






## Research Article

# Associations of environmental and lifestyle factors with spatial navigation in younger and older adults

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### Abstract

**Objective:** Advanced age is associated with prominent impairment in allocentric navigation dependent on the hippocampus. This study examined whether age-related impairment in allocentric navigation and strategy selection was associated with sleep disruption or circadian rest-activity fragmentation. Further, we examined whether associations with navigation were moderated by perceived stress and physical activity. **Method:** Sleep fragmentation and total sleep time over the course of 1 week were assayed in younger ( $n = 42$ ) and older ( $n = 37$ ) adults via wrist actigraphy. Subsequently, participants completed cognitive mapping and route learning tasks, as well a measure of spontaneous navigation strategy selection. Measurements of perceived stress and an actigraphy-based index of physical activity were also obtained. Circadian rest-activity fragmentation was estimated via actigraphy post-hoc. **Results:** Age was associated with reduced cognitive mapping, route learning, allocentric strategy use, and total sleep time ( $ps < .01$ ), replicating prior findings. Novel findings included that sleep fragmentation increased with advancing age ( $p = .009$ ) and was associated with lower cognitive mapping ( $p = .022$ ) within the older adult cohort. Total sleep time was not linearly associated with the navigation tasks ( $ps > .087$ ). Post-hoc analyses revealed that circadian rest-activity fragmentation increased with advancing age within the older adults ( $p = .026$ ) and was associated with lower cognitive mapping across the lifespan ( $p = .001$ ) and within older adults ( $p = .005$ ). Neither stress nor physical activity were robust moderators of sleep fragmentation associations with the navigation tasks ( $ps > .113$ ). **Conclusion:** Sleep fragmentation and circadian rest-activity fragmentation are potential contributing factors to age effects on cognitive mapping within older adults.

**Keywords:** cognitive mapping; route learning; physical activity; sleep fragmentation; circadian rhythms

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### Introduction

Existing research has focused on characterizing age-related differences in spatial navigation, with evidence of particular deficits in processes dependent upon the hippocampus (Lester et al., 2017). However, it is important to also consider factors that may contribute to the deficits, particularly ones that may be modifiable. While several factors may contribute to hippocampal aging and related impairments in spatial navigation, the role of age-related disruption in sleep quality remains unclear. Thus, the current study focused on understanding the role of sleep disturbance in age effects on spatial navigation.

The ability to navigate an environment to a goal location involves two separable strategies and neural systems (Burgess, 2008; Maguire, 1998; Wolbers et al., 2004). Allocentric navigation strategies involve a flexible, world-centered (object-to-object) representation (i.e., a “cognitive map”) and are hippocampal dependent. Egocentric navigation strategies involve environmental information represented from the perspective of the navigator

(i.e., route based) and are dependent on the caudate nucleus and medial parietal cortex. In dual-solution paradigms, there is individual variability in which strategy is predominately used, paralleling structural and functional variance in the hippocampus and caudate (e.g., Bohbot et al., 2007; Iaria et al., 2003; Marchette et al., 2011). While both strategies may be used during navigation, there is also evidence of competitive interactions between the systems (Packard & McGaugh, 1996; Poldrack & Packard, 2003).

While advancing age is associated with deterioration of the neural substrates of both navigation strategies (Raz & Rodrigue, 2006), the magnitude of hippocampal atrophy exceeds that of caudate atrophy (Raz et al., 2010; Walhovd et al., 2011). Consistent with this, there is greater age-related decrement on tasks assessing the formation, retention, and use of a cognitive map relative to learning a route (Head & Isom, 2010; Iaria et al., 2009; Lester et al., 2017). Additionally, older adults exhibit a shift from allocentric to egocentric strategies in dual-solution paradigms consistent with competitive interactions between the systems (Rodgers et al.,

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2012; Wiener *et al.*, 2013). Lastly, associations between hippocampal volume and allocentric tasks have been observed in older adults (Daugherty *et al.*, 2015; Head & Isom, 2010).

Several lines of evidence support poor sleep quality as a potential contributor to these age effects on allocentric navigation. Total sleep deprivation is associated with reduced hippocampal plasticity, a shift from allocentric to egocentric strategy use and a differential deficit in allocentric compared to egocentric navigation task performance in rodents (Hagewoud *et al.*, 2010; Murata *et al.*, 2018; Soto-Rodriguez *et al.*, 2016). Sleep fragmentation, a measure of brief arousals during a bout of sleep, is more ecologically valid and common than sleep deprivation. Experimentally induced sleep fragmentation negatively impacts hippocampal plasticity and hippocampal-dependent learning in rats (Guzman-Marin *et al.*, 2007; Lee *et al.*, 2016; Sportiche *et al.*, 2010; Tartar *et al.*, 2010). Furthermore, sleep fragmentation is associated with disruptions in electrophysiological signals that support hippocampal-dependent memory processes (Astori *et al.*, 2013; Fogel & Smith, 2011; Ondze *et al.*, 2003). The incidence of sleep fragmentation rises with advancing age (Ohayon *et al.*, 2004) and is modestly associated with impaired cognitive performance in older adults (André *et al.*, 2019; Blackwell *et al.*, 2011; Kaneshwaran *et al.*, 2019; Luik *et al.*, 2015). However, much of this work was conducted with clinical populations or limited to general psychometric measures. Thus, targeted research exploring the impact of sleep fragmentation on spatial navigation processes associated with the hippocampus in healthy older adults is necessary.

