



Shift-work-related sleep disruption and the risk of decline in cognitive function: The CRUISE Study

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Abstract

Acute total sleep deprivation and partial sleep deprivation have negative impacts on cognitive performance. Studies in subjects who regularly experience sleep loss, however, are rare and often restricted to examination of internal sleeping disorders. To address this issue, we set up a pilot study to explore the effects of a week characterized by sleep disruption on cognitive functioning, using a case-control setting in a maritime pilot group with chronic exposure to intermittent extrinsic, work-related sleep disruption. Twenty maritime pilots (aged 30–50 years) were compared to sex- and education-matched controls with normal sleep behaviour, from the same age range. We assessed subjective and objective cognitive function, including attention, psychomotor speed, memory and executive function using the Cambridge Neuropsychological Test Automated Battery (CANTAB). Although we were able to confirm poorer sleep in maritime pilots and subjective complaints in some cognitive domains, we did not find objective cognitive deficits in the maritime pilot group compared to controls without sleep disruption. This could suggest that in this group of healthy, young maritime pilots, exposure to sleep disruption resulted in some subjective cognitive complaints, but objective deficits of cognitive function were not detected in comparison with a non-pilot control group. However, given the small sample size, the absence of an effect does not exclude the possibility that sleep disruption could result in cognitive deficits in general. Therefore, our findings have to be confirmed in future prospective studies with a larger sample size and matched controls, regarding age, education and work history.

KEYWORDS

cognitive function, shift work, sleep deprivation, sleep disruption

1 | INTRODUCTION

Sleep deprivation is associated with a higher risk of cardiovascular diseases, increased chances of accidents (Åkerstedt, 2003), and has

a negative effect on mood and cognitive function (Killgore, 2010; Killgore, Balkin, Yarnell, & Capaldi, 2017; McCoy & Strecker, 2011; Medic, Wille, & Hemels, 2017; Pilcher & Huffcutt, 1996). More specifically, poor sleep has been shown to decrease attention, learning,

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memory and executive function (Javaheipour et al., 2019; McCoy & Strecker, 2011; Medic et al., 2017). Sufficient sleep, especially deep sleep, on the other hand, might facilitate cognitive function and the generation of memory consolidation (Kang, Lee, & Lim, 2017; Mander et al., 2015). Brain regions affected by sleep deprivation are the superior parietal lobe, bilateral occipital lobe, thalamus (Javaheipour et al., 2019) and the prefrontal cortex (PFC) (Killgore, 2010), and their interconnectivity (Verweij et al., 2014), which are important for planning, cognitive control, visuospatial perception, memory, reasoning, personal goal setting and higher-order cognitive processes (Javaheipour et al., 2019; Miller & Cohen, 2001). As a result, one night of acute total sleep deprivation is sufficient to slow reaction times and worsen attention, working memory, decision making and short-term memory (Aidman, Jackson, & Kleitman, 2019; Alhola & Polo-Kantola, 2007). Several nights of sleep restriction to 6 hr or less can lead to cognitive deficits that resemble the cumulative effects of two nights of total sleep deprivation (Van Dongen, Maislin, Mullington, & Dinges, 2003). These studies focused on acute, short-term effects of sleep deprivation in experimental settings. In contrast, studies in subjects who regularly experience sleep loss are scarce, mostly limited in duration and vary in methodology and participant selection (Alhola & Polo-Kantola, 2007; Deary & Tait, 1987). Such studies are furthermore often restricted to the internal nature of sleep disruption, for example sleeping disorders such as insomnia, apnea and REM sleep behavioural disorders (El-Ad & Lavie, 2005; Galbiati, Carli, Hensley, & Ferini-Strambi, 2018; Meng, Zheng, & Hui, 2013). These sleeping disorders might share common pathways, in which poor sleep is a symptom of an underlying disease that might cause the detrimental effects on health in general, rather than poor sleep alone being a risk factor.

