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Original Article

Work Hours and Cognitive Function: The Multi-Ethnic Study of Atherosclerosis

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ABSTRACT

Background: Cognitive impairment is a public health burden. Our objective was to investigate associations between work hours and cognitive function.
Methods: Multi-Ethnic Study of Atherosclerosis (MESA) participants ($n = 2{,}497$; 50.7% men; age range 44–84 years) reported hours per week worked in all jobs in Exams 1 (2000–2002), 2 (2002–2004), 3 (2004–2005), and 5 (2010–2011). Cognitive function was assessed (Exam 5) using the Cognitive Abilities Screening Instrument (version 2), a measure of global cognitive functioning; the Digit Symbol Coding, a measure of processing speed; and the Digit Span test, a measure of attention and working memory. We used a prospective approach and linear regression to assess associations for every 10 hours of work.
Results: Among all participants, associations of hours worked with cognitive function of any type were not statistically significant. In occupation-stratified analyses (interaction $p = 0.051$), longer work hours were associated with poorer global cognitive function among Sales/Office and blue-collar workers, after adjustment for age, sex, physical activity, body mass index, race/ethnicity, educational level, annual income, history of heart attack, diabetes, apolipoprotein E-epsilon 4 allele (ApoE4) status, birth-place, number of years in the United States, language spoken at MESA Exam 1, and work hours at Exam 5 ($\beta = -0.55$, 95% CI $= -0.99, -0.09$) and ($\beta = -0.80, -1.51, -0.09$), respectively. In occupation-stratified analyses (interaction $p = 0.040$), we also observed an inverse association with processing speed among blue-collar workers (adjusted $\beta = -0.80, -1.52, -0.07$). Sex, race/ethnicity, and ApoE4 did not significantly modify associations between work hours and cognitive function.
Conclusion: Weak inverse associations were observed between work hours and cognitive function among Sales/Office and blue-collar workers.

1. Introduction

Cognitive impairment is a public health burden. Findings from the 1999–2001 National Health Interview Survey revealed that there were approximately 800,000 community-based persons aged 65 years and older in the United States who had confusion or memory loss and 2.3 million adults with reported limitation of activity caused by late life cognitive impairment or dementia [1]. In 2010, the estimated prevalence of Alzheimer's disease in the US population aged ≥65 years was 4.7 million [2]. Of great concern is

Abbreviations: ApoE4, apolipoprotein E-epsilon 4 allele; BMI, body mass index; CASI, Cognitive Abilities Screening Instrument; CVD, cardiovascular disease; DS, Digit Span; DSC, Digit Symbol Coding; GED, General Education Development; MESA, Multi-Ethnic Study of Atherosclerosis; MET-min, metabolic equivalent minutes.

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the aging of the population and that the number of persons with Alzheimer's disease is projected to rise to 13.8 million by the year 2050 [2,3]. It is therefore important to study factors, including those that are work-related, that may be associated with or contribute to cognitive impairment.

Psychological stress has been shown to be a risk factor for decreased cognitive function [4]. Under some circumstances, working overtime may be considered an occupational stressor. Americans in certain sectors work long hours [5–7] and the consequence of such a practice has substantial public health ramifications. Long working hours have been shown to be associated with physical and mental health problems such as coronary heart disease, sleep problems, depression, and anxiety [8–10]. Working long hours regularly leads to fatigue and a greater need for recovery [11,12]. Those who have a greater need for recovery from fatigue are known to be at increased risk of cardiovascular disease (CVD) [13], which is associated with a greater risk for cognitive impairment [14].

In at least one study, long working hours have been found to be directly associated with poor cognitive performance. Using a prospective study design, Virtanen et al [15] showed that working more than 55 hours per week was associated with lower scores on two of the five tests of cognitive function among British civil servants. Furthermore, long working hours predicted decline in performance on the reasoning test over a 50-year follow-up period. These associations persisted after adjustments for several factors, such as education, occupational position, physical diseases (CVD dysfunction), psychosocial stress factors, sleep problems, and health-risk behaviors. The population in this study by Virtanen et al was composed of a mostly homogeneous occupational (and racial/ethnic) group and the authors did not assess for effect modification by occupational category or racial/ethnic group. We intend to investigate similar associations in a different population. Our cohort is composed of several occupational groups, which may be different from those in the British sample. Our sample is also composed of persons from four racial/ethnic populations and the cognitive instruments used were different from those used in the UK study.