Circadian rest-activity rhythm fragmentation, in the form of daytime napping and/or nighttime arousals, may also contribute to age effects on allocentric navigation. The intradaily variability, an actigraphy-derived measure of rest-activity rhythm fragmentation, increases with older age (Huang *et al.*, 2002; Luik *et al.*, 2013; Musiek *et al.*, 2018; Oosterman *et al.*, 2009). Furthermore, higher intradaily variability has been associated with medial temporal lobe atrophy and dysfunction across the lifespan (Van Someren *et al.*, 2019). The impact of circadian disruption on navigation strategies remains unclear.

Relevant to our central goal of understanding the effects of sleep fragmentation on allocentric navigation is consideration of other lifestyle factors. Exercise and stress have both been shown to regulate hippocampal plasticity, with exercise conferring benefits and stress imparting a negative impact in rodents and humans. (Erickson *et al.*, 2011; Gianaros *et al.*, 2007; Kleemeyer *et al.*, 2016; Lucassen *et al.*, 2010; Machida *et al.*, 2021; Niemann *et al.*, 2014). As an initial step in building models of how these factors may play a role in age effects on hippocampal-dependent navigation, we considered interactive effects of stress and exercise with sleep fragmentation. That is, neurophysiological changes with aging could make older adults' hippocampal system simultaneously more vulnerable to cumulative damage from sleep fragmentation and stress as well as more likely to benefit from protective factors like physical activity and exercise (Graham *et al.*, 2006; Miller & O'Callaghan, 2005).

The current study collected one-week measures of sleep quality, perceived stress, and physical activity as assays of trait-like characteristics to address several novel aims. First, we examined associations between sleep disturbance and spatial navigation. We hypothesized that sleep fragmentation would have a particularly negative impact on allocentric navigation performance and be associated with a shift from allocentric strategy use to egocentric strategy use. A second goal was to determine the role of sleep disturbance in age-related differences in spatial navigation. We

hypothesized that sleep fragmentation would mediate age-related effects on allocentric navigation. Our third aim was to determine whether perceived stress or physical activity moderates the effects of sleep disturbance. We hypothesized that individuals with greater perceived stress would evidence greater negative effects of sleep fragmentation, and that this moderating effect would be greater for older adults. Additionally, we hypothesized that greater physical activity would mitigate the negative effects of sleep fragmentation, and this moderating effect would be greater for older adults. Total sleep time was also examined as a secondary measure of sleep quality, with the hypotheses that shorter sleep duration would serve a similar role as greater sleep fragmentation.

The fourth aim was to determine whether circadian rest-activity rhythm fragmentation was associated with spatial navigation in post-hoc analyses. We hypothesized that intradaily variability would be negatively associated with allocentric navigation performance and strategy use and would mediate age effects on these tasks.

## Methods

### Participants

Younger adult participants (aged 18–25) were recruited via an undergraduate participant pool in the Department of Psychological & Brain Sciences at Washington University or Volunteers for Health (VFH), a research volunteer registry at Washington University. Older adult participants (aged 60–89) were recruited via VFH. Participants were compensated monetarily or with course credit. All participants were right-handed with normal or corrected vision. Participants with a current or past psychological disorder or neurological disorder (e.g., stroke, dementia, traumatic brain injury), current sleep disorder, reduced mobility, or use of sleep-promoting medications were excluded. In total, 80 participants were enrolled (42 younger adults (27 females); 37 older adults (19 females); see Supplemental Table 1). There was a non-significant trend for higher education in older adults ( $p = .08$ ). One older individual was excluded due to sleep medication use. Participants provided written consent in accordance with Washington University Human Research Protection Office guidelines.

### Experimental procedures

#### General

Participants had two lab visits approximately one week apart. During the first visit, participants were given an actigraphy watch and instructions on completing a sleep diary. During the second visit, participants completed experimental tasks. A psychomotor vigilance task was first. Spatial navigation task order was counter-balanced. Participants completed stress, physical activity, computer expertise, health, and sense of direction questionnaires via REDCap before or after the second visit. A summary of study measures is in Table 1 and descriptive statistics are in Supplemental Table 2.

#### Measures

*Sleep fragmentation, total sleep time, and intradaily variability* Sleep measures were obtained using Actigraph GT9X watch (ActiGraph; Pensacola, FL) with a tri-axial accelerometer. With the exception of bathing or swimming, participants continuously wore the watch on the non-dominant wrist for three–eight consecutive nights (82% with 5+ days; mean = 6.2;  $SD = 1.4$ ).