We set up the CRUISE study (Cognitions Relationship to Unfrequent and Irregular Sleep Events) to study the effects of external (work-induced) sleep disruption on cognitive functioning in healthy adults (aged 30–50 years). To do so, we recruited a unique population of Dutch maritime pilots. Maritime pilots work irregular shifts, resulting in weeks of normal sleep alternating with work weeks characterized by disrupted sleep with periods of sleep deprivation (missing a full night of sleep due to work), sleep restriction (a shorter night of sleep) and sleep fragmentation (short sleep periods interrupted by calls to work). This group is therefore well suited to test the hypothesis that sleep disruption may lead to deficits in cognitive function. We hypothesize that this specific work schedule of week-long sleep disruptions leads to poor sleep that might facilitate deficits in cognitive function. Testing this hypothesis is of relevance for a broader population of people who suffer from sleep disruption or work irregular shifts. To test the cognitive function of the maritime pilot cohort, we made use of the Cambridge Neuropsychological Test Automated Battery (CANTAB), including tests of attention and psychomotor speed (reaction time [RTI] and rapid visual information processing [RVP]), working memory (spatial working memory [SWM]) and episodic memory (paired associates learning [PAL]), and executive function (multitasking test [MTT] and one-touch stockings of Cambridge [OTS]).

2 | METHODS

2.1 | Participants

We recruited 20 male maritime pilots (30–50 years old) from the national organization of Dutch maritime pilots (Nederlandse Loodswezen) who had an average employment time of 10.9 years \pm 3.5 (range, 5–16 years). The inclusion of men only was due to the fact that maritime pilots in the Netherlands are almost entirely men. The task of a maritime pilot is to guide large international ships into Dutch harbours. They exclusively work irregular shifts, in which working hours depend on the number and type of ships that arrive. Working these unpredictable and irregular shifts results in fragmented and shorter sleep over a period of 24 hr for seven consecutive days, which is followed by a week off. More details about the study population have been reported in previous publications (Thomas, Ooms, et al., 2019; Thomas, Overeem, & Claassen, 2019). In addition, we recruited 20 control participants (30–50 years old), matched on sex and educational attainment. Controls had an average of 19.5 \pm 1.96 years of education, which is comparable to the 18 \pm 0 years of education the maritime pilots completed. Controls were employed in various different professions, comparable in cognitive demand with the maritime pilots, for example in academic environments. All controls, however, had normal sleep (self-reported). All enrolled participants had a body mass index of 18–35 kg/m², did not use neuroactive medication and were physically healthy (self-report). Controls did not report any cognitive deficits, indicated by a general health questionnaire and examination of medical history.

2.2 | Ethical approval

The CRUISE study was approved by the institutional review board (CMO Region Arnhem-Nijmegen, file number 2017-3950) and performed according to good clinical practice (GCP) guidelines. The study took place from November 2018 until August 2019. Written informed consents were obtained from all participants after they received detailed study information. Participants did not receive a stipend for taking part in the study.

2.3 | Design

The CRUISE study is an observational case-control study. All participants were scheduled for one visit to fill out five questionnaires about general health, cognitive state, sleep, quality of life (QoL) and mood. After completing the questionnaires, they underwent cognitive testing of approximately 1 hr. The maritime pilot group was scheduled for the first day off after a work week to measure short-term effects of sleep disruption of the preceding work week on cognitive functions.

2.4 | Questionnaires

2.4.1 | Pittsburgh Sleep Quality Index (PSQI) and sleep-wake diary

The PSQI provides information on individual sleep-related dysfunctions and general sleep behaviour. The questionnaire was divided into six sub-categories: sleep quality (SQ), sleep latency (SOL), total sleep time (TST), sleep efficiency (SEF), sleep disturbances and daytime dysfunction. For the maritime pilot group, we administered the questionnaire twice, for a rest week and a work week. The control group completed the questionnaire once for a normal week. Scores on the subcategories were added up. The PSQI has a maximum score of 21; a total score of 5 was used as cut-off point for sleep disturbances and a score of ≥ 7 indicates severe/abnormal sleep behaviour (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). Additionally to the PSQI and to get a comprehensive measure of day-to-day variation in sleep behaviour, participants were instructed to maintain a sleep-wake diary for 10 days.