Certain groups of workers such as salaried and highly-paid workers, nurses, residents, and long-haul truck drivers are known to experience longer work hours than workers in other groups [5–7]. It is possible that the association between long work hours and cognitive function may differ due to attributes within each occupational category that are expected to affect this association. For example, professional workers may experience greater decision latitude and job control compared to blue-collar workers, which may attenuate any association between long work hours and cognitive impairment. Workers in certain professions may also have a higher cognitive reserve compared to other workers, which may be protective of a cognitive decline [16–18]. In addition, differences in the association between long work hours and cognitive function may be observed among women and men due to sex-related physiological differences, different racial or ethnic groups, or persons of a different apolipoprotein E (ApoE) genetic status. The allele of $\varepsilon 4$ of ApoE is known to be a prevalent and strong genetic risk factor for Alzheimer's disease [19–21]. Our main objective was to determine if longer working hours are associated with any of three cognitive function measures 5 to 10 years later. Secondary objectives were to assess potential effect modification in associations, if any, by occupational category, sex, race/ethnicity, and ApoE epsilon 4 status (ApoE4).

2. Materials and methods

2.1. Study design and participants

Participants in our study were examined in the Multi-Ethnic Study of Atherosclerosis (MESA) that was initiated in July 2000. Details of the study design and protocol have been previously published [22]. Briefly, the original cohort of 6,814 men and women aged 45–84 years consisted of participants from four racial and ethnic backgrounds (Whites, African-Americans, Hispanics, and Chinese Americans) and from six US communities. All participants signed written informed consent forms. The institutional review boards of the six field centers, the data coordinating center, and the National Heart, Lung, and Blood Institute approved the study protocol.

This study examines data from the MESA Exam 1 (July 2000–August 2002), Exam 2 (September 2002–February 2004), Exam 3 (March 2004–September 2005), and Exam 5 (April 2010–December 2011). The total number of participants in each examination were as follows: Exam 1 (n = 6,814), Exam 2 (n = 6,233), Exam 3 (n = 5,947), and Exam 5 (n = 4,716). The decrease in sample sizes across examinations was due to numerous factors, including unwillingness to continue participation, death, moving outside of the area of recruitment, etc. Between Exams 1 and 5, a 10-year gap, there was a loss to follow-up of 39% (6,814–4,176/6,814), which is within an acceptable range.

To be included in these analyses, participants must have reported at Exam 1 that they worked to earn money (n = 3,700 of 6,814). We also excluded persons who had not been tested for cognitive function at Exam 5, that is, those with missing data on the Cognitive Abilities Screening Instrument (CASI; n = 850), the Digit Span test (DS; n = 859), and the Digit Symbol Coding (DSC; n = 1,106) for a total exclusion of 1,115 persons. From this sample size of 2,585, we excluded participants with missing data on work hours at Exams 2 (n = 44), 3 (n = 50), and 5 (n = 12) leaving a final sample size of 2,497 participants (49.3% women and 50.7% men) (Fig. 1). The analyses for the current study were conducted during 2016–2018.

2.2. Assessment of hours of work

"Hours of work" was used from the data collected in MESA Exam 1 (July 2000–August 2002). Participants answered questions on occupational activities. They were asked to estimate the amount of time spent in all jobs ("How many days per week and hours per day do you work in all jobs?"). The total number of hours of work per week was calculated by multiplying the two responses. Hours of work were also collected in MESA Exam 5.

2.3. Occupational data

Occupational information was collected by questionnaire at Exam 1 [23]. Four open-ended questions modeled on the US Census occupational questions were used to determine the respondent's current (or last, if no longer working) occupation: "For whom do/did you work?" "What type of business or industry is/was this?" "What kind of work do/did you do?" "What was your job title?" The responses were coded by trained staff at NIOSH using the Census 2000 Occupational Codes and categorized from 413 occupations [23].