**Table 1.** Summary of key tasks and variables

|                     | Construct  | Task description  | Outcome scores   |
|---------------------|--|---|--|
| Navigation          | Allocentric navigation ability (cognitive mapping)             | Study phase: Learn object locations by freely exploring a virtual environment for four minutes. Test phase: Mark the locations of the landmarks by making an X on a two-dimensional map             | Average number of correctly placed landmarks across four trials.<br>(0–12; higher = better performance)  |
|                     | Egocentric navigation ability (route learning)                 | Study phase: Learn a route by following arrows along a path in an environment of interconnected hallways with landmarks. Test phase: Recreate learned path as quickly as possible                   | Average time in seconds to traverse a route across four trials.<br>(higher = worse performance)  |
|                     | Spatial navigation strategy use                                | Study phase: Learn object locations by watching a video tour of an environment with interconnected pathways and landmarks. Test phase: Navigate to a target landmark from random locations          | Ratio of trials with shortcut use vs. original route across 16 trials.<br>(0–1; higher = more allocentric strategy use)  |
| Sleep               | Sleep fragmentation  | Tri-axial accelerometer worn on non-dominant wrist for 3–8 consecutive days and nights  | Average daily sleep fragmentation index. Movement Index (total awake minutes/total hours in bed × 100) + Fragmentation Index (total one-minute sleep bouts/total sleep bouts × 100).<br>(0+; higher = more fragmented sleep) |
|                     | Sleep duration (total sleep time)                              | Tri-axial accelerometer worn on non-dominant wrist for 3–8 consecutive days and nights  | Average minutes of sleep per 24-hr period<br>(0+; higher = longer sleep duration)  |
|                     | Circadian rest-activity fragmentation (intradaily variability) | Tri-axial accelerometer worn on non-dominant wrist for 3–8 consecutive days and nights  | Variability between successive hours of activity/variability of activity in one day<br>(0–1; higher = more fragmented rest-activity cycle)   |
| Moderators          | Physical activity  | Tri-axial accelerometer worn on non-dominant wrist for 3–8 consecutive days and nights  | Average daily minutes of moderate to vigorous physical activity (>1952 counts per 60-s epoch)<br>(0+; higher = more physical activity)   |
|                     | Perceived stress   | Ten-item version of the Perceived Stress Scale; rate frequency of stressful events occurring in past month on a 0–4 Likert scale  | Sum of items<br>(0–40; higher = more perceived stress)   |
| Additional measures | Psychomotor vigilance  | Attend to a crosshair centered on the screen and press spacebar as quickly as possible when a red dot appears at randomly varying time intervals  | Standardized composite of average reciprocal of response times, average response time for slowest 10% of trials, and number of trials with response time > 500 s (reverse coded).<br>(higher = better performance)           |
|                     | Visuomotor expertise   | Traverse hallway with alternating turns in virtual environment as quickly as possible   | Time in seconds to traverse<br>(0+; higher = worse performance)  |
|                     | Computer experience  | Rate computer experience, experience playing computer games, and experience with computer games involving virtual reality on a 0–7 Likert scale   | Sum of items scored 0–7<br>(0–21; higher = more experience)  |
|                     | Subjective sleepiness  | Stanford Sleepiness Scale; Rate current alertness on a 1–7 scale from “1-Feeling active, vital, alert, or wide awake” to “7- No longer fighting sleep, sleep onset soon; having dreamlike thoughts” | Single-item score<br>(1–7; higher = more subjective sleepiness)  |

Movement sampling frequency was set to 30 Hz and binned in 60-s epochs without the low frequency extension filter (Feito et al., 2017). A wear-time validation algorithm was applied before further processing (Choi et al., 2011). Sleep periods were determined in ActiLife (Pensacola, FL) using the Cole–Kripke algorithm (Cole et al., 1992). If entire nights of sleep were not detected by the Cole–Kripke algorithm but were indicated in participant’s sleep diary, self-reported sleep and wake times were manually entered ( $n = 23$ , no age group difference,  $p < .92$ ). The sleep fragmentation index was computed as the sum of the movement index (total scored awake minutes/total time in bed in hours × 100) and the fragmentation index (total one-minute scored sleep bouts/total number of sleep bouts of any length × 100) (ActiLife 6 User’s Manual, 2012). Total sleep time was the average minutes of sleep per 24 hr.

Intradaily variability, a measure of rest-activity fragmentation, was calculated as a ratio of the variability between successive hours of activity and overall variability of activity in 1 day (Witting et al., 1990). Greater intradaily variability is consistent with greater fragmentation of rest-activity cycles. Intradaily variability was derived from full days of raw activity counts binned in 60-s epochs using the R package “nparACT” (Blume et al., 2016).

#### Sleep diary

Participants completed the Consensus Sleep Diary (Maich et al., 2018) as soon as possible each morning via REDCap or a paper form.

#### Psychomotor vigilance

This task was administered using Psychology Experiment Building Language (Mueller & Piper, 2014). Participants attended to a crosshair centered on the screen and quickly pressed the spacebar when a red dot appeared at randomly varying time intervals. Response time appeared after each trial. The index of performance was a standardized composite score of average reciprocal of response times, average response times for the slowest 10% of trials, and number of trials where response time exceeded 500 milliseconds (Basner & Dinges, 2011).

#### Spatial navigation tasks

Spatial navigation tasks were administered in Unity (San Francisco, CA) on 24-inch monitors (see Supplementary Figure 1). Participants first practiced using a joystick in a virtual environment of a long hallway with alternating turns. Next,

visuomotor expertise was tested by requiring participants to traverse the environment within 60 seconds. All participants passed this test.

#### *Cognitive mapping*

For this task, the indoor environment consisted of interconnected hallways with twelve landmarks (Allison et al., 2016). During study, participants freely explored a virtual environment for four minutes and were instructed to discover as many objects as they could and to pay attention to the objects and their locations. For the test phase, participants indicated the locations of the landmarks by making an X on a two-dimensional map. These study-test phases were repeated for four trials. Cognitive mapping performance was quantified as the average number of correctly placed landmarks across trials.

#### *Route learning*

During study, participants followed a path marked by arrows in an environment consisting of interconnected hallways and twenty-six landmarks (Allison et al., 2016). For the test phase, participants were instructed to accurately traverse the route as quickly as possible without the arrows. These study-test phases were repeated for four trials. Route learning performance was quantified as average time to traverse the route across trials in seconds.

#### *Spatial navigation strategy use*

Participants were administered a dual-solution task (Marchette et al., 2011). First, participants studied pictures of each landmark with its associated name two times for familiarization. Next, participants encoded a route through an outdoor environment that included the twelve landmarks, interconnecting pathways, and four unique surrounding mountains by viewing a video across nine trials. To ensure sustained attention, five matching trials were randomly interspersed with experimental route trials. Matching trials were in a different environment from the experimental route environment with no landmarks, but instead with colored spheres along a route. Participants answered yes/no questions about number, color, or sequence in which spheres were presented.

