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RESEARCH ARTICLE

The interaction effect of physical activity and sleep on cognitive function in stroke

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Abstract

INTRODUCTION: Having a stroke increases risk for dementia two-fold. Poor sleep quality and quantity are common after a stroke and are associated with cognitive impairment. Physical activity benefits cognitive function. Whether there is an interaction effect of physical activity and sleep on cognitive function among persons living with chronic stroke is unknown.

METHODS: A cross-sectional study used baseline data acquired from 97 community-dwelling adults aged ≥55 years, living with chronic stroke (71±9 years; $n = 38$, female), and enrolled in a 6-month randomized controlled trial. We measured physical activity (i.e., moderate to vigorous physical activity [MVPA] and light physical activity [PA]) and sleep quality and quantity (i.e., efficiency, latency, duration) using wrist-worn accelerometry. Global cognitive function was measured with the 13-item Alzheimer's Disease Assessment Scale–Cognitive Subscale (ADAS-Cog-13). We assessed whether

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the interaction of physical activity (MVPA and light PA) with sleep quality and quantity (interaction term: physical activity * sleep) was associated with ADAS-Cog-13 score: (1) in the full sample and (2) among males and females separately (i.e., sex-stratified). Significant moderations were plotted as continuous simple slopes.

RESULTS: In the full sample, there was a significant interaction effect between MVPA and sleep duration on the ADAS-COG-13 score ($\beta = 1.636 \pm 0.787$; $p = 0.041$). Specifically, among individuals with shorter sleep duration (i.e., one standard deviation below mean sleep duration), those with greater MVPA had better ADAS-Cog-13 performance. In the sex-stratified analysis, the interaction effect of MVPA and sleep duration on cognitive function was significant in males ($\beta = 3.417 \pm 1.374$; $p = 0.016$) but not females.

DISCUSSION: Moderate to vigorous physical activity may mitigate the negative impact of shorter sleep on cognitive function among persons living with stroke, particularly males.

KEYWORDS
accelerometry, chronic stroke, cognitive function, physical activity, randomized controlled trial, sleep quality

Highlights

- Physical activity and sleep are associated with cognitive function following stroke.
- Physical activity may ameliorate the negative effects of poor sleep on cognitive function.
- Females suffer greater health consequences of sleep dysregulation than males.
- Physical activity moderates the association of sleep duration and cognitive function.
- Physical activity may promote cognitive function in males with short sleep duration.

1 | BACKGROUND

Stroke is the leading cause of disability and the second leading cause of death, with 13.7 million recorded global incidents in 2016.[1] The consequences of stroke include impaired physical and cognitive function.[2] Notably, a stroke doubles the risk of dementia.[3] Thus, it is important to identify modifiable factors that mitigate the negative impact of stroke on cognitive health. Sleep quality and quantity and physical activity (PA) are each modifiable behaviors that impact recovery and outcomes among persons living with stroke.[4,5]

Good sleep quality and quantity are critical for cognitive health.[6] Sleep quality and quantity, broadly speaking, represent how well an individual sleeps at night.[7] Some indicators of sleep quality include (1) *sleep efficiency* (%; the ratio of time spent sleeping to time spent trying to sleep); (2) *sleep latency* (minutes; the amount of time it takes to fall asleep). One measure of sleep quantity includes (3) *sleep duration* (minutes; the time spent actually sleeping after going to bed).[7] Poor sleep quality and quantity are associated with cognitive impairment in attention, working memory, memory consolidation, alertness, and decision-making ability.[8] Among older adults, cognitive function decreases with worsening sleep quality and quantity.[9]

Sleep quality and quantity may be especially critical for cognitive health in individuals with stroke. Poor sleep quality and quantity may be predictive of cognitive impairment of vascular origins.[10] Poor sleep is common among persons who are living with stroke.[4] Notably, poor sleep quality and quantity are associated with a greater magnitude of deficits in cognitive function among people living with stroke than their non-stroke peers.[11]

Another key lifestyle factor associated with cognitive health is PA.[12,13] Briefly, PA is any bodily movement that requires energy expenditure from skeletal muscles, including activities of daily living.[14] Among older adults, greater levels of PA are associated with maintained memory and executive function and a decreased risk of cognitive decline compared with sedentary older adults.[15,16]

PA is imperative for cognitive health in people living with stroke. People living with stroke have reduced levels of accelerometry device-measured PA compared with their non-stroke peers.[5] Among individuals living with stroke, greater levels of PA are associ-

ated with decreased cognitive impairment 6 months after stroke incidence.[17]

