hygiene, extended sedentary behavior, and low physical activity are associated with adverse health consequences.[48,49] Poor sleep hygiene may also lead to reduced sleep quality, higher depressive symptoms, and more sleep disturbances overall.[40] As such, improving sleep hygiene may be an important intervention target to consider for reducing depressive symptoms and improving physical function.

Physical activity is recognized as being important for older adult sleep quality.[50] Our study builds upon previous literature by highlighting that daytime dysfunction is significantly associated with 3 unique measures of physical function that assess overall mobility, balance, and fatigue. While our analyses do not account for physical activity level, future research should examine whether older adult stroke survivors who are more physically active have (1) greater physical function; and (2) better sleep quality.

This study contains a number of limitations. The sample size for this study is small and the exploratory analyses are strictly intended as hypothesis generating tools. The cross-sectional design of our study did not allow us to ascertain the temporal or the bidirectional relationships between subjective sleep quality and cognition, depression, and physical function. As such, our findings do not imply directionality in the relationship between sleep,

depression, and cognition among individuals with stroke. Participants were not screened based on a diagnosed sleep disorder; sleep quality was measured subjectively using the PSQI via participant self-report and thus subject to self-report bias. As such, the PSQI should be validated in a stroke population using polysomnography. Our study also included a specific population of poststroke older adults and thus these findings cannot be generalized to a more heterogeneous population. Further, because participants did not receive a formal diagnosis for sleep disorders, our findings cannot be generalized to specific types of sleep disorders.

Conclusion

Our data highlight the link between modifiable subjective sleep parameters that are significantly associated with depression and trainable subjective sleep parameters that are significantly associated with physical function among stroke survivors. These results provide clinicians with evidence-based options to target various sleep parameters as a means of reducing the severity of stroke-related deficits in depression and physical function.

Acknowledgments

We thank the Vitality study participants.

Conflict of Interest

The authors have declared that no competing interests exist.

Author Contributions

TLA and JCD had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: TLA, JCD.

Acquisition, analysis, or interpretation of data: TLA, JCD, RSF, JRB.

Drafting of the manuscript: JCD, TLA, RSF.

Critical revision of the manuscript for important intellectual content: JCD, RSF, TLA, JRB.

Statistical analysis: JCD, RSF.

Obtained funding: TLA, JRB.

Administrative, technical, or material support: TLA.

Study supervision: TLA, JCD, JRB, RSF.

Sponsor's Role

None.

Data sharing

Unpublished data are available upon request. Please email Dr. Teresa Liu-Ambrose: teresa.ambrose@ubc.ca

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.jstrokecerebrovasdis.2019.04.010.

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