For the test phase, participants were placed at one landmark in the maze and asked to locate a target landmark indicated at the top of the screen by name. Twenty-four combinations of starting landmarks and target landmarks were administered in random order. For 16 of these trials, participants could either find the target by following the path originally shown or by taking a shortcut route.

We used a protocol to classify trials similar to past work (Furman et al., 2014; Marchette et al., 2011). Shortcut routes were defined as paths that were shorter than the original path and with more than half of the path deviating from the original path. Original routes were defined as having more than half of the participants' trajectory on the original path. Inefficient routes were defined as being longer than the original path. Unsuccessful routes were defined as not reaching the target location. The navigation strategy index was defined as the proportion of trials in which a shortcut was taken (0 = no shortcut use; 1 = shortcut used on all trials). Unsuccessful and inefficient routes were not included when calculating the strategy index.

Shortcut use is considered an allocentric strategy because it requires knowledge of object locations and their relative distances irrespective of viewpoint. Conversely, following an original route is considered an egocentric strategy, where the navigator uses knowledge of local landmarks and associated body turns from a first-person perspective. Therefore, higher values on the navigation

strategy index, indicating greater use of shortcuts, is interpreted as reflecting greater allocentric strategy use. Greater shortcut use on this task correlates with relative activation of the hippocampus versus caudate (Furman et al., 2014; Marchette et al., 2011).

#### *Perceived stress*

Psychological stress over the prior month was measured with the ten-item version of the Perceived Stress Scale (Cohen et al., 1994). This scale has demonstrated strong internal consistency, strong test-retest reliability, and moderate criterion validity in both younger and older adults (Lee, 2012).

#### *Physical activity*

Physical activity was measured via actigraphy. Acquisition parameters and wear-time validation were the same as for sleep measures (Choi et al., 2011). ActiLife software was set to indicate wrist-worn watch, which scales the scoring algorithms accordingly via an internal algorithm (ActiLife 6 User's Manual, 2012). The Freedson algorithm (Freedson et al., 1998) was used for cut-points to classify intensity levels into sedentary (<100 counts per epoch), light (100–1952), moderate (1952–5723), and vigorous activity (>5724) categories. Physical activity was quantified as average minutes in moderate to vigorous physical activity per valid wear day. Minutes of physical activity only included bouts activity, defined as at least 10 minutes of continuous physical activity allowing for two minutes of interruption (Physical Activity Guidelines Advisory Committee, 2008).

#### *Computer experience*

Participants rated computer experience, experience playing computer games, and experience with computer games involving virtual reality on a 0–7 Likert scale (higher number = more experience).

#### *Subjective sleepiness*

The Stanford Sleepiness Scale (Hoddes et al., 1973) was completed after the experimental tasks. Participants rated their current state on a 7-point scale (higher number = greater sleepiness).

#### *Analytic approach*

##### *Covariates*

Gender, computer experience, visuomotor expertise, subjective sleepiness, psychomotor vigilance, and number of nights of actigraphy measurement were considered as potential covariates. Variables significantly associated with age were included as covariates. Computer experience, subjective sleepiness, and number of measurement nights were significantly different between age group ( $ps < .05$ ; see Table 1).

##### *Outliers*

Outliers were defined as data points > 2.5 standard deviations from the mean and with Cook's D value greater than  $4/n$  (Cook, 1977). Results are presented with outliers removed (see Supplemental Tables 2–5 for results with outliers included).

##### *Aims 1 and 2 analyses: associations amongst age, sleep characteristics, and spatial navigation*

For these analyses, we used age group as the predictor, navigation measures as the outcomes, and sleep fragmentation (primary) and total sleep time (secondary) as mediators. All analyses were conducted in Stata 16.0 (StataCorp) using the "sem" command and

**Table 2.** Stress as a moderator of sleep characteristics

|                   |        | Age          | Stress    | SFI       | SFI × stress | Age × SFI  | Age × stress | Age × stress × SFI |
|-------------------|--------|--------------|-----------|-----------|--------------|------------|--------------|--------------------|
| Strategy index    | Step 1 | -.51(.12)*** | -.22(.14) | .09(.11)  | -.12(.10)    | –          | –            | –                  |
|                   | Step 2 | -.45(.14)**  | -.22(.16) | -.03(.13) | -.14(.13)    | .34(.25)   | .06(.19)     | .24(.23)           |
| Cognitive mapping | Step 1 | -.72(.08)*** | .10(.11)  | -.01(.07) | .10(.08)     | –          | –            | –                  |
|                   | Step 2 | -.72(.07)*** | .05(.12)  | .11(.12)  | .06(.09)     | -.27(.11)* | .08(.11)     | -.13(.13)          |
| Route learning    | Step 1 | .71(.11)***  | .15(.13)  | .13(.12)  | .02(.10)     | –          | –            | –                  |
|                   | Step 2 | .73(.13)***  | .20(.13)  | -.03(.15) | .15(.13)     | .15(.17)   | -.05(.17)    | -.04(.17)          |

|                   |        | Age          | Stress    | TST       | TST × Stress | Age × TST | Age × Stress | Age × Stress × TST |
|-------------------|--------|--------------|-----------|-----------|--------------|-----------|--------------|--------------------|
| Strategy index    | Step 1 | -.52(.14)*** | -.16(.14) | -.20(.12) | -.02(.13)    | –         | –            | –                  |
|                   | Step 2 | -.52(.14)**  | -.11(.16) | -.03(.12) | -.07(.14)    | -.31(.18) | -.07 (.18)   | -.07(.23)          |
| Cognitive mapping | Step 1 | -.69(.08)*** | .05(.11)  | .09(.07)  | .09(.09)     | –         | –            | –                  |
|                   | Step 2 | -.65(.07)*** | -.03(.14) | .04(.09)  | .10(.11)     | .10(.12)  | .17(.10)     | .06(.13)           |
| Route learning    | Step 1 | .76(.12)***  | .11(.12)  | .09(.11)  | -.10(.09)    | –         | –            | –                  |
|                   | Step 2 | .69(.14)***  | .12(.12)  | .22(.15)  | -.08(.11)    | -.23(.16) | -.03(.18)    | -.15(.17)          |

SFI = sleep fragmentation index; TST = total sleep time.