Evidence suggests that there is a complex and interactive relationship between PA and sleep quality and quantity with cognitive function among older adults.[18–20] Higher levels of PA have been shown to mitigate the negative effects of suboptimal sleep on cognitive outcomes.[18] In another cross-sectional analysis of 121 older adult females, Lambiase and colleagues[19] determined that greater levels of PA attenuated the negative effects of poor sleep efficiency on executive function outcomes. Longitudinally, a secondary analysis of a randomized controlled trial (RCT) of 121 adults living with stroke, determined that PA in the form of exercise training had a more robust effect on cognitive function for individuals with poor sleep compared with those with good sleep.[21] Exercise training differs from PA such that it is planned, structured, and repetitive with the goal of improving physical health.[14] PA may be more representative of the relationship between daily behaviors and health outcomes. In a 10-year longitudinal study of 8958 individuals aged 50 to 95, higher PA and optimal sleep were independently associated with better cognitive outcomes; the authors also determined that participants with high PA and shorter sleep duration had faster rates of cognitive decline than those with high PA and optimal sleep duration after a median 10-year follow-up.[20] Given the high prevalence of sleep disorders and reduced sleep quality and quantity among persons living with stroke, PA may be critical to maintaining cognitive health in this population. There is limited evidence of the moderating role sleep plays on the relationship between PA and cognitive function observationally.[22] Wei and colleagues[6] determined that older adults who had less than 7 h of sleep per night and engaged in greater levels of PA had better executive function.[6] However, more research is required on how sleep interacts with PA and cognitive function among older adults and those living with stroke. To our knowledge, no study has examined the interactive associations of objective, device-measured PA, and sleep with cognitive performance in people with stroke. Further, the effect of the interaction of PA (i.e., light PA and moderate to vigorous PA) with sleep quality and quantity on cognitive performance has yet to be established.

The effect of the interaction of PA and sleep quality and quantity on cognitive function in persons living with stroke may also vary as a function of biological sex. Evidence suggests that sleep dysregulation impacts females more severely.[23] Given that an estimated 50% of individuals have sleep disorders after a stroke,[24] this may contribute to the observation that females have worse outcomes after stroke – including dementia.[25]

This study explored the question of whether there was an effect of the interaction of PA and sleep quality and quantity on cognitive function in persons living with chronic stroke (i.e., ≥1 year since stroke incident). Further, we stratified the sample by biological sex to explore whether this interaction differed between males and females who had had a stroke. We hypothesize that PA attenuates the negative associations of poor sleep quality and quantity with cognitive function in males and females living with chronic stroke. Further, we propose that the effect of the interaction of sleep quality and quantity and PA on cognitive function varies by biological sex.

RESEARCH IN CONTEXT

1. **Systematic review**: The authors reviewed the literature using traditional sources (e.g., PubMed). Among individuals living with stroke, there is growing research on the individual associations of objectively measured PA and objectively measured sleep with cognitive function, but how one moderates the other's relationship with cognitive function is underdeveloped.
2. **Interpretation**: Our findings expand the current body of literature by identifying the interaction effect of PA and sleep on cognitive function in individuals living with stroke. We further determine that this relationship differs by biological sex.
3. **Future directions**: Longitudinal analysis of a RCT that explores the relationship of PA and sleep quality among individuals living with chronic stroke is required to assess the causality of the identified moderation. Analysis of a biological sex-balanced sample will more clearly define sex differences.

2 | METHOD

2.1 | Study Design

This was a cross-sectional subset analysis from baseline data of 97 community-dwelling adults living with chronic stroke from a 6-month proof-of-concept RCT that examined if twice weekly exercise training or twice weekly social and cognitive training improved cognitive function in adults living with chronic stroke (ClinicalTrials.Gov Identifier: NCT01916486).[26] Ethical approval was obtained from the Vancouver Coastal Health Research Institute and the University of British Columbia's Clinical Research Ethics Board (H13-00715). All participants provided written informed consent.

2.2 | Participants

The study protocol is published.[26] Briefly, our baseline sample of adults living with chronic stroke consisted of 120 community-dwelling males and females who (1) were aged ≥55 years old, (2) had an ischemic or hemorrhagic stroke (confirmed by previous magnetic resonance imaging (MRI) or computed tomography scan) at least 1 year prior to study enrollment, (3) had a Mini-Mental State Examination (MMSE) score of ≥20/30,[27] (4) could read, write, and speak English with acceptable visual and auditory acuity, (5) were not expected to start or were stable on a fixed dose of cognitive medications (e.g. donepezil and galantamine), (6) were able to walk ≥6 m with rest intervals, (7) were not currently participating in any regular therapy or exercise training, and (8) had not been diagnosed with dementia of any type or another neurodegenerative or neurological condition.