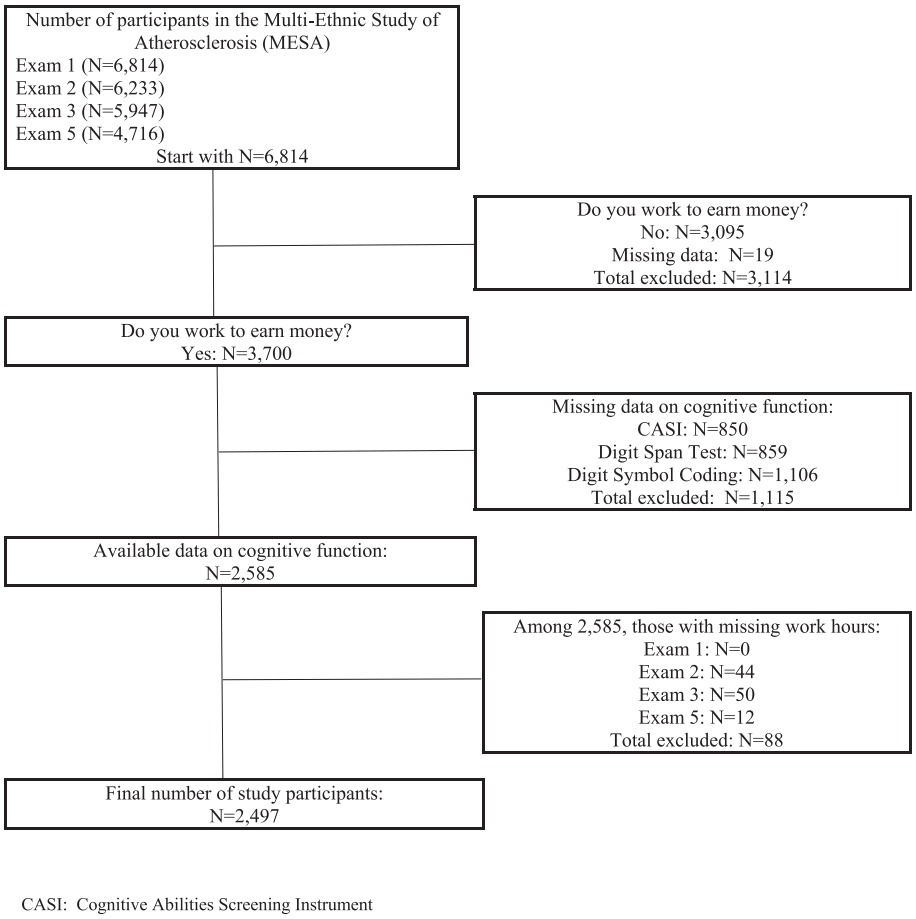

Fig. 1. Flowchart of participants included in the present study. CASI, Cognitive Abilities Screening Instrument; MESA, Multi-Ethnic Study of Atherosclerosis.

2.4. Assessment of cognitive function

General instructions for the cognitive examination were translated into Spanish and Mandarin Chinese and then independently back-translated by native speakers and pretested [24]. A centralized training was held before the fifth MESA examination to standardize administration and additional training was provided as needed. Examiners were certified to administer the tests and conference calls were held throughout the data collection period to maintain high fidelity.

Cognitive function was evaluated during the fifth MESA follow-up examination (2010–2011) and was assessed using the CASI (version 2), a measure of global cognitive functioning [25]; the DSC task, a measure of processing speed [26]; and the DS, a measure of attention and working memory [26].

The CASI includes items assessing attention/concentration, orientation, recent and remote memory, visual confrontational naming, verbal fluency, abstraction, judgment, and constructional praxis with possible scores ranging from 0 to 100 [25]. Lower scores indicate worse cognitive function.

The DSC measures how quickly simple perceptual or mental operations can be performed [26]. A key at the top of the test page displays a series of nine simple symbols (e.g., +, >) uniquely paired with numbers from 1 to 9. For 120 seconds, the participant is asked to copy the corresponding symbol into empty boxes directly below randomly-ordered numbered boxes. The DSC score is the number of correctly transposed symbols and ranges from 0 to 133.

The DS test requires respondents to repeat increasing spans of random numbers presented orally, first in the order they are presented and then backwards [26]. A point is awarded for each span correctly recalled (range 0–28).