Note. Data represent standardized path coefficients with standard errors in parentheses. Higher scores on the strategy index indicate greater relative shortcut use. Higher scores on cognitive mapping indicate better performance. Higher scores on route learning indicate worse performance.

\* $p < 0.05$ .

\*\* $p < 0.01$ .

\*\*\* $p < 0.001$ .

full information maximum likelihood estimation to address missing data (see Table 1). The first step examined whether the necessary conditions for mediation were met (i.e., the predictor and outcome variable were significantly related to the mediator). Based on current recommendations, a significant association between predictor and outcome was not required to assess for mediation (MacKinnon et al., 2002; Rucker et al., 2011). Mediation analyses implemented a regression-based approach to estimate effects in conjunction with bootstrapping. The total effect represents the association of age group with spatial navigation, including both direct and indirect effects. The direct effects indicate the degree of association between: (a) age group and the mediator; (b) the mediator and spatial navigation controlling for age group; and (c) age group and spatial navigation controlling for the mediator. Indirect effects indicate the degree to which age group influences spatial navigation via the mediator. Indirect effects were examined using 5,000 bootstrapping samples and 95% percentile confidence intervals (CIs).

#### Aim 3 analyses: stress and physical activity as moderators of sleep associations with spatial navigation

Regression analyses were conducted to examine moderating effects. Analyses were conducted in Stata 16.0 (StataCorp) using the “sem” command and full information maximum likelihood estimation to address missing data (see Table 1). Continuous variables were standardized using a Z-transformation prior to creating interaction terms. In all analyses, covariates, age group, the sleep variable, perceived stress (or physical activity), and the primary 2-way interaction of interest (sleep variable × perceived stress (or physical activity) were entered in the first step. Remaining 2-way interactions with age group (age group × sleep variable; age group × perceived stress (or physical activity) as well as the 3-way interaction of primary interest were entered in the second step. Standardized coefficients and standard errors (SE) are presented.

#### Aim 4 post-hoc analyses: associations amongst age, intradaily variability, and spatial navigation

Analyses were conducted as described under Aim 1, except intradaily variability was the mediator.

## Results

### Aims 1 and 2: associations amongst age, sleep characteristics, and spatial navigation

#### Age-related differences

The age groups did not differ in sleep fragmentation, but older age was associated with reduced total sleep time (sleep fragmentation index:  $\beta = .183$  [ $SE = .129$ ],  $p = .153$ ; total sleep time:  $\beta = -.386$  [ $SE = .104$ ],  $p < .001$ ). There were age group differences in cognitive mapping, route learning, and navigation strategy use. Older adults were less able to form a cognitive map, recreate a learned route, and use shortcuts ( $\beta = -.732$  [ $SE = .072$ ],  $p < .001$ ;  $\beta = .620$  [ $SE = .091$ ],  $p < .001$ ;  $\beta = -.373$  [ $SE = .117$ ],  $p = .001$ , respectively).

#### Sleep fragmentation

Sleep fragmentation was not associated with cognitive mapping, route learning, or navigation strategy use ( $\beta = -.041$  [ $SE = .068$ ],  $p = .547$ ;  $\beta = .094$  [ $SE = .108$ ],  $p = .35$ ;  $\beta = .131$  [ $SE = .103$ ],  $p = .203$ , respectively).

However, we did observe that the association of sleep fragmentation with cognitive mapping differed by age group (see Tables 2 and 3) in the moderation models. The interaction remained significant when examined independently from stress or physical activity (stress model:  $\beta = -.265$  [ $SE = .113$ ],  $p = .019$ ; physical activity model:  $\beta = -.298$  [ $SE = .111$ ],  $p = .008$ ; independent model:  $\beta = -.250$  [ $SE = .103$ ],  $p = .015$ ). Specifically, greater sleep fragmentation was associated with worse cognitive mapping performance among older adults but not younger adults (older:  $\beta = -.344$  [ $SE = .156$ ],  $p = .022$ ; younger:  $\beta = .203$  [ $SE = .168$ ],  $p = .227$ ; see Figure 1). However, sleep fragmentation did not mediate age effects on cognitive mapping within the older adults in a post-hoc analysis ( $\beta = -.155$ ;  $b = -.032$ ; 95% CI:  $-.088$ – $.009$ ).

We also examined whether sleep fragmentation was more strongly associated with cognitive mapping relative to route learning within the older adults. While the association between sleep fragmentation and route learning was not significant ( $\beta = .123$  [ $SE = .216$ ],  $p = .570$ ), the magnitude of the association was not significantly lower than the association with cognitive mapping ( $\chi^2 = 2.27$ ,  $p = .132$ ).

