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Brief Original Contribution

Shift Work and Cognition in the Nurses' Health Study

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Rotating night-shift work, which can disrupt circadian rhythm, may adversely affect long-term health. Experimental studies indicate that circadian rhythm disruption might specifically accelerate brain aging; thus, we prospectively examined shift-work history at midlife as associated with cognitive function among older women in the Nurses' Health Study. Women reported their history of rotating night-shift work in 1988 and participated in telephone-based cognitive interviews between 1995 and 2001; interviews included 6 cognitive tests that were subsequently repeated 3 times, at 2-year intervals. We focused on shift work through midlife (here, ages 58–68 years) because cognitive decline is thought to begin during this period. Using multivariable-adjusted linear regression, we evaluated mean differences in both "average cognitive status" at older age (averaging cognitive scores from all 4 interviews) and rates of cognitive decline over time across categories of shift-work duration at midlife (none, 1–9, 10–19, or ≥20 years). There was little association between shift work and average cognition in later life or between shift work and cognitive decline. Overall, this study does not clearly support the hypothesis that shift-work history in midlife has long-term effects on cognition in older adults.

circadian rhythm; cognition; nurses; shift work

Abbreviations: CI, confidence interval; TICS, Telephone Interview of Cognitive Status.

Shift work is common in the United States and Europe (1), but rotating night shifts have recently been linked to adverse health outcomes, including obesity, type 2 diabetes, and cardiovascular disease (2, 3), all of which have been associated with poor cognition in older adults (4, 5). Because important biological functions operate on a 24-hour cycle (i.e., circadian rhythms), inappropriate light exposure during night shifts, which can disrupt circadian rhythm, might adversely affect shift workers' health (6, 7). Experimental data indicate that circadian rhythm disruption may directly affect cognitive health; for example, sleep deprivation in mice, which causes circadian disruption (8), can decrease neurogenesis in the hippocampus (the center of learning and memory in the brain) (9) and increase β-amyloid deposition in the brain (the pathological hallmark of Alzheimer's disease) (10). In addition, administration of melatonin—a hormone necessary for circadian signaling—can reduce β-amyloid accumulation in the brains of mice (11). Moreover, a recent epidemiologic study found that more fragmented circadian rhythms (as measured by actigraphy) were associated with greater risks of cognitive impairment and dementia in older women (12). Thus, several lines of evidence suggest that rotating shift work might directly or indirectly contribute to decrements in cognitive function.

To our knowledge, only 1 cross-sectional study has explored how shift work might affect cognition in young to middle-aged adults; results were inconsistent between men and women, although the lack of association in women might have been due to limited shift-work exposure in this group (13). Still, because pathology associated with cognitive impairment begins years prior to clinical symptoms, midlife exposures may be particularly influential for cognitive function in later life; indeed, previous studies have identified strong associations between midlife exposures and cognition in older adults (14). To explore this association prospectively, we evaluated midlife shift-work history in relation to average cognitive function and cognitive decline in later life among 16,190 participants in the Nurses' Health Study.

MATERIALS AND METHODS

The Nurses' Health Study began in 1976, when 121,701 female nurses in the United States, aged 30–55 years, responded to a mailed questionnaire about their health and lifestyle (15). Since then, women have returned biennial questionnaires updating this information; follow-up rates have been ≥90% for each questionnaire cycle. The 1988 questionnaire asked women to report their history of rotating night-shift work, and a telephone-based cognitive study was conducted between 1995 and 2000. Women who were ≥70 years of age and had no history of stroke were eligible to participate in the cognitive study, and 19,415 (92% of eligible participants) completed an initial cognitive interview. This interview was repeated 3 times at 2-year intervals (the median time from first interview to fourth interview was 6.4 years), and participation remained ≥90% among women who were still alive at each assessment. In this study, "midlife" refers to the age at which the women returned the 1988 mailed questionnaire (ages 58–68 years). The institutional review board of Brigham and Women's Hospital (Boston, Massachusetts) approved this study.

Assessment of rotating night-shift work

In 1988, women were asked, "What is the total number of years during which you worked rotating night shifts (at least 3 nights/month in addition to days or evenings in that month)?" There were 8 prespecified response categories: never, 1–2 years, 3–5 years, 6–9 years, 10–14 years, 15–19 years, 20–29 years, and ≥30 years.

Assessment of cognitive function

Initially, we administered the Telephone Interview of Cognitive Status (TICS), a telephone version of the Mini-Mental State Examination; the 2 tests are highly correlated ($P = 0.97$) (16). Once we established high participation rates, we gradually added 5 cognitive tests to our battery: 1) immediate and 2) delayed recall of the East Boston Memory Test, 3) category fluency, 4) delayed recall of the TICS 10-word list, and 5) digit span backward. We previously reported that our cognitive battery is highly valid compared with a detailed, in-person cognitive assessment in older women and is highly reliable across multiple cognitive interviewers in our cohort (17).