2.5. Assessment of covariates

Questionnaires that were self-administered at Exam 1 provided information on demographic variables, which included age, sex, self-identified race/ethnicity (Caucasian, Chinese-American, African-American, Hispanic), educational attainment (≤high school graduate/General Equivalency Diploma), some college/technical school, bachelor's degree, graduate/professional), and lifestyle behaviors (pack-years of smoking for current and former smokers, current smoking status). Cigarette smoking was defined as current, former, or never. Also included in these questionnaires were annual household income, medical history, primary spoken language, number of years living in the United States, and place of birth. Place of birth was coded as United States (i.e., within the 50 US states) and whether West, Midwest, South, or Northeast, or foreign-born.

Height and weight were measured with participants wearing light clothing and no shoes. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. The MESA Typical Week Physical Activity Survey, adapted from the Cross-Cultural Activity Participation Study [27], was used to obtain the time and frequency spent in various physical activities during a typical week in the previous month at Exam 1. Minutes of activity

were summed for each discrete activity type and multiplied by metabolic equivalent level to derive composite physical activity levels.

Blood was drawn from participants at Exam 1 after they had fasted for a minimum of 12 hours, and aliquots were prepared for analysis and for storage at −70°F at the University of Vermont and the University of Minnesota. Laboratory analysis was performed for lipids. Low-density lipoprotein cholesterol was calculated by the Friedewald equation [28].

Resting blood pressure was measured three times in the seated position using a Dinamap model Pro 100 automated oscillometric sphygmomanometer (Critikon, Wipro GE Healthcare, Waukesha, WI, USA). The average of the last two measurements was used in the analysis. Hypertension was defined as systolic pressure ≥140 mmHg, diastolic pressure ≥90 mmHg, or current use of antihypertensive medication. Genotyping was conducted in MESA participants in 2013 and from those analyses, ApoE isoforms were estimated from single nucleotide polymorphisms rs429358 and rs7412.

2.6. Statistical analysis

Initial analyses included descriptive results to characterize the demographic and lifestyle characteristics of the study sample overall and by gender [mean and standard deviation (SD) for continuous variables and *n* (%) for categorical variables are presented]. For the current analyses, work hours per week (at Exams 1, 2, and 3) served as the main exposure or predictor variables of interest, whereas cognitive function measures assessed at Exam 5 served as the main outcome variables of interest. Occupation was treated as potential effect modifier of the main association of interest between work hours and cognitive function. Other covariates (demographic and lifestyle characteristics, health outcomes) served as potential confounders. The associations of these covariates with the exposure variables (work hours) and the outcome variables (cognitive function) were examined using linear regression and analysis of variance and covariance; the results from these analyses were used a guide to select covariates that were significantly associated with both the exposure and outcome variables. Variables were selected as confounders if they were significantly associated with both the exposure (average hours worked/week) and outcome (cognitive measures); based on this criteria, the variables selected as confounders were age, sex, race/ethnicity, physical activity, BMI, and annual income. We also included in the model, variables that are known risk factors for or may influence cognitive function and they include educational level, family history of heart attack, diabetes, ApoE4 allele status, place of birth, number of years lived in the United States, language spoken at Exam 1.

The main associations of interest between work hours (for every 10-hour increase) and cognitive function were examined using multiple linear regression analyses; separate analyses were conducted using work hours at each of the three examinations. First, age-adjusted associations between work hours at the three examinations (separately) with cognitive function were examined. Next, the associations were further adjusted by including demographic and lifestyle characteristics (sex, physical activity, BMI, race/ethnicity, education, annual income, place of birth, number of years in the United States, language at MESA Exam 1) and health outcomes (history of heart attack, diabetes, ApoE4 allele status). Next, effect modification was assessed for sex, race/ethnicity, occupational category, and ApoE4 allele status in the fully-adjusted association between work hours and the cognitive function measures by including an interaction term consisting these variables and work hours. If the effect modification was significant (i.e., significant interaction term), subsequent analyses were stratified by the relevant variable. In all analyses, model assumptions were tested. Although the CASI variable was slightly skewed, we decided not to log-transform it because such transformation increased the skewness. The other dependent variables were normally distributed. Statistical significance was determined at $p = 0.05$ for all analyses. Analyses were conducted using SAS version 9.3 (SAS, Cary, NC, USA).