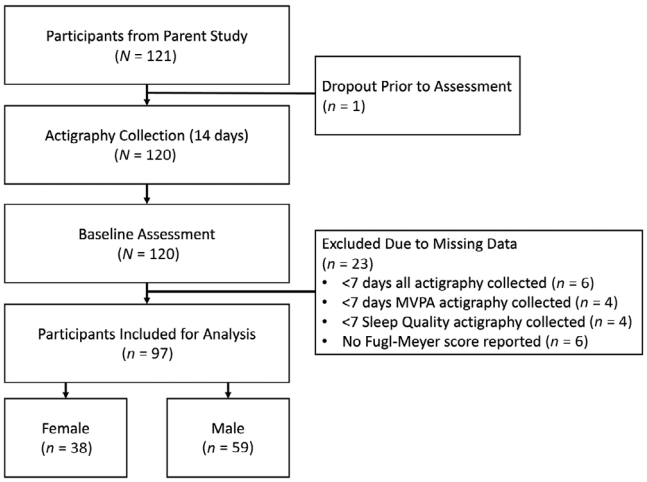

FIGURE 1 Strobe flow chart.

2.3 | Measures

All measures were collected at study baseline prior to randomization. We collected demographics and conducted neuropsychological testing to index cognitive function (Figure 1). Age in years, education level, height in centimeters, weight in kilograms, resting systolic and diastolic blood pressure, stroke type, and duration since most recent stroke were measured. All measures were collected by trained research personnel using standard protocols.

2.3.1 | Descriptors

General cognition and cognitive status (i.e., presence of probable mild cognitive impairment) was assessed using the MMSE[27] and the Montreal Cognitive Assessment (MoCA).[28] We assessed post-stroke motor function using the Fugl–Meyer motor score.[29] Balance and mobility were assessed by the Short Physical Performance Battery (SPPB); gait speed was derived from its 4-m walk component.[30] Subjectively rated sleep quality was assessed with the Pittsburgh Sleep Quality Index (PSQI).[31] Participants were asked if they had previously been diagnosed with obstructive sleep apnea.

2.3.2 | Accelerometry measurement of sleep quality and quantity and PA

At study entry, objective sleep quality and quantity and PA were measured using the MotionWatch8 (MW8) – a uniaxial, wrist-worn accelerometer with evidence of validity and reliability for indexing sleep quality and quantity[32] and PA.[33] The MW8 can provide reliable estimates of sleep quality and quantity after 7 days of observation[34] and was designed to observe acceleration ranging in magnitude from 0.01 to 8 g with a frequency of 3 to 11 Hz. The filtered acceleration signal is digitized and the magnitude summed over a user-specified time interval. At the end of each interval, the summed value or activity "count" is stored in memory, and the integrator is reset. For the current study, we used 60-s epochs.[35]

Sleep quality and quantity

Participants were fitted with the MW8 by trained research personnel who provided detailed information on the MW8 features (i.e., the light sensor, event marker button, and status indicator). Participants were instructed to press the event marker button each night when they started trying to sleep and again each morning when they finished trying to sleep. Consistent with established protocol for MW8, participants wore the device on the non-dominant wrist for a period of >7 days. This protocol was modified for adults with stroke; if the non-dominant side was the stroke-affected side, then we placed the MW8 on the dominant wrist.

Participants completed the nine-item Consensus Sleep Diary (CSD)[36] each morning upon waking. The CSD was used to confirm time-stamped event markers from the MW8 of "lights out" at the start of the sleep window and "lights on" at the end of the sleep window. We used light sensor data to determine "lights out" and activity data to determine "lights on" in cases where CSD and MW8 event markers did not match. Total awake time started each day when participants reported being awake and out of bed (as per responses to the CSD and confirmed via event marker time stamps from MW8) and ended at "lights out." Data prior to recorded wake time on the first full day of recording were manually removed to only investigate full 24-h recordings of activity.

After collection, stored activity counts were downloaded and saved using the MotionWare 1.0.27 (camntech) for subsequent data reduction and analysis. MotionWare was used to estimate different parameters of sleep quality and quantity including sleep efficiency (time asleep expressed as a percentage of time in bed), sleep latency (time between "lights out" and falling asleep), and sleep duration (total time spent sleeping).

Physical activity

Daily PA was determined by MW8 counts per minute during total awake time on full days of recording (i.e., lights on to lights out). Total awake time spent in PA was split into two categories 1) light PA (light PA; 1.5 – 3.0 METs) and 2) moderate-to-vigorous physical activity (moderate to Vigorous Physical Activity (MVPA);>3.0 METs). We included both light PA and MVPA as independent variables in the analysis. Physical activity levels were established using predetermined cut points established by Falck and colleagues[37] that consider (1) whether the accelerometer is worn on the stroke-affected side and (2) Fugl–Meyer stroke severity (mild ≥79/100, moderate to severe <79/100).[38]

2.3.3 | Cognitive function

The 13-item Alzheimer's Disease Assessment Scale–Cognitive Subscale (ADAS-Cog-13) measured global cognitive function.[39] The 13-item version assesses word recall, commands, constructional praxis,

naming, ideational praxis, orientation, word recognition, remembering instructions, comprehension of spoken language, word-finding difficulty in spontaneous speech, spoken language ability, delayed word recall, and number cancellation.[40] Higher scores on ADAS-Cog-13 indicate poorer cognitive performance (range 0 to 85 points).