We focused on 3 primary outcomes based on a priori considerations: 2 measures of general cognition (the TICS score and a global composite score averaging all 6 cognitive tests) and a verbal memory composite score (averaging immediate and delayed recalls of the East Boston Memory Test and the TICS 10-word list). Verbal memory is an important cognitive domain that is particularly affected in early Alzheimer's disease (18–20). Because our cognitive tests have different scales, we created *z* scores for the composite scores by calculating the difference between individual test scores and the mean score for our population, divided by the population standard deviation.

Population for analysis

Of the 19,415 participants who completed the initial cognitive assessment, we excluded 3,225 women who provided no information in 1988 on rotating night-shift work; thus, our analytical sample included 16,190 women with information on both shift-work history and cognitive function. At the time of the initial cognitive interview, women who provided shift-work information on the 1988 questionnaire were similar in age compared with women who did not provide this information (mean age = 74.3 years for both groups), but had higher average cognition (mean global composite scores = −0.05 vs. −0.12 standard units).

Statistical analysis

We used 2 analytical approaches when evaluating the association between rotating night-shift work and cognition in later life. The first approach was to estimate "average cognitive status" at older age by averaging scores from all 4 of our repeated cognitive interviews, and then utilizing multivariable-adjusted linear regression models to estimate mean differences in average cognitive status across categories of duration of rotating night-shift work at midlife (never, 1–9 years, 10–19 years, and ≥20 years); "never" was the reference category in all analyses. The second approach was to analyze cognitive trajectories over time, as was done previously in this cohort (21).

We considered multiple potential confounding factors, including: age (continuous, in years), education (registered nurse degree, bachelor's degree, graduate degree), alcohol intake (none, 1–14, ≥15 g/day), smoking status (never, former, current), physical activity (quartiles, in metabolic-equivalent task-hours/week), living alone (yes, no), presence of depressive symptoms (yes, no), history of high blood pressure (yes, no), sleep duration (≤5, 6, 7, 8, ≥9 hours/day), and use of tranquilizer medications (yes, no). Initial models were adjusted for age and education, and additional models included other covariates; covariate information was determined based on each participant's status at the time of the initial cognitive interview.

RESULTS

Table 1 shows participants' characteristics at the time of the initial cognitive interview, which were generally similar across categories of rotating shift-work history. However, women with ≥20 years of shift-work history were more likely to have lower educational attainment compared with women with no shift-work history. Women with longer durations of shift work also had higher body mass index, on average.

In age- and education-adjusted models, there were few associations between shift-work history at midlife and average cognitive status at older age (Table 2). For example, when comparing women with ≥20 years of shift-work history with women with no shift-work history, mean differences in average cognition were similar for both global and verbal composite scores (mean difference: −0.03 standard units, 95% confidence interval (CI): −0.07, 0.01, and mean difference 0.02 standard units, 95% CI: −0.03, 0.06, respectively). However, women with ≥20 years of shift-work had significantly lower TICS scores than women with no shift-work history (mean difference: −0.20 points, 95% CI: −0.36, −0.03). Further adjustment for possible confounding factors yielded similar results, with worse cognitive scores being evident for the TICS score

Table 1. Characteristics of Participants ($n = 16,190$) at the Initial Cognitive Interview, Across Categories of Rotating Shift-Work History, Nurses' Health Study, 1995–2001

	Shift Work History											
	None ($n = 6,136$)			1–9 Years ($n = 7,685$)			10–19 Years ($n = 1,341$)			≥20 Years ($n = 1,028$)		
	%	Mean (SD)	Median (IQR)	%	Mean (SD)	Median (IQR)	%	Mean (SD)	Median (IQR)	%	Mean (SD)	Median (IQR)
Total participants	38			48			8			6		
Age, years		74.3 (2.3)			74.2 (2.3)			74.4 (2.3)			74.5 (2.3)	
Registered nurse degree only[a]	77			76			82			86		
Body mass index[b]		25.7 (4.8)			25.9 (4.8)			26.8 (5.2)			27.0 (5.2)	
Alcohol intake, g/day			0.9 (0–5.8)			0.9 (0–6.0)			0 (0–4.4)			0 (0–2.4)
Never smoker	48			46			45			48		
Physical activity, metabolic-equivalent task-hours/week			9.1 (2.7–20.4)			10.2 (3.4–22.4)			9.0 (2.9–21.1)			9.0 (2.9–22.7)
Lives alone	31			32			38			35		
Presence of depressive symptoms	4			4			6			5		
History of high blood pressure	54			55			59			61		
Sleep duration ≤6 hours/day	27			28			29			34		
Use of tranquilizer medications	6			5			6			4		

Abbreviations: IQR, interquartile range; SD, standard deviation.
[a] Highest educational attainment.
[b] Weight (kg)/height (m)^2.