2.4.2 | General Information Questionnaire

This questionnaire assessed medical background, medication use, alcohol intake and smoking behaviour. Additionally, working schedules and working years for maritime pilots were recorded.

2.4.3 | Cognitive Failure Questionnaire (CFQ)

The CFQ measures the burden of daily subjective cognitive errors. Participants answered 25 statements, indicating how often they experience certain cognitive errors on a scale from 0 (never) to 4 (very often). The scores were summed, resulting in a maximum score of 100 and a minimum score of 0. Normative values for the Dutch population have been reported, with a mean of 32.8 and a standard deviation (SD) of 11.2 for a normal population (mean age = 45.5 ± 4.1 years) (Ponds, Van Boxtel, & Jolles, 2006). There is no evidence for an age-dependent effect on the CFQ (Ponds et al., 2006); we can therefore interpret the results without constraint. A score of 55.2 was used as cut-off point for severe cognitive complaints (> 2 SDs above the mean).

2.4.4 | RAND-36 (QoL)

The RAND-36 is a validated questionnaire for QoL and health status assessment. It contains nine different subscales, with variations in minimum and maximum scores: functional state (min. 10, max. 30), social functioning (min. 2, max. 10), physical restraints (min. 4, max. 8), emotional restraints (min. 3, max. 6), mental health (min. 5, max. 30), vitality (min. 4, max. 24), pain (min. 11, max. 60), general health (min. 5, max. 25) and change in health (min. 1, max. 5) (Van der Zee & Sanderman, 1993). Items are transformed to calculate a scale score that ranges from 0 to 100. The higher the scale score, the better the

health status and QoL. Standardized age norms have been established for different age groups, we used age-adjusted (35–44 years) normative data to interpret our results (data not shown).

2.4.5 | Hospital Anxiety and Depression Scale (HADS)

The HADS is a well-validated questionnaire that measures mood disorders related to anxiety and depression. Participants indicated how often they experience certain emotions or behaviours related to emotional distress. The HADS contains seven items for depression and seven for anxiety. The maximum score for each component is 21. A score of 0–7 is interpreted as normal, whereas a score of ≥ 11 indicates severe mood problems (Spinhoven et al., 1997; Zigmond & Snaith, 1983).

2.5 | Neuropsychological Assessment (CANTAB)

To assess cognitive function, we chose tests from the validated CANTAB test battery (Cambridge Cognition) that were sufficiently sensitive to detect cognitive differences between maritime pilots and controls (Barnett, Blackwell, Sahakian, & Robbins, 2016; Égerházi, Berecz, Bartók, & Degrell, 2007; J. Fray, W. Robbins, & J. Sahakian, 1996; Sahakian & Owen, 1992). CANTAB is a well-validated battery of tests that is relatively robust to ceiling effects due to its digital nature, in which difficulty levels can adjust to participants' performance. CANTAB has been proven to be a valid tool for the assessment of cognitive functions of healthy individuals (Pettersen, 2017; Savulich et al., 2019). Tests focused on attention and psychomotor speed (RTI and RVP), working memory (SWM) and episodic memory (PAL), and executive function (MTT and OTS). These tests seem to be addressing some of the functions most affected by sleep deprivation effects (Majer et al., 2008).

2.5.1 | Reaction time (RTI)

The RTI task measures attention; that is, reaction times for motor and mental responses. During the task, circles (one for the simple task and five for the five-choice mode) are shown at the top of the screen in which a random yellow light appears. Participants have to hold a button on the bottom of the screen and release it to select the circle above in which they detected the yellow light as fast as possible and then return their finger to the hold button. Outcome measures include simple median reaction time (SMDRT), five-choice median reaction time (FMDRT) and error scores (simple error score and five-choice error score).