2.4 | Statistical Analysis

All statistical analyses were completed in R version 4.1.2. We averaged physical activity (i.e., MVPA and light PA) and sleep quality and quantity (i.e., efficiency, latency, and duration) estimates across the first 7 days of observation.

Mean values, standard deviations, and distribution of participant characteristics and measures were analyzed using R version 4.1.2.

To examine whether there is an effect of the interaction of physical activity and sleep on cognitive function, linear regressions were conducted. Independent variables were (1) sleep quality and quantity, (2) physical activity, and (3) the interaction of sleep quality and quantity with physical activity. ADAS-Cog-13 was the dependent variable of interest. A total of six separate regression models were conducted for each sleep quality and quantity metric (i.e., efficiency, latency, and duration) and each level of physical activity (i.e., light PA and MVPA) in the study sample. We included biological sex, age, MoCA, and Fugl–Meyer score as covariates. All independent variables and covariates were mean centered to reduce multicollinearity and improve interpretation of results.[41] Significant interaction effects were then explored using model-based estimates of simple slopes in which the relationship between physical activity and ADAS-Cog-13 score was estimated separately at mean sleep quality and quantity, one standard deviation (SD) below mean sleep quality and quantity, and one SD above sleep quality and quantity.[42] All significant associations were plotted with ggplot2 3.3.5. Given the exploratory and hypothesis-developing nature of this analysis, we did not correct for multiple comparisons.

To examine whether the interaction of physical activity and sleep differed by biological sex, we conducted stratified regression analysis based on biological sex. Covariates were Fugl–Meyer motor score, MoCA, and age. Significant interaction effects of sleep quality and quantity and physical activity were then then further explored by using model-based estimates of simple slopes in which the relationship between physical activity and ADAS-Cog-13 score was estimated separately at mean sleep quality and quantity, one standard deviation (SD) below mean sleep quality and quantity, and one SD above mean sleep quality and quantity. Given the exploratory and hypothesis developing nature of this analysis we did not correct for multiple comparisons.

3 | RESULTS

One hundred twenty community-dwelling adults living with chronic stroke were enrolled and randomized to the trial at baseline (Figure 1). Following a quality check of sleep and physical activity accelerometry data acquired from the MW8 device, 97 participants were included on the basis that they had at least seven consecutive days and nights of accelerometry data collected and had a reported Fugle–Meyer motor score to determine activity cut points (Figure 1). Twenty-three participants were excluded due to incomplete MW8 data.

3.1 | Participant characteristics

Table 1 provides participant characteristics. Participants were primarily male (60.8%). The mean age was 71 years (SD = 9) with a BMI of 27.74 kg/m^2 (SD = 4.46). Mean PSQI was 6.18 (SD = 3.07), indicating a poor sleep quality (i.e., a score >5 indicates poor sleep quality).[43] Mean accelerometry measured sleep efficiency (M = 85.31%; SD = 7.34; range = 63.34% to 97.29%), sleep latency (M = 6.36 min; SD = 5.75; range = 0.00 to 28.64 min), and sleep duration M = 427.26 min; SD = 66.22; range = 284.21 to 652.79 min) are reported in Table 1. Mean daily MVPA and light PA were 33 min (SD = 41.23; range = 0.00 to 250.00 min) and 198.74 min (SD = 123.83; range = 3.71 to 443.86 min; Table 1). The mean ADAS-Cog-13 score was 16.64 (SD = 7.00).

There were no differences in objectively measured sleep efficiency, latency, or duration, as well as MVPA or light PA between sexes (Table 1). Females (M = 14.64, SD = 5.10) had lower ADAS-Cog-13 compared to males (M = 17.93, SD = 7.76; Table 1).

3.2 | Interaction of PA and sleep on cognitive function

There was a significant effect of the interaction of mean daily MVPA and sleep duration on ADAS-Cog-13 score (β = 1.636 ± 0.787; p = 0.041; Table 2) when controlling for Fugl–Meyer motor score, MoCA, age, and sex (Table 2). Specifically, as shown in Figure 2, among persons with low sleep duration (i.e., mean sleep duration – one standard deviation), those with greater mean daily MVPA had better ADAS-Cog-13 scores despite low sleep duration. Greater mean daily MVPA was not associated with higher ADAS-Cog13 scores among individuals with mean and high sleep duration. Mean daily MVPA did not significantly interact with the sleep quality metrics of efficiency or latency. Mean daily light PA did not significantly interact with any sleep quality and quantity metrics (Table 2).