3. Results

Ages of participants ranged from 44 to 84 years (mean ± SD = 56.3 ± 8.0), 50.7% were male, 42.4% were white, and 49.5% were in the Management/Professional occupational category (Table 1). The mean scores of global cognitive function (as measured by the CASI) were similar between women and men. Mean scores for attention/working memory (DS test) were only slightly higher for men compared to women (15.8 ± 5.2 vs. 15.4 ± 4.9; $p = 0.041$). However, women had a significantly higher mean score for processing speed (DSC) compared with men (56.6 ± 17.9 vs. 53.4 ± 16.9; $p < 0.0001$). Sex was significantly associated with hours of work per week, with men reporting a slightly higher mean number of hours worked than women (40.8 ± 18.0 vs. 37.3 ± 18.3 hours; $p < 0.0001$).

We investigated associations of selected variables with the number of hours worked per week (See Supplemental Table S-I). Younger mean age and higher mean levels of physical activity were significantly associated with longer work hours ($p < 0.001$). Occupational category was one of several variables that was significantly associated with hours worked per week ($p < 0.001$). Among those who worked 41–49 hours and ≥50 hours, a higher percentage held jobs in the Management/Professional category than in the other three occupational categories.

Age- and education-adjusted associations of selected variables with the three cognitive function measures are presented in Table S-II. Systolic and diastolic blood pressure and depressive symptoms at Exam 1 were inversely and significantly correlated with global cognitive function at Exam 5. Physical activity, BMI, waist circumference, systolic and diastolic blood pressure, and depressive symptoms at Exam 1 were inversely and significantly correlated with attention/working memory and processing speed at Exam 5. High-density lipoprotein cholesterol was positively and significantly correlated with attention/working memory and processing speed at Exam 5. Occupational categories were significantly associated with all three cognitive function measures where participants in the Service and blue-collar groups had somewhat lower mean cognitive scores compared to those in the other two categories. Race/ethnicity was also significantly associated with all three cognitive function measures where Chinese Americans had higher mean scores in attention/working memory and processing speed and whites had a higher mean score in global cognitive function compared to the other racial/ethnic groups (all associations, $p < 0.0001$). Diabetic status was significantly associated with all three measures with persons who had impaired fasting glucose or untreated diabetes having lower mean scores across all measures. There was no difference in the mean scores of global cognitive function and attention/working memory between persons with and without the ApoE4 allele, but those with the ApoE4 allele had a slight but significantly lower mean score for processing speed (54.13 ± 0.52 vs. 55.57 ± 0.39; $p = 0.028$).

Table 1
Descriptive statistics of all variables in the study sample.