**Table 3.** Physical activity as a moderator of sleep characteristics

|                   |        | Age          | Physical activity | SFI       | SFI × physical activity | Age × SFI   | Age × physical activity | Age × physical activity × SFI |
|-------------------|--------|--------------|-------------------|-----------|-------------------------|-------------|-------------------------|-------------------------------|
| Strategy index    | Step 1 | -.33(.12)**  | .15(.15)          | .06(.13)  | -.01(.13)               | -           | -                       | -                             |
|                   | Step 2 | -.26(.11)*   | .27(.14)          | -.16(.13) | .09(.13)                | .62(.20)**  | -.13(.16)               | .31(.20)                      |
| Cognitive mapping | Step 1 | -.74(.07)*** | -.03(.09)         | -.05(.07) | -.04(.09)               | -           | -                       | -                             |
|                   | Step 2 | -.77(.08)*** | -.08(.13)         | .16(.09)  | -.23(.10)*              | -.30(.11)** | -.05(.11)               | .18(.13)                      |
| Route learning    | Step 1 | .67(.09)***  | .01(.12)          | .10(.12)  | .03(.11)                | -           | -                       | -                             |
|                   | Step 2 | .69(.11)***  | .11(.16)          | -.05(.16) | .11(.15)                | .08(.16)    | -.14(.16)               | -.10(.18)                     |

|                   |        | Age          | Physical activity | TST       | TST × Physical Activity | Age × TST | Age × physical activity | Age × physical activity × TST |
|-------------------|--------|--------------|-------------------|-----------|-------------------------|-----------|-------------------------|-------------------------------|
| Strategy index    | Step 1 | -.38(.12)*   | .16(.13)          | -.15(.12) | .21(.16)                | -         | -                       | -                             |
|                   | Step 2 | -.31(.13)**  | .27(.15)          | .06(.13)  | -.15(.15)               | -.23(.17) | .05(.17)                | .51(.22)*                     |
| Cognitive mapping | Step 1 | -.65(.10)*** | .01(.11)          | .09(.08)  | .01(.11)                | -         | -                       | -                             |
|                   | Step 2 | -.65(.10)*** | .05(.18)          | .11(.12)  | -.00(.13)               | -.02(.11) | -.07(.13)               | -.02(.11)                     |
| Route learning    | Step 1 | .71(.09)***  | .05(.10)          | .16(.10)  | .27(.10)**              | -         | -                       | -                             |
|                   | Step 2 | .73(.10)***  | .10(.15)          | .24(.17)  | .13(.14)                | -.08(.13) | .00(.15)                | .20(.14)                      |

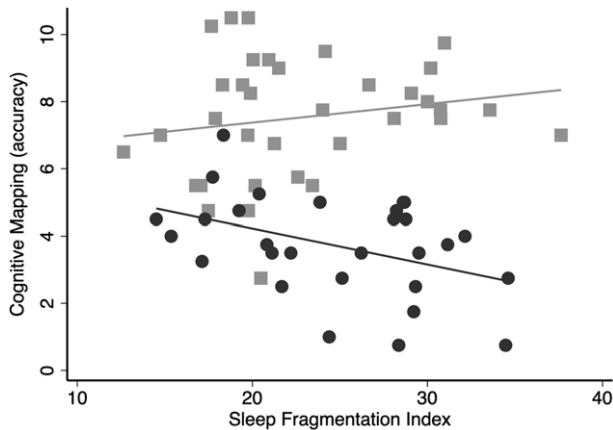
MVPA = moderate-to-vigorous physical activity; SFI = sleep fragmentation index; TST = total sleep time.

Note. Data represent standardized path coefficients with standard errors in parentheses. Higher scores on the strategy index indicate greater relative shortcut use. Higher scores on cognitive mapping indicate better performance. Higher scores on route learning indicate worse performance.

\* $p < 0.05$ .

\*\* $p < 0.01$ .

\*\*\* $p < 0.001$ .



**Figure 1.** Sleep fragmentation association with cognitive mapping. Scatter plot of the significant age group × sleep fragmentation interaction with separate regression lines for younger adults (gray squares;  $\beta = .203$  [ $SE = .168$ ],  $p = .227$ ) and older adults (black circles;  $\beta = -.354$  [ $SE = .154$ ],  $p = .022$ ). See text for details.

While there was also evidence of an age × sleep interaction for the strategy index in the physical activity model, the interaction was not significant when physical activity was removed from the model ( $\beta = .624$  [ $SE = .196$ ],  $p = .001$ ;  $\beta = .271$  [ $SE = .152$ ],  $p = .075$ , respectively).

**Total sleep time**

Total sleep time was not associated with cognitive mapping, route learning, or the spatial navigation strategy index ( $\beta = .084$  [ $SE = .075$ ],  $p = .258$ ;  $\beta = .119$  [ $SE = .104$ ],  $p = .252$ ;  $\beta = -.199$  [ $SE = .117$ ],  $p = .087$ , respectively).

**Aim 3: stress and physical activity as moderators of sleep associations with spatial navigation**

**Sleep fragmentation**

There were no significant interactions involving either stress or physical activity with sleep fragmentation predicting navigation outcomes ( $ps > .113$ ; see Tables 2 and 3).

**Total sleep time**

There were no significant interactions involving stress and total sleep time for any of the navigation outcomes ( $ps > .250$ ; see Table 2). Physical activity did not moderate the association of total sleep time with cognitive mapping ( $ps > .894$ ; see Table 3).

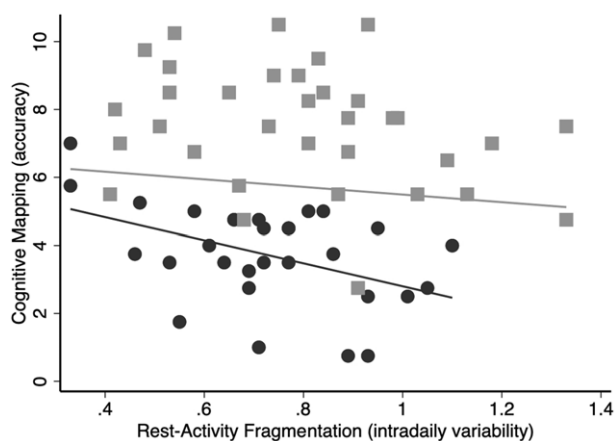
There was a significant total sleep time × physical activity interaction for route learning ( $\beta = .270$  [ $SE = .098$ ],  $p = .006$ ). However, the interaction reflected that longer sleep duration was associated with worse performance at higher physical activity levels but was not associated with performance at lower physical activity levels (high PA:  $\beta = .238$  [ $SE = .099$ ],  $p = .016$ ; low PA:  $\beta = .062$  [ $SE = .201$ ],  $p = .758$ ).