3.3 | Effect of interaction of PA and sleep on cognitive function stratified by sex

In the sex-stratified analysis, there was a significant effect of the interaction of mean daily MVPA and sleep duration on ADAS-Cog-13 score (β = 3.417 ± 1.374; p = 0.020) in males (Table 3). As shown in Figure 3, among males with low sleep duration (i.e., mean sleep duration – one standard deviation), males with greater mean daily MVPA had better ADAS-Cog-13 scores despite low sleep duration. Greater mean daily MVPA was not associated with higher ADAS-Cog-13 scores among males with mean and high sleep duration. We did not find any signifi-

TABLE 1 Participant characteristics.

	Mean standard deviation (SD) or *n* (%)			
	Parent study sample	Total	Female	Male
Measure *	*n* = 120	*n* = 97	*n* = 38	*n* = 59
Age (years)	70.73 (8.56)	70.80 (8.71)	71.95 (9.26)	70.07 (8.34)
Sex = male	74 (61.7)	59 (60.8)	-	-
Stroke type				
Hemorrhagic	33 (27.5)	30 (30.9)	7 (18.4)	23 (39.0)
Ischemic	73 (60.8)	54 (55.7)	23 (60.5)	31 (52.5)
Ischemic and lacunar	1 (0.8)	1 (1.0)	1 (2.6)	0 (0.0)
Lacunar	7 (5.8)	6 (6.2)	4 (10.5)	2 (3.4)
Unknown	6 (5.0)	6 (6.2)	3 (7.9)	3 (5.1)
Stroke hemisphere				
Bilateral	4 (3.3)	2 (2.1)	1 (2.6)	1 (1.7)
Left	61 (50.8)	48 (49.5)	20 (52.6)	28 (47.5)
Right	51 (42.5)	44 (45.4)	17 (44.7)	27 (45.8)
Unknown	4 (3.3)	3 (3.1)	0 (0.0)	3 (5.1)
Time since last stroke (months)	66.48 (53.77)	66.73 (54.64)	66.45 (55.64)	66.92 (54.46)
Fugl-Meyer score (/100)	81.21 (23.85)	80.98 (23.33)	77.82 (27.93)	83.02 (19.81)
Obstructive sleep apnea	17 (14.2)	14 (14.4)	5 (13.2)	9 (15.3)
CES-D (/60)	9.32 (8.24)	9.74 (8.49)	11.34 (10.10)	8.69 (7.15)
Education				
High school diploma or less	24 (20.0)	18 (18.6)	7 (18.4)	11 (18.6)
Some university	36 (30.0)	28 (28.9)	12 (31.6)	16 (27.1)
University or higher	60 (50.0)	51 (52.6)	19 (50.0)	32 (54.2)
Height (cm)	167.37 (9.80)	167.28 (10.10)	158.40 (6.39)	173.00 (7.59)
Weight (kg)	77.95 (15.85)	78.19 (16.53)	68.26 (13.66)	84.58 (15.07)
BMI (kg/m^2)	27.68 (4.43)	27.74 (4.46)	27.13 (5.13)	28.14 (3.96)
MMSE (/30)	27.27 (2.47)	27.38 (2.45)	27.53 (2.18)	27.29 (2.62)
MoCA (/30)	21.89 (4.15)	22.31 (4.12)	22.47 (3.27)	22.20 (4.60)
Mild cognitive impairment	109 (90.8)	87 (89.7)	36 (94.7)	51 (86.4)
SPPB (/12)	8.18 (2.67)	8.32 (2.68)	8.03 (2.68)	8.51 (2.68)
Gait speed (m/s)	0.86 (0.32)	0.88 (0.33)	0.79 (0.35)	0.94 (0.31)
ADAS-Cog-13 (/85)	17.25 (7.37)	16.64 (7.00)	14.64 (5.10)	17.93 (7.76)
Physical activity behavior				
MVPA (min)	-	33.00 (41.23)	31.71 (49.87)	33.83 (35.00)
Light PA (min)	-	198.74 (123.83)	192.89 (144.92)	202.51 (109.29)
Sleep quality				
PSQI (/21)	6.06 (3.02)	6.18 (3.07)	6.95 (2.77)	5.68 (3.17)
Sleep Efficiency (%)	-	85.31 (7.34)	85.56 (8.29)	85.14 (6.73)
Sleep Latency (min)	-	6.36 (5.75)	6.06 (5.79)	6.56 (5.77)
Sleep Duration (min)	-	427.26 (66.22)	422.29 (48.81)	430.47 (75.58)

Abbreviations: BMI, body mass index; ADAS-Cog-13, 13-item Alzheimer's Disease Assessment Scale–Cognitive Subscale; MMSE, Mini-Mental State Exam; MoCA, Montreal Cognitive Assessment; MCI, mild cognitive impairment (i.e., MoCA score ≤ 26); CES-D, Center for Epidemiological Studies Depression Scale; SPPB, Short Physical Performance Battery; MVPA, moderate to vigorous physical activity; PA, physical activity; PSQI, Pittsburgh Sleep Quality Index.