	All (n = 2497)	Women (n = 1231)	Men (n = 1266)
	Mean ± SD	Mean ± SD	Mean ± SD
Age (*range* 44–84 y)	56.3 ± 8.0	55.8 ± 7.7	56.8 ± 8.1
Physical activity (MET-min/wk)	7034.8 ± 6587.6	6327.6 ± 5332.5	7722.5 ± 7551.1
Body mass index (kg/m^2)	28.4 ± 5.4	28.8 ± 6.3	28.0 ± 4.3
Waist circumference (cm)	97.2 ± 14.2	95.5 ± 16.0	98.9 ± 11.9
Global cognitive function (CASI)	88.8 ± 9.7	88.5 ± 10.1	89.2 ± 9.3
Attention/working memory (total DS)	15.7 ± 5.1	15.4 ± 4.9	15.8 ± 5.2
Processing speed (DSC)	54.9 ± 17.5	56.6 ± 17.9	53.4 ± 16.9
Hours of work per week	39.1 ± 18.2	37.3 ± 18.3	40.8 ± 18.0
	n (%)	*n* (%)	*n* (%)
Race/Ethnicity			
White	1059 (42.4)	502 (40.8)	557 (44.0)
Chinese-American	291 (11.7)	122 (9.9)	169 (13.4)
African-American	630 (25.2)	354 (28.8)	276 (21.8)
Hispanic	517 (20.7)	253 (20.6)	264 (20.9)
Educational status			
≤High school grad/GED	614 (24.6)	338 (27.5)	276 (21.8)
Some college/Tech school	744 (29.8)	413 (33.6)	331 (26.2)
Bachelor's degree	514 (20.6)	228 (18.5)	286 (22.6)
Graduate/professional	624 (25.0)	252 (20.5)	372 (29.4)
Annual household income ($)			
<20k	261 (10.7)	153 (12.6)	108 (8.7)
20–50k	880 (35.9)	510 (42.2)	370 (29.8)
50–75k	526 (21.5)	258 (21.3)	268 (21.6)
>75k	784 (32.0)	289 (23.9)	495 (39.9)
Occupational categories			
Management/ Professional	1218 (49.5)	565 (46.5)	653 (52.5)
Sales/Office	508 (20.7)	337 (27.8)	171 (13.7)
Service	369 (15.0)	231 (19.0)	138 (11.1)
Blue-collar	364 (14.8)	81 (6.7)	283 (22.7)
Smoking status			
Never	1285 (51.5)	722 (58.7)	563 (44.5)
Former	889 (35.6)	361 (29.3)	528 (41.7)
Current	322 (12.9)	148 (12.0)	174 (13.8)
Marital status			
Married/living as married	1620 (65.5)	653 (53.9)	967 (76.6)
Widowed/divorced/ separated	617 (25.0)	423 (34.9)	194 (15.4)
Never married	236 (9.5)	135 (11.2)	101 (8.0)
Alcohol use			
Never	411 (16.5)	289 (23.6)	122 (9.7)
Former	510 (20.5)	218 (17.8)	292 (23.2)
Current	1567 (63.0)	720 (58.7)	847 (67.2)
Body mass index (kg/m^2)			
Normal (18.5–24.9)	703 (28.2)	387 (31.4)	316 (25.0)
Overweight (Grade 1, 25–29.9)	985 (39.5)	399 (32.4)	586 (46.3)
Overweight (Grade 2, 30–39.9)	718 (28.8)	372 (30.2)	346 (27.3)
Overweight (Grade 3, ≥40)	91 (3.6)	73 (5.9)	18 (1.4)
Heart attack (family history)			
No	1386 (58.5)	649 (55.2)	737 (61.6)
Yes	985 (41.5)	526 (44.8)	459 (38.4)
Diabetes mellitus* (Exam 1)			
Normal	1994 (80.2)	1031 (84.2)	963 (76.4)
Impaired fasting glucose	284 (11.4)	105 (8.6)	179 (14.2)
Untreated diabetes	52 (2.1)	17 (1.4)	35 (2.8)
Treated diabetes	156 (6.3)	72 (5.9)	84 (6.7)
Hypertension†			
No	1688 (67.6)	834 (67.8)	854 (67.5)
Yes	809 (32.4)	397 (32.3)	412 (32.5)
Lipid-lowering medication			
No	2,192 (87.9)	1,110 (90.3)	1,082 (85.5)
Yes	303 (12.1)	119 (9.7)	184 (14.5)
Hours of work per week			
<40	1,016 (40.7)	584 (47.4)	432 (34.1)
40	631 (25.3)	304 (24.7)	327 (25.8)
41–49	359 (14.4)	150 (12.2)	209 (16.5)
≥50	491 (19.7)	193 (15.7)	298 (23.5)
ApoE4 allele status			
No	1,501 (64.3)	708 (62.4)	793 (66.2)
Yes	832 (35.7)	427 (37.6)	405 (33.8)
Place of birth			
US—West	122 (4.9)	65 (5.3)	57 (4.5)
US—Midwest	646 (25.9)	305 (24.8)	341 (27.0)
US—South	688 (27.6)	350 (28.5)	338 (26.7)
US—Northeast	284 (11.4)	139 (11.3)	145 (11.5)
Foreign-born	754 (30.2)	371 (30.2)	383 (30.3)
No. of years in the United States			
US born	1,815 (72.7)	887 (72.0)	928 (73.3)
<15 y	142 (5.7)	66 (5.4)	76 (6.0)
15–20 y	110 (4.4)	57 (4.6)	53 (4.2)
>20 y	430 (17.2)	221 (18.0)	209 (16.5)
Language at MESA Exam 1			
English	2,079 (83.3)	1,041 (84.6)	1,038 (82.0)
Spanish	215 (8.6)	103 (8.4)	112 (8.9)
Chinese	203 (8.1)	87 (7.1)	116 (9.2)

ApoE4, apolipoprotein E-epsilon 4 allele; CASI, Cognitive Abilities Screening Instrument; DS, Digit Span; DSC, Digit Symbol Coding; GED, General Education Development; MESA, Multi-Ethnic Study of Atherosclerosis; MET-min: metabolic equivalent minutes; SD, standard deviation.

* Diabetes mellitus by 2003 fasting criteria.