2.5.2 | Spatial working memory (SWM)

The SWM test is a measure of visuospatial working memory. Participants have to search for a yellow token that is hidden in one

of the boxes placed at different locations on the computer screen through process of elimination. The number of boxes increases during the task depending on the level of difficulty (max. 12 boxes). Outcome measures include total errors (TE), errors due to selecting boxes that have already been found to be empty (within errors) or re-opening boxes that contained a token already (between errors [BE]).

2.5.3 | Paired associates learning (PAL)

The PAL test assesses visual episodic memory. Participants are presented with boxes on the screen in which different visual patterns are shown one by one. After the encoding phase, the different patterns are shown in the middle of the screen and participants have to select the box in which the pattern was previously presented. Outcome measures include the total number of errors adjusted for the level of difficulty (total errors adjusted).

2.5.4 | Rapid visual information processing (RVP)

The RVP test measures response sensitivity under time pressure. The task is to detect target sequences of digits. Participants are confronted with digits from 2 to 9 one-by-one in a pseudo-randomized order and have to press a button in the centre of the screen as quickly as possible when they detect a target sequence. Outcome measures include a sensitivity score (A') calculated using the number of hits, false alarms and omissions.

2.5.5 | Multitasking test (MTT)

The MTT measures the ability to ignore task-irrelevant information, as part of executive function. An arrow is presented on either side of the screen pointing in either direction (right or left). Participants have to pay attention to either the side of the screen where the arrow appears or the direction of the arrow (indicated by SIDE or DIRECTION on the screen), by pressing a button on the left or right corner on the screen, respectively. Outcome measures include the total correct and incorrect responses (TC and TIC), the incongruency cost (congruent trials vs. incongruent trials, ICOST) and median reaction latency (LMD).

2.5.6 | One-touch stockings of Cambridge (OTS)

The OTS test assesses spatial planning and working memory, as part of executive function. The screen is divided into two displays, presented in a way that resembles stockings or socks. In the upper display, three coloured balls are presented, forming a pattern. The task is to copy the pattern by selecting the number of steps necessary to move the balls in the lower half of the screen. Outcome measures include the number of problems that are solved on first choice (PSFC) and the mean of choices needed for correction (MCC).

TABLE 1 Baseline characteristics

Measures	Controls (n = 20)	Maritime pilots (n = 20)
Age, years	36.5 ± 5.71	43.6 ± 4.36
Educational attainment, years	19.45 ± 1.96	18 ± 0
BMI	23.17 ± 2.24	25.23 ± 2.37
History of diabetes	0	0
History of hypertension	0	0
Medication use	4 (20)	1 (5)
Smoking	1 (5)	1 (5)
Habitual caffeine intake, p/d	2.9 ± 2.47	4.6 ± 2.64

Note: Data are shown as mean ± SD or number (%). BMI, body mass index.

2.6 | Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 20.0 (IBM Corp.). Alpha was set at .05. All outcomes were tested for normal distribution by inspection of the Shapiro-Wilk test and visual inspection of histograms. Independent samples t tests were performed to compare outcome measures that were normally distributed between maritime pilots and controls. Normal data are presented as mean ± SD. For data that were not normally distributed, we performed Mann-Whitney U -tests, for which the data are reported as median and interquartile range (IQR). A Bonferroni correction was applied for analyses from the CANTAB to correct for multiple comparisons. Using 15 different outcome variables, a $p < .003$ was considered significant (Table 4). To adjust for age as a possible confounder for CANTAB outcomes, we ran a bivariate correlation analysis using Pearson's correlation coefficient.