*Higher scores indicate better performance: FMS; MMSE; MoCA; SPPB.

*Higher scores indicate worse performance: ADAS-Cog-13; PSQI; CES-D.

TABLE 2 Interaction of mean daily physical activity with sleep quality on ADAS-Cog-13 scores.

Term	B	SE	*t*	*p*
Sleep Efficiency × Light PA	−0.065	0.566	−0.114	0.91
Sleep Efficiency × MVPA	−0.145	0.741	−0.196	0.85
Sleep Latency × Light PA	−0.290	0.660	−0.439	0.66
Sleep Latency × MVPA	−0.895	0.708	−1.265	0.21
Sleep Duration × Light PA	0.671	0.596	1.126	0.26
Sleep Duration × MVPA	1.636	0.787	2.078	**0.04**
MVPA at simple slope levels				
Low sleep duration	−0.824	0.684	−1.205	0.23
Mean sleep duration	1.023	0.807	1.267	0.21
High sleep duration	2.870	1.479	1.941	0.06

Note: ADAS-Cog-13 is the dependent variable on all models. Age, biological sex, Montreal Cognitive Assessment score, and Fugle-Meyer score are included as covariates. $p < 0.05$ indicates statistical significance.
Abbreviations: ADAS-Cog-13, 13-item Alzheimer's Disease Assessment Scale–Cognitive Subscale; β, adjusted standardized beta estimate; MVPA, moderate to vigorous physical activity; PA, physical activity; SE, standard error; *t*, *t* statistic.

cant effect of interactions between sleep quality and quantity and PA on ADAS-Cog-13 in females alone (Table 3).

4 | DISCUSSION

The interaction of mean daily MVPA and sleep duration was associated with cognitive function in persons living with chronic stroke. These findings align with the current body of evidence that MVPA engagement may attenuate the negative effects of poor sleep on cognitive function.[6,18,19] To our knowledge, this is the first study to identify this interaction among persons living with chronic stroke using objective, device-measured PA and sleep quality and quantity.

Among participants with shorter sleep duration, those who engaged in greater levels of MVPA had better cognitive function. However, longer sleep duration may mitigate the benefits of greater MVPA engagement on cognitive function. The current literature suggests that sleep duration may share an inverse-U relationship with cognitive function, where abnormally high (>9 h) and abnormally low (<6 h) sleep duration negatively impact cognitive function[44] and increase the risk of dementia.[45] Based on our findings, PA may be beneficial in promoting cognitive function among persons who have lower sleep duration. However, in a longitudinal cohort analysis, Bloomberg and colleagues[20] determined that there were no differences in cognitive performance across sleep duration at baseline in adults aged 50 to 95 but participants with high PA and shorter sleep duration had faster rates of cognitive decline than those with higher PA and optimal sleep duration after a median 10-year follow-up.[20]

Longer, but not shorter, sleep duration is associated with increased frailty in older adults.[46] In the present baseline analysis, participants with more than 8 h of average sleep duration had a mean SPPB score 1.5 points lower than persons with less than 8 h of sleep, which may indicate a greater degree of frailty. Additionally, within this sample of persons living with chronic stroke, persons with longer sleep duration (i.e., >8 h) engaged in far less MVPA (M = 5.17 min MVPA; SD = 6.60) than those with 6 to 8 h of sleep duration (M = 32.96 min MVPA; SD = 35.89) and <6 h (M = 61.05 min MVPA; SD = 64.52). Therefore, it is possible that persons with longer sleep duration engage in less MVPA due to increased frailty which impacts their cognitive function.