† Hypertension by JNC VI (1997) criteria.

3.1. Work hours and global cognitive function

Associations between work hours (every 10 hours of work per week) at the three examinations and global cognitive function are presented in Table 2. Among participants overall, associations between hours of work per week reported at all three examinations and global cognitive function were not statistically significant. However, occupational category significantly modified the associations at the 0.10 level (p = 0.051). In the occupation-stratified analyses, longer work hours at Exam 1 was inversely associated with poorer global cognitive function among persons in the Sales/Office category, after adjustment for age, sex, physical activity, BMI, race/ethnicity, educational level, annual income, history of heart attack, diabetes, ApoE4 allele status, place of birth, number of years in the United States, language spoken at MESA Exam 1, and work hours at Exam 5 (final adjusted model: raw regression coefficient = −0.55, 95% CI = −0.99, −0.09). We did not observe significant associations for work hours at Exams 2 or 3 with global cognitive function in this occupational group. Among blue-collar workers, longer work hours at Exam 3 were significantly associated with global cognitive function at Exam 5 after adjustment for confounders and risk factors (final adjusted model: raw regression coefficient = −0.80, 95% CI = −1.51, −0.09). Sex, race/ethnicity, and ApoE did not significantly modify the association between work hours and global cognitive function.

3.2. Work hours and attention/working memory

Associations between hours of work (every 10 hours of work per week) at all three examinations and attention/working memory at Exam 5 were not statistically significant (Table 3). Occupational category, sex, race/ethnicity, and ApoE did not significantly modify the association between work hours and attention/working memory.

Table 2
Association between 10 work hours per week at three examinations and global cognitive function (CASI at Exam 5) among all participants and also stratified by occupational categories.

	n	Exam 1 (2000–2002)	Exam 2 (2002–2004)	Exam 3 (2004–2005)
		β-coeff. (95% CI); *p*-value	β-coeff. (95% CI); *p*-value	β-coeff. (95% CI); *p*-value
All participants	2,497			
Model 1		−0.099 (−0.317, 0.119); 0.372	0.189 (−0.015, 0.393); 0.069	0.106 (−0.090, 0.301); 0.289
Model 2		−0.072 (−0.296, 0.152); 0.530	0.022 (−0.183, 0.226); 0.835	−0.005 (−0.205, 0.195); 0.960
Model 3		−0.074 (−0.299, 0.151); 0.521	0.020 (−0.186, 0.227); 0.849	−0.008 (−0.212, 0.196); 0.938
Management/Professional	1,218			
Model 1		−0.006 (−0.275, 0.264); 0.968	0.170 (−0.086, 0.426); 0.192	0.073 (−0.165, 0.311); 0.548
Model 2		0.071 (−0.211, 0.352); 0.623	0.064 (−0.195, 0.323); 0.630	0.031 (−0.216, 0.278); 0.806
Model 3		0.059 (−0.227, 0.344); 0.687	0.048 (−0.217, 0.314); 0.721	0.014 (−0.239, 0.267); 0.914
Sales/Office	508			
Model 1		**−0.694 (−1.107, −0.281); 0.001**	−0.014 (−0.440, 0.412); 0.949	0.105 (−0.302, 0.512); 0.613
Model 2		**−0.553 (−1.005, −0.101); 0.017**	−0.016 (−0.466, 0.434); 0.944	0.228 (−0.206, 0.662); 0.303
Model 3		**−0.547 (−0.999, −0.094); 0.018**	−0.017 (−0.467, 0.434); 0.942	0.255 (−0.184, 0.693); 0.255
Service	369			
Model 1		**0.679 (0.084, 1.275); 0.026**	**0.562 (0.017, 1.107); 0.043**	**0.663 (0.120, 1.207); 0.017**
Model 2		0.493 (−0.206, 1.192); 0.167	0.208 (−0.402, 0.819); 0.503	0.388 (−0.247, 1.023); 0.231
Model 3		0.479 (−0.222, 1.180); 0.180	0.186 (−0.429, 0.800); 0.553	0.353 (−0.295, 1.002); 0.285
Blue-collar	364			
Model 1		−0.260 (−1.086, 0.566); 0.537	0.127 (−0.487, 0.741); 0.685	−0.514 (−1.134, 0.105); 0.104
Model 2		−0.458 (−1.350, 0.435); 0.314	−0.108 (−0.776, 0.560); 0.751	**−0.810 (−1.511, −0.109); 0.024**
Model 3		−0.455 (−1.349, 0.438); 0.317	−0.085 (−0.759, 0.589); 0.804	**−0.797 (−1.506, −0.088); 0.028**