3 | RESULTS

Twenty maritime pilots and 20 controls completed the study. Controls were on average 7 years younger than maritime pilots (Table 1; 95% CI, -10.35 to -3.85; $p < .001$). No other differences were found between the groups in baseline characteristics (Table 1). All participants were Dutch and had the same level of educational attainment.

3.1 | Sleep

There were no significant differences between controls' PSQI scores and maritime pilots' rest week PSQI scores. However, when comparing the PSQI scores of a work week (maritime pilots) to the scores of controls, maritime pilots had a significantly higher overall score, indicating more sleep complaints (Table 2). Furthermore, for maritime

pilots the average overall PSQI score for work weeks was almost twice as high as the score for rest weeks, with values exceeding the validated cut-off point for abnormal sleep behaviour (≥ 7) (Table 2). Results from the PSQI thus confirm impaired sleep during work weeks for maritime pilots, while indicating normal sleep during rest weeks (Table 2).

The 10-day sleep-wake diary entries contain a mixture of work-days and rest days for the maritime pilots. A mean was calculated for the three most relevant variables: sleep onset latency (SOL), total sleep time (TST) and number of awakenings. Maritime pilots reported significantly less TST compared to controls ($381 \text{ min} \pm 59$ vs. 443 ± 24 ; $p < .001$), further confirming PSQI results. Of the total 40 participants, two controls and two maritime pilots did not complete the diaries and were therefore excluded from the analyses.

3.2 | Questionnaires

All test scores on the CFQ, RAND-36 and HADS were within normal ranges based on available normative data adjusted for participants' age and education (data not shown). Maritime pilots reported slightly more cognitive complaints on the CFQ compared to controls and reported more depressive symptoms on the HADS, while scoring slightly higher (better) on the mental health subscale (RAND-36) (Table 3). Furthermore, controls reported better physical functioning on the RAND-36 than maritime pilots (Table 3).

3.3 | Cognitive testing

For maritime pilots, cognitive assessment was administered approximately $26 \text{ hr} \pm 10.7$ after the end of their last shift. One maritime pilot had to be excluded, because cognitive testing was administered after his vacation, resulting in more than 10 days between the last shift and testing.

Overall, in the group of maritime pilots we did not find differences on tests of attention and psychomotor speed (RTI and RVP), memory (SWM) and executive function (MTT and OTS) (Table 4). Maritime pilots performed slightly better on the spatial working memory (SWM) task, expressed in less total error (TE) scores and less BE scores compared to controls (Table 4). These differences were not statistically significant after correction for multiple comparisons. Results from the correlation analysis remained insignificant. We found no correlation between participants' age and CANTAB results, suggesting that the age difference between the two groups did not affect outcomes of cognitive assessment.

4 | DISCUSSION

We explored whether exposure to sleep loss, in this case defined as effects of a week with work-related sleep disruption, resulted in cognitive deficits in a group of maritime pilots. We found that the

TABLE 2 PSQI differences between work weeks for maritime pilots and normal weeks for controls and between rest weeks and work weeks for maritime pilots

Measures	Controls (n = 20)	Maritime pilots (n = 20)	p-value
	PSQI		
SQ	1 (0-1)	1 (1-2)	.02*
SOL	1 (0-1)	1 (0-2)	.15
TST	0 (0-0)	1 (1-2)	<.001**
SEF	0 (0-0)	1 (1-1)	<.001**
Sleep disturbances	1 (1-1)	1 (1-1)	.67
Daily dysfunction	1 (0-1)	1.5 (1-2)	.007*
Overall	3 (2-4)	7 (6-9)	<.001**
Measures	Rest week (maritime pilots, n = 20)	Work week (maritime pilots, n = 20)	p-value
	PSQI		
SQ	1 (0-1)	1 (1-2)	.001*
SOL	0 (0-1)	1 (0-2)	.02*
TST	0 (0-0)	1 (1-2)	<.001**
SEF	0 (0-0)	1 (1-1)	<.001**
Sleep disturbances	1 (1-1)	1 (1-1)	.08
Daily dysfunction	0.5 (0-1)	1.5 (1-2)	.001*
Overall	3 (1.25-4)	7 (6-9)	<.001**

Note: Data are shown as median (IQR).