The interaction of MVPA and sleep duration on cognitive function was significant in males but not females. Thus, greater engagement in MVPA may be beneficial for preserving cognitive function in adults living with chronic stroke who have short sleep duration, particularly

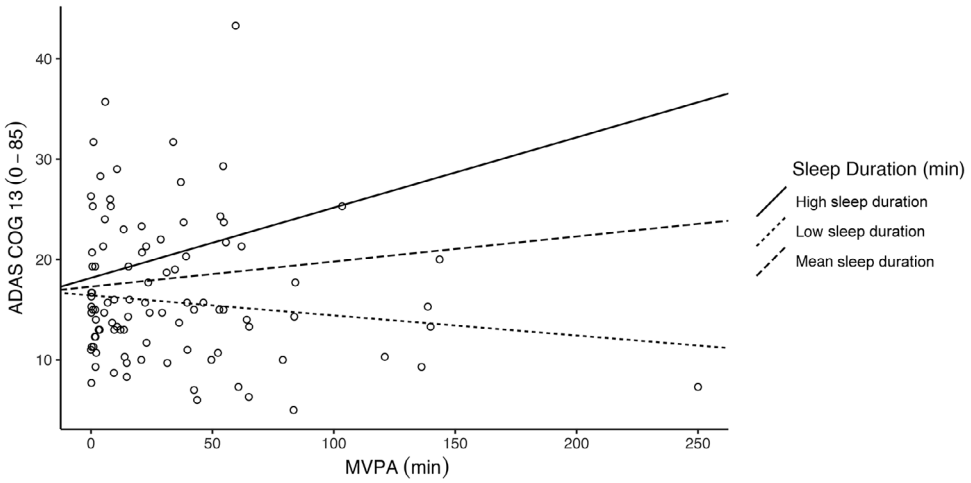

FIGURE 2 The interaction of mean daily moderate to vigorous physical activity (MVPA) and sleep duration with 13-item Alzheimer's Disease Assessment Scale–Cognitive Subscale (ADAS-Cog-13) among males and females ($n = 97$), where higher ADAS-Cog-13 scores indicate lower cognitive performance. Greater MVPA attenuated the association between lower sleep duration and cognitive function, where greater MVPA was associated with improved cognitive function (adjusted $R^2 = 51.4\%$). Mean sleep duration = 427.26 min; higher sleep duration (mean + 1 SD) = 493.49 min; lower sleep duration (mean−SD) = 361.04 min.

TABLE 3 Interaction of mean daily physical activity with sleep quality on ADAS-Cog-13 scores stratified by sex.

Interaction Term	B	SE	*t*	*p*
Males				
Sleep Efficiency × Light PA	0.642	1.016	0.632	0.53
Sleep Efficiency × MVPA	0.608	1.294	0.469	0.64
Sleep Latency × Light PA	−1.117	0.992	−1.126	0.27
Sleep Latency × MVPA	−1.616	0.949	−1.704	**0.09**
Sleep Duration × Light PA	1.289	0.840	1.534	0.13
Sleep Duration × MVPA	3.417	1.374	2.487	**0.02**
MVPA at simple slope levels				
Low sleep duration	−2.901	1.471	−1.973	0.05
Mean sleep duration	0.999	1.071	0.933	0.36
High sleep duration	4.900	2.246	2.181	**0.03**
Females				
Sleep Efficiency × Light PA	−0.259	0.562	−0.462	0.65
Sleep Efficiency × MVPA	−0.394	0.773	−0.509	0.61
Sleep Latency × Light PA	0.501	0.780	0.641	0.53
Sleep Latency × MVPA	0.904	1.019	0.887	0.38
Sleep Duration × Light PA	0.331	0.843	0.392	0.70
Sleep Duration × MVPA	1.097	0.954	1.150	0.26

Note: ADAS-Cog-13 is the dependent variable on all models. Age, Montreal Cognitive Assessment score, and Fugle-Meyer score are included as covariates.

Abbreviations: ADAS-Cog-13, 13-item Alzheimer's Disease Assessment Scale–Cognitive Subscale; MVPA, moderate to vigorous physical activity; PA, physical activity. β, adjusted standardized beta estimate; SE, standard error; *t*, *t* statistic; $p < 0.05$ indicates statistical significance.

among males. Poor sleep quality and quantity is reported to impact brain health and cognitive function in females more than males.[47] Given the prevalence of poor sleep quality and quantity after a stroke, this may contribute to the observation that females have worse cognitive outcomes after a stroke[48] and PA engagement may not overcome the negative impact of poor sleep quality and quantity on cognitive function.

4.1 | Limitations and future directions

First, although MW8 has evidence of validity against polysomnography,[32] it is plausible that sleep variables are being both overestimated and underestimated. Individuals with poor sleep quality and quantity may reduce agreement between accelerometry and polysomnography since these people tend to lie in bed motionless, but awake, for long periods of time.[49] However, due to the ease of use and minimally invasive nature of the MW8, it is still a valuable tool in sleep quality and quantity detection as it allows the inclusion of more participants than traditional polysomnography.