We also observed an age group × physical activity × total sleep time interaction for navigation strategy that was inconsistent with hypotheses ( $\beta = .506$  [ $SE = .219$ ],  $p = .021$ ; see Table 3). For older adults, less sleep was particularly associated with greater shortcut use (i.e., greater allocentric strategy use) at higher physical activity levels compared to lower physical activity levels (interaction:  $\beta = .484$  [ $SE = .190$ ],  $p = .011$ ; high PA:  $\beta = -.239$  [ $SE = .109$ ],  $p = .028$ ; low PA:  $\beta = -.924$  [ $SE = .096$ ],  $p < .001$ ). The physical activity × total sleep time interaction was not significant for younger adults ( $\beta = -.200$  [ $SE = .140$ ],  $p = .155$ ).

Post-hoc analyses were conducted to better understand these interactions. Considering evidence of an inverted U-shape relationship between sleep duration and cognitive outcomes (Mohlenhoff et al., 2018; van Oostrom et al., 2018), we assessed for quadratic (i.e., nonlinear) associations for our navigation outcomes in the full sample by including the quadratic (squared) term for total sleep time in the regression models. There were significant quadratic associations of total sleep time with navigation strategy use and route learning (Supplemental Figure 2) ( $\beta = .275$  [ $SE = .099$ ],  $p = .005$ );  $\beta = .223$  [ $SE = .101$ ],  $p = .027$ , respectively). Thus, it is conceivable that observed interactions with physical activity are spurious (Belzak & Bauer, 2019; Cohen et al., 2003).

**Aim 4: Associations amongst age, intradaily variability, and spatial navigation in post-hoc analyses**

Older adults evidenced lower intradaily variability compared to younger adults indicating reduced rest-activity fragmentation,



**Figure 2.** Circadian rest-activity fragmentation association with cognitive mapping. Scatter plot of the significant association of circadian rest-activity fragmentation with cognitive mapping. Younger adult data are depicted with gray squares and older adult data depicted with black circles. The separate regression lines represent the association in the full sample (gray line;  $\beta = -.235$  [ $SE = .074$ ],  $p = .001$ ) and in the older adults (black line;  $\beta = -.437$  [ $SE = .175$ ],  $p = .005$ ). See text for details.

which is opposite from the expected age-related increase ( $\beta = -.287$  [ $SE = .112$ ],  $p = .015$ ). Greater intradaily variability was associated with lower cognitive mapping but was not related to route learning or strategy use ( $\beta = -.235$  [ $SE = .074$ ],  $p = .001$ ;  $\beta = .134$  [ $SE = .089$ ],  $p = .129$ ;  $\beta = -.095$  [ $SE = .112$ ],  $p = .413$ , respectively).

Within the older adult sample, there was the expected increase in intradaily variability with advancing age ( $\beta = -.449$  [ $SE = .172$ ],  $p = .009$ ;  $\beta = -.389$  [ $SE = .174$ ],  $p = .026$ , respectively). In addition, greater intradaily variability was associated with lower cognitive mapping (see Figure 2), but not with route learning ( $\beta = -.437$  [ $SE = .175$ ],  $p = .005$ ;  $\beta = .252$  [ $SE = .153$ ],  $p = .100$ , respectively) among older adults. However, intradaily variability was not differentially associated with cognitive mapping relative to route learning ( $\chi^2 = .91$ ,  $p = .341$ ). Lastly, intradaily variability did not mediate age effects on cognitive mapping within the older adults ( $\beta = -.170$ ;  $b = -.035$ ; 95% CI:  $-.099$ – $.006$ ).

## Discussion

The current study replicated age differences in spatial navigation tasks (Lester et al., 2017; Wiener et al., 2012) and extended this literature in several ways. The novel goals of this study were to examine: (a) associations between sleep disturbance and spatial navigation; (b) whether sleep disturbance mediated age differences in spatial navigation; (c) whether perceived stress and physical activity moderated sleep associations with spatial navigation; and (d) associations amongst rest-activity fragmentation, spatial navigation, and age in post-hoc analyses. We discuss the results for the each these aims below.

### Associations amongst age, sleep characteristics, rest-activity fragmentation, and spatial navigation

Novel convergent findings were observed regarding the fragmentation measures and cognitive mapping. There was a significant age-related increase in sleep fragmentation within the older adult sample, which is consistent with previous findings (Boulos et al., 2019; Ohayon et al., 2004). Sleep fragmentation has been linked to neurophysiological changes in the hippocampus including

reduced neurogenesis (Guzman-Marin et al., 2007), metabolic dysregulation (Nair et al., 2011; Williams et al., 2016), and reduced long-term potentiation (Tartar et al., 2006). Consistent with these adverse physiologic effects, greater sleep fragmentation was associated with reduced cognitive map formation in older adults. Circadian rest-activity fragmentation also exhibited an age-related increase within the older adults in post-hoc analyses, similar to past observations (Luik et al., 2013; Musiek et al., 2018; Oosterman et al., 2009; but see Park et al., 2021). Importantly, greater circadian rest-activity fragmentation was also related to lower cognitive mapping performance. This is consistent with evidence linking circadian rest-activity fragmentation with hippocampal activity and atrophy (Sherman et al., 2015; Van Someren et al., 2019). Neither the sleep nor circadian fragmentation measure significantly mediated age effects on cognitive mapping within the older adults in post-hoc analyses. This may be attributable to the modest effect sizes combined with a smaller sample size.