Abbreviations: PSQI, Pittsburgh Sleep Quality Index; SEF, sleep efficiency; SOL, sleep onset latency; SQ, sleep quality; TST, total sleep time.

*significant at $p < .05$;

**significant at $p < .001$.

cohort of maritime pilots reported some subjective cognitive complaints, but did not score worse on objective cognitive assessment compared to the control group.

Results of the PSQI and the sleep-wake diaries confirmed worse sleep quality and less TST in maritime pilots compared to controls and worse sleep quality during work weeks of the maritime pilots compared to their rest weeks.

Regarding the questionnaires, maritime pilots reported more cognitive complaints (CFQ) and mood problems (HADS), without exceeding clinically relevant cut-off points. Although the differences were subtle, these questionnaires were administered after a work week for maritime pilots and might reflect mood and complaints during that week, which could explain the higher amount of tense feelings. The higher (better) scores of maritime pilots on mental health on the QoL questionnaire (RAND-36) first seemed contradictory with findings from the HADS; however, the RAND-36 is not bound to a specific time (work week/rest week), but rather reflects general satisfaction with life. Controls reported better physical functioning than maritime pilots, which could be due to less confrontation

TABLE 3 Results of questionnaires

Measures	Controls (n = 20)	Maritime pilots (n = 20)	p-value
CFQ			
Overall	22.5 (20.25–26.75)	34 (29.25–36.75)	.004*
Confusion	4.65 ± 2.80	6.9 ± 3.24	.03*
Social confusion	5.1 ± 2.49	6.3 ± 2.60	.15
Names and words	5 (5–6)	7.5 (6–8.75)	<.001**
Orientation	1 (0.25–2)	2 (1–3)	.07
Rand-36			
Physical functioning	100 (100–100)	95 (95–100)	.02*
Social functioning	100 (87.5–100)	100 (87.5–100)	.59
Physical restriction	100 (100–100)	100 (100–100)	.62
Emotional restriction	100 (75.03–100)	100 (100–100)	.07
Mental health	80 (62–88)	88 (80–88)	.03*
Vitality	68.25 ± 12.70	69.24 ± 11.48	.80
Pain	100 (89.8–100)	100 (89.8–100)	.62
General health	82.5 ± 13.13	77.45 ± 15.13	.27
Health change	50 (50–50)	50 (50–75)	.32
HADS			
Anxiety	4.35 ± 2.48	3.8 ± 2.86	.52
Depression	2 (1–3.75)	3 (2–5.75)	.04*

Note: Data are shown as median (interquartile range [IQR]) or mean ± standard deviation (SD)

Abbreviations: CFQ, Cognitive Failure Questionnaire; HADS, Hospital Anxiety and Depression Scale; PSQI, Pittsburgh Sleep Quality Index.

*significant at $p < .05$;

**significant at $p < .001$.

with physically challenging situations, which maritime pilots encounter more often on a daily basis than controls.

Based on studies claiming that cognitive function, especially memory consolidation, depends on generating sufficient deep sleep and that poor sleep may impair cognitive function (Killgore et al., 2017; Mander et al., 2015; McCoy & Strecker, 2011), we initially hypothesized that sleep disruption would lead to worse episodic memory, slowing of reaction times, or inaccuracy on cognitive assessment. Although maritime pilots are exposed to poorer sleep quality, we did not observe worse performance compared to controls on any of the cognitive tests (attention, psychomotor speed, memory, executive function). Cognitive assessment was administered on the first day off after a work week for maritime pilots, making sure that the recovery period between the end of the last shift and cognitive assessment would not exceed 48 hr. This decision was based on findings from the literature suggesting that the effect of partial sleep deprivation is restored after two to three nights (Åkerstedt, 2003; Ikegami et al., 2009), and that sleep restriction of 4–5 hr for seven consecutive nights is restored after two nights of 10 hr of sleep (Balkin, Rupp, Picchioni, & Wesensten, 2008). Our participants followed a 7–7 schedule, in which a 7-day work week is followed by a 7-day rest period. According to the literature, the maritime pilots would need two nights of 10 hr of sleep over a 48-hr period to restore baseline cognitive functions (Balkin et al., 2008). By administering the cognitive assessment within approximately