Second, given that females are at greater risk of poor sleep quality[23] and have worse cognitive outcomes following stroke,[25] an insignificant interaction effect of PA and sleep on cognitive function in females was unexpected. However, we included more males than females in our analysis. It is possible that we were underpowered (i.e., type II error or false negative) to detect an interactive effective of PA and sleep quality on cognitive function in females.[21] Further, we explored potential sex differences in the interaction of PA and sleep on cognitive function by stratified analysis versus a three-way interaction (i.e., sex * MVPA *

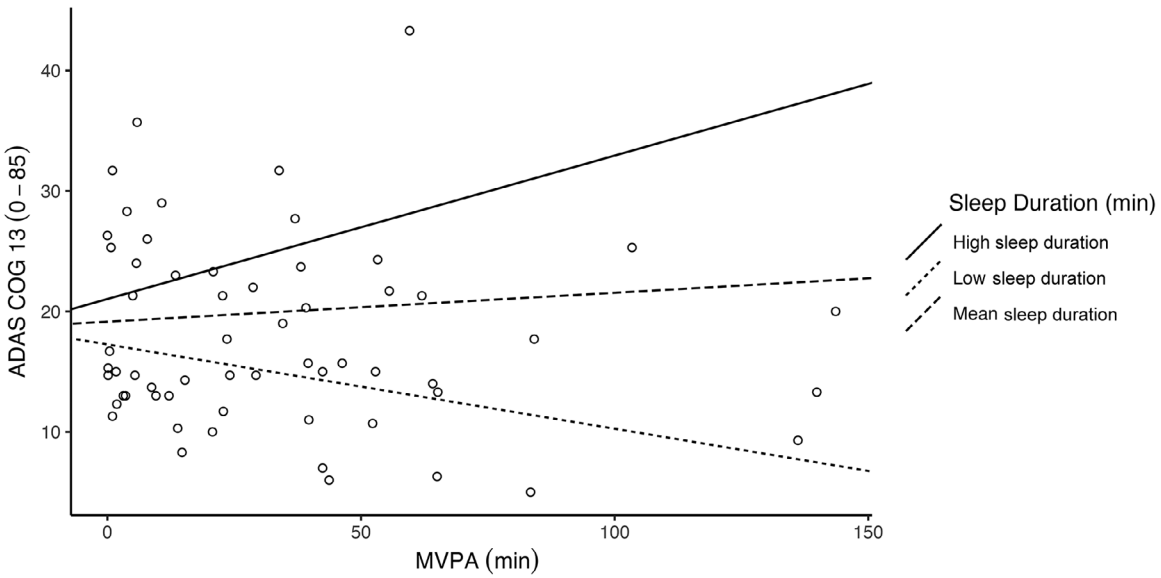

FIGURE 3 Interaction of mean daily moderate to vigorous physical activity (MVPA) and sleep duration on 13-item Alzheimer's Disease Assessment Scale–Cognitive Subscale (ADAS-Cog-13) among males ($n = 59$), where higher ADAS-Cog-13 score indicates lower cognitive performance. Greater MVPA attenuated the association between lower sleep duration and cognitive function, where greater MVPA was associated with improved cognitive function (adjusted $R^2 = 51.7\%$). Mean sleep duration = 430.47 min; longer sleep duration (mean + 1 SD) = 506.04 min; shorter sleep duration (mean—SD) = 354.89 min.

sleep) due to our smaller sample size. Future studies with larger samples are needed to robustly examine sex differences in the effect of the interaction of PA and sleep on cognitive function.

Third, we did not comprehensively screen for clinical sleep disorders such as restless leg syndrome; we only screened for prior diagnosis of obstructive sleep apnea and insomnia. Individuals living with stroke are at an elevated risk of sleep disorders, such as restless leg syndrome, which can significantly impact sleep, cognitive, and functional outcomes.[50]

Fourth, we did not conduct multiple comparisons adjustments due to the exploratory and hypothesis-developing nature of this analysis. Thus, there is an increased false positive risk (i.e., type I error).

Fifth, although there is an established inverse-U relationship between sleep duration and cognitive function,[44] this relationship was not observed in this sample with an exploratory quadratic function. It is likely that the sample size was not sufficient to observe this known relationship.

Longitudinal studies are needed to confirm our current findings. Future RCTs involving exercise are needed to determine whether exercise can improve sleep and whether exercise-induced changes in sleep is a pathway by which exercise improves cognition in stroke.

5 | CONCLUSIONS

Our results suggest that MVPA is beneficial for global cognitive function among stroke survivors with shorter sleep duration. We also identified an interaction of MVPA and sleep duration on cognitive function in males but not females. These findings may suggest that males living with chronic stroke respond differently to PA engagement than females with regard to cognitive function.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest. Author disclosures are available in the Supporting Information.

CONSENT STATEMENT

All human subjects provided informed consent.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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