Table 2. Mean Differences in Average Cognitive Function in Later Life (Averaging Scores from 4 Cognitive Assessments) Across Categories of Rotating Shift-Work History, Nurses' Health Study, 1995–2008

	Shift Work History						
	None (Mean Difference = 0)[a]	1–9 Years		10–19 Years		≥20 Years	
		Mean Difference	95% CI	Mean Difference	95% CI	Mean Difference	95% CI
Global score							
Model 1[b]	0	0.01	−0.01, 0.03	−0.01	−0.05, 0.02	−0.03	−0.07, 0.01
Model 2[c]	0	0.00	−0.01, 0.02	−0.01	−0.05, 0.02	−0.03	−0.07, 0.01
Verbal score							
Model 1	0	0.02	−0.01, 0.04	0.01	−0.03, 0.05	0.02	−0.03, 0.06
Model 2	0	0.01	−0.01, 0.03	0.01	−0.03, 0.05	0.01	−0.03, 0.06
TICS score							
Model 1	0	0.08	−0.01, 0.16	−0.04	−0.19, 0.11	−0.20	−0.36, −0.03
Model 2	0	0.07	−0.01, 0.15	−0.02	−0.16, 0.13	−0.18	−0.35, −0.02

Abbreviations: CI, confidence interval; TICS, Telephone Interview of Cognitive Status.

[a] Reference category.

[b] Adjusted for age (continuous, in years) and education (registered nurse degree, bachelor's degree, or graduate degree).

[c] Additionally adjusted for alcohol intake (none, 1–14, ≥15 g/day), smoking status (never, past, or current smoker), physical activity (quartiles, in metabolic-equivalent task-hours/week), living alone (yes, no), presence of depressive symptoms (yes, no), history of high blood pressure (yes, no), sleep duration (≤5, 6, 7, 8, or ≥9 hours/day), and use of tranquilizer medications (yes, no).

only (for ≥20 years of rotating shift work vs. none, mean difference = −0.18 points, 95% CI: −0.35, −0.02).

When we analyzed cognitive trajectories over time, we found no associations with shift-work history at midlife in fully adjusted models; for example, the mean difference in rates of global score decline over follow-up was 0.01 standard units (95% CI: −0.05, 0.06) when comparing extreme shift-work categories.

DISCUSSION

We found that a history of rotating night-shift work at midlife was not consistently associated with cognitive status in this cohort of nurse participants. Although shift work was modestly related to diminished cognition when we considered the TICS assessment (a test of general cognition), there were no associations between shift-work history and composite measures of general cognition and verbal memory. Additionally, there were no associations between shift-work history and cognitive decline among these women. Based on these results, there appears to be little indication that a strong association between shift-work history at midlife and cognition exists among older women.

To our knowledge, this is the first epidemiologic study of midlife shift-work history and later-life cognitive function to have been conducted prospectively. Previously, a cross-sectional study of 3,237 French workers aged 32–62 years found that current shift work was associated with lower cognitive performance in men, although the association was not evident for men who reported past shift work only; this is consistent with our findings (13). There was some, albeit inconsistent, evidence for a dose-response relationship between increasing duration of shift work and cognitive function in men. In contrast, there were no associations between shift work and cognition among women, although women performing shift work appeared to have more regular schedules than men (e.g., 15% of women vs. 45% of men reported not being able to sleep before midnight, and 20% of women vs. 37% of men reported missing night sleep); therefore, limited exposure may explain the lack of association among these women.

Although the Nurses' Health Study does not include detailed information on work schedules, we calculated shift-work history based on women's reports of "rotating night-shift work" at least 3 nights per month in addition to day and evening work; thus, our exposure classification is likely to have captured women with the least regular schedules and therefore the most circadian disruption. Unlike the French study, the Nurses' Health Study does not include data on current shift work; hence, results of these 2 studies together may indicate that shift work has acute but not long-term effects on cognitive health. Clearly, more research is needed in this area.

This study had several limitations. First, we asked women about their history of rotating night-shift work but did not separately query women about their history of permanent night work; as a result, women who had engaged in permanent night work may have mistakenly reported their shift-work experience as rotating night-shift work. If this occurred, such misreporting would have contributed to exposure misclassification and possible underestimation of the association of interest, since permanent night-shift workers are thought to experience less circadian disruption than rotating night-shift workers. However, other studies in this cohort have utilized this exposure metric to identify important associations with health outcomes, suggesting that our shift-work classification contains important information for identifying associations with health status among these women. Second, exposure information was limited to shift-work history reported through midlife, but not beyond. The lack of data on shift work in later life may have led to misclassification of our exposure and could have biased our findings toward the null. Third, our cognitive assessment certainly contains some amount of random misclassification, which may have limited our ability to observe associations between shift work and cognition. A previous validation study found that our telephone-based cognitive battery performed well compared with a detailed, in-person neuropsychological assessment, and numerous associations between health and lifestyle factors and cognitive function have been identified in this cohort; thus, our cognitive function assessment appears to provide substantially valid information on women's later-life cognitive status for detection of associations with a variety of exposures. Finally, cognitive scores were considerably higher, on average, for women who provided shift-work information than for those who did not; thus, it is possible that curtailment of our outcome distribution in this way contributed to our null results.

In summary, we observed no consistent association between shift-work history at midlife and cognition in later life in this cohort of older women. Further research is necessary to examine whether rotating night-shift work may have shorter- versus longer-term effects on cognitive health and whether these effects may vary according to different durations and intensities of shift work.

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