26 hr after the last shift, we reduced the possibility that full recovery of cognitive function would obscure any cognitive deficits related to the work week with sleep deprivation.

What could explain our findings? First, it is suggested that sleep loss affects stage 2 and rapid-eye-movement sleep but not slow-wave sleep (Åkerstedt, 2003), which could explain why maritime pilots did not show signs of memory disruption, which in the long run appears to be more closely associated with slow-wave sleep (Kang et al., 2017). Second, in a meta-analysis of a total sample of 1,932 individuals, sleep loss is suggested to have the largest effect on mood but the smallest effect on motor tasks (Pilcher & Huffcutt, 1996), which might be one of the reasons why maritime pilots did not perform significantly worse on reaction time tasks. Third, the extent to which sleep loss affects cognitive functions depends on several aspects, such as age, gender (Alhola & Polo-Kantola, 2007) and the extent of compensatory mechanisms (Killgore, 2010). It is possible that maritime pilots have developed excellent compensatory mechanisms for their sleep loss, because they have to accurately execute their job while being sleep disrupted most of the times. These compensatory mechanisms could include either sufficient deep sleep during work weeks, due to efficient sleeping skills that have been developed over the course of their employment years, or excessive rebound sleep in rest periods after work weeks as compensatory for the disruption of deep sleep during work weeks. Belenky et al. accentuate this suggestion by claiming that the brain is able to adapt to chronic sleep restriction sufficient enough

TABLE 4 Results of cognitive assessment presented in raw scores

Measures	Controls (n = 20)	Maritime pilots (n = 19)	p-value
RTI			
SMDRT	330.9 ± 26.2	326.7 ± 21.6	.59
FMDRT	372.0 ± 31.5	361.3 ± 30.1	.29
SES	0 (0–0.75)	0 (0–0)	.25
FES	0 (0–0)	0 (0–0)	.37
SWM			
TE	7 (1–9)	1 (0–6)	.03*
BE	6.5 (1–9)	1 (0–6)	.03*
WE	0 (0–0)	0 (0–0)	.96
PAL			
TEA	5.5 (0.25–8.75)	6 (4–11)	.20
RVP			
A'	0.95 (0.93–0.96)	0.93 (0.91–0.96)	.46
MTT			
TC	157.5 (155.25–159)	158 (157–159)	.67
TIC	2 (1–3)	1 (1–3)	.51
ICOST	56.1 ± 35.7	81.4 ± 50.3	.08
LMD	615.1 ± 90.83	615.4 ± 55.8	.99
OTS			
PSFC	13 (11–13.75)	13 (11–14)	.61
MCC	1.3 ± 0.2	1.2 ± 0.18	.72

Note: Data are shown as mean ± standard deviation (SD) or median (interquartile range [IQR]). Significance level: * $p < .05$; ** $p < .003$ (corrected for multiple comparison).