We also hypothesized specific negative effects of fragmented sleep and circadian rhythms on hippocampal-dependent navigation. However, we did not observe significant differential associations of either sleep fragmentation or circadian rest-activity fragmentation with cognitive mapping relative to route learning. In addition, there were no indications of fragmentation-related shifts from allocentric to egocentric strategies. Thus, it is relevant to consider that sleep fragmentation and circadian rest-activity fragmentation might instead lead to broad rather than selective deficits. Both types of fragmentation have been associated with reduced processing speed, memory, visuospatial abilities, executive functions, and general cognitive status to varying degrees (André et al., 2019; Lim et al., 2012; Luik et al., 2015; McSorley et al., 2019; Oosterman et al., 2009; Swanson et al., 2021). This literature has generally used neuropsychological tests and no consistent pattern has emerged in terms of domain specificity. Thus, larger-scale studies using more targeted experimental tasks, such as those employed here, may be beneficial for determining the degree to which certain cognitive domains are differentially sensitive to sleep or circadian rest-activity fragmentation.

In terms of total sleep time, duration was not associated with any of the spatial navigation measures, except within the context of interactions with physical activity. However, linear associations were in the opposite directions from those hypothesized for route learning and navigation strategy. One potential contributing factor is the presence of nonlinear associations between total sleep time and both tasks in post-hoc analysis, which can lead to spurious interactions (Belzak & Bauer, 2019; Cohen et al., 2003). Such nonlinear associations are observed in the literature particularly for self-report measures of sleep (Devore et al., 2016). However, findings are also mixed in terms of whether such quadratic associations are observed in younger versus older adults, and in terms of differences across cognitive domains (e.g., Devore et al., 2014; Lo et al., 2016; Mohlenhoff et al., 2018; van Oostrom et al., 2018; Wilckens et al., 2014). We observed the best route learning performance associated with a sleep duration of approximately seven hours, which is consistent with prior literature implicating short and long sleep duration with poorer cognitive outcomes (Lo et al., 2016). In contrast, short and long sleep durations were associated with *more optimal* performance for the navigation strategy task (i.e., taking shortcuts reflective of an allocentric strategy). Considering this heterogeneity in findings, large-scale, systematic investigations are necessary to enhance mechanistic understanding of conditions, cognitive domains, and populations in which nonlinear effects are most likely to be observed.

### Stress and physical activity as moderators of sleep associations with spatial navigation

Surprisingly, neither perceived stress nor physical activity moderated associations of sleep disruption with spatial navigation tasks (Minkel et al., 2014; Van Reeth et al., 2000). In terms of stress, the null effects may be related to its measurement, which was a single retrospective self-report of the past week. Self-reported stress has previously exhibited mixed findings in terms of associations with the stress hormone cortisol (O'Brien et al., 2013). Whereas modulation of navigation strategy use by experimentally induced acute stress has been more consistently associated with elevated cortisol (Diamond & Rose, 1994; Schwabe et al., 2009). Furthermore, stress exposure may affect specific aspects of sleep physiology, such as slow wave activity (Sanford et al., 2015), which would not be captured here. Lastly, studies have indicated that acute and chronic sleep deprivation lead to increased hypothalamic-pituitary-adrenal (HPA) axis reactivity to experimentally induced stressors (Suchecki et al., 2002). Thus, the ecological sleep changes observed here may not be potentiated by stress. Overall, it may be important to systematically incorporate polysomnography to determine sleep architecture, measures of chronic stress exposure, and HPA axis reactivity via cortisol.

Another consideration is that lower physical activity and greater perceived stress may instead be directly associated with greater sleep fragmentation and circadian rest-activity fragmentation (Hooghiemstra et al., 2015; Lambiase et al., 2013). Furthermore, there are age-related reductions in physical activity and complex age effects on stress appraisal (Watson et al., 2016; Surachman & Almeida, 2018). Thus, these two lifestyle factors may also instead directly mediate age effects on spatial navigation processes, rather than interact with sleep quality as examined here. Future work in larger samples should test more complex models (e.g., multiple mediator and/or moderated mediation).

### Limitations

One potential limitation is the use of measures derived from wrist-worn actigraphy devices. Wrist actigraphy may be less sensitive to sleep fragmentation compared to polysomnography (de Souza et al., 2003), and may underestimate physical activity levels in older adults relative to hip placement (Kwan et al., 2020). These factors may have influenced the lack of expected age group differences in sleep fragmentation (Boulos et al., 2019; Ohayon et al., 2004), as well as the lack of modulation by physical activity. In addition, the finding of greater circadian rest-activity fragmentation in younger compared to older adults may be due to the recruitment of college students, as this group self-reports irregular sleep-wake patterns (Lund et al., 2010). Lastly, although we excluded individuals with a known neurological condition, including dementia, we did not screen older adults for global cognitive status.

### Conclusions

In conclusion, we provide novel evidence of associations of both sleep fragmentation and circadian rest-activity fragmentation with hippocampal-dependent spatial navigation in a non-clinical population. These results demonstrate that increased sleep fragmentation and circadian rest-activity fragmentation are associated with reduced cognitive mapping performance in older adults. There was no support for moderating influences of physical activity or psychosocial stress. These and other factors should be further examined to determine mediators and moderators of sleep

fragmentation and circadian rest-activity fragmentation on spatial navigation.

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**Conflicts of interest.** None.

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