Abbreviations: A', sensitivity (A-prime); BE, between errors; FES, five-choice error score; FMDRT, five-choice median reaction time; ICOST, incongruency cost; LMD, median response latency; MCC, mean choice to correct; MTT, multitasking test; OTS, one-touch stockings of Cambridge; PAL, paired association learning; PSFC, problems solved on first choice; RTI, reaction time; RVP, rapid visual information processing; SES, simple error score; SMDRT, simple median reaction time; SWM, spatial working memory; TC, total correct; TE, total errors; TEA, total errors adjusted; TIC, total incorrect; WE, within errors.

to stabilize performance (Belenky et al., 2003). These compensatory mechanisms may be pre-existing, as self-selection is likely to have occurred in maritime pilots who have been working for years. However, the CRUISE study is a pilot study, thus the absence of a short-term effect of sleep disruption on cognitive functions in our study does not exclude the possibility that sleep disruption could result in cognitive deficits in general. One of the strongest limitations of our study is the small sample size ($n = 40$), which reduces the power to identify cognitive effects related to poor sleep. However, one could argue that if much larger samples are needed to detect statistically significant, but very small differences, the clinical relevance of these findings is debatable. Regardless, future prospective studies should extend this study by recruiting larger samples to clarify the effect of sleep disruption on cognitive function.

Our study is further limited by the self-reported sleep assessment and the fact that we did not control caffeine intake right before administering cognitive tests. Participants were allowed to consume their normal amount of coffee. Routine intake was slightly higher in maritime pilots compared to controls (Table 1). Furthermore, the maritime pilot group and controls were not precisely matched for age: controls were on average 7 years younger and therefore could theoretically have performed better on cognitive tests, even though there is no evidence for an effect on CANTAB results in this age range. However, we did not find any group differences in cognitive performance in our study, indicating that this potential confound might not have affected our results. Another limitation is the unique group of maritime pilots, which might have led to a selection bias. Maritime pilots are professionally trained to perform under difficult and stressful conditions. Controls, although matched for sex and education, might not have been matched entirely with respect to, for example, personality, resilience or cognitive skills/general intelligence. In future studies with the maritime pilots, a longitudinal study design should be considered with specific quantification of chronic and acute sleep disruption with highly matched controls, regarding age, general intelligence, and especially work environment. For example, a control group of airline pilots with normal sleep could be an interesting match. In theory, it is possible that maritime pilots started on a higher cognitive level and their occupation-related sleep disruption brought them down to the level of the control participants. However, long-term effects of sleep on cognitive function are likely to take longer and manifest in older age. Moreover, the control group was highly educated and had an average of almost 20 years of education. Another approach to test the effect of work-related sleep disruption on cognitive functions would have been a within-subjects, repeated-measures approach in which larger samples of maritime pilots are tested after a rest week and a work week to observe an actual decline in cognitive functions after a work week compared to a rest week. The results obtained after a rest week could then be compared to controls' performance to measure the long-term effect of sleep disruption, ideally by recruiting maritime pilots with varying durations of exposure. By applying such a design we would be able to model both individual levels of acute sleep disruption and effects of extended exposure to the shift-work schedules.

Strengths of our study are the use of well-validated and sensitive cognitive tests for the assessment of work-related cognitive distortion regarding the domains known to be disturbed in early stages of cognitive decline. Furthermore, we made sure that maritime pilots had minimal recovery time between the end of their last shift and cognitive assessment.

5 | CONCLUSION

In this group of healthy maritime pilots, we found that exposure to intermittent weeks characterized by sleep disruption led to small subjective cognitive complaints. However, we were unable

to show that it led to objective deficits of cognitive performance. These findings must be interpreted in the context of the limitations of our study, as discussed previously. The effect of sleep disruption on cognitive decline remains complex and future studies should extend this pilot study by recruiting larger samples and focus on investigating the relationship under different research designs.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

AUTHOR CONTRIBUTIONS

JT was involved in designing the project, setting up the study, recruiting participants, acquisition of data, analysing and interpretation of data, and writing this manuscript. SO and MD were major contributors to interpretation of the data and results, and revision of the manuscript. RPCK contributed to designing the study, advice on and interpretation of cognitive data, and contributed to revising the manuscript. JAHRC was a major contributor in designing the project, obtaining funding and setting up the study, and was involved in writing and revising the manuscript. All authors approved the final version of the manuscript.

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