The bold values are statistically significant. Raw regression coefficients and *p*-values were obtained from linear regression models.
Model 1: Adjusted for age.
Model 2: Adjusted for age, sex, physical activity, BMI, race/ethnicity, education, annual income, history of heart attack, diabetes, ApoE4 allele status, place of birth, number of years in the United States, and language at MESA Exam 1.
Model 3: Adjusted for age, sex, physical activity, BMI, race/ethnicity, education, annual income, history of heart attack, diabetes, ApoE4 allele status, place of birth, number of years in the United States, language at MESA Exam 1, and work hours at Exam 5.
Effect modification by occupational category: $p = 0.051$ (Model 3).
CI, confidence interval.

3.3. Work hours and processing speed

The association between hours of work (every 10 hours of work per week) at all three examinations and processing speed at Exam 5 were not statistically significant overall among participants (Table 4). However, occupational category did modify the association (interaction $p = 0.040$). After stratification by occupational category, we observed a significant association between work hours at Exam 2 and processing speed after full adjustment among blue-collar workers. No other significant associations were

Table 3
Association between 10 work hours per week at three examinations and attention/working memory scores (Digit Span test backward and forward combined scores at Exam 5) among all participants and also stratified by occupational categories.

	n	Exam 1 (2000–2002)	Exam 2 (2002–2004)	Exam 3 (2004–2005)
		β-coeff. (95% CI); *p*-value	β-coeff. (95% CI); *p*-value	β-coeff. (95% CI); *p*-value
All participants	2,497			
Model 1		−0.033 (−0.134, −0.068); 0.518	**0.127 (0.033, 0.221); 0.008**	0.060 (−0.030, 0.150); 0.190
Model 2		0.021 (−0.077, −0.119); 0.673	0.057 (−0.032, 0.147); 0.211	0.038 (−0.050, 0.125); 0.401
Model 3		0.023 (−0.076, −0.121); 0.655	0.060 (−0.030, 0.150); 0.194	0.041 (−0.048, 0.131); 0.363
Management/Professional	1,218			
Model 1		−0.067 (−0.213, −0.079); 0.365	0.093 (−0.046, 0.231); 0.190	0.064 (−0.065, 0.193); 0.331
Model 2		0.001 (−0.153, −0.154); 0.994	0.055 (−0.086, 0.196); 0.446	0.085 (−0.049, 0.219); 0.215
Model 3		−0.001 (−0.156, −0.154); 0.992	0.056 (−0.089, 0.200); 0.450	0.087 (−0.050, 0.225); 0.213
Sales/Office	508			
Model 1		−0.146 (−0.349, −0.058); 0.159	−0.007 (−0.215, 0.201); 0.950	−0.136 (−0.335, 0.062); 0.179
Model 2		−0.116 (−0.329, −0.098); 0.287	0.014 (−0.197, 0.225); 0.898	−0.079 (−0.283, 0.124); 0.445
Model 3		−0.109 (−0.322, −0.104); 0.316	0.013 (−0.198, 0.224); 0.902	−0.060 (−0.265, 0.146); 0.568
Service	369			
Model 1		0.192 (−0.048 to 0.433); 0.117	**0.331 (0.113, 0.549); 0.003**	0.087 (−0.133, 0.308); 0.438
Model 2		0.175 (−0.071 to 0.421); 0.163	0.173 (−0.041, 0.387); 0.114	0.079 (−0.145, 0.304); 0.486
Model 3		0.169 (−0.078 to 0.415); 0.180	0.164 (−0.052, 0.379); 0.136	0.060 (−0.168, 0.289); 0.604
Blue-collar	364			
Model 1		−0.039 (−0.340, −0.262); 0.798	0.140 (−0.083, 0.363); 0.218	0.172 (−0.054, 0.397); 0.136
Model 2		0.011 (−0.251, −0.273); 0.935	0.014 (−0.181, 0.210); 0.884	−0.024 (−0.231, 0.184); 0.823
Model 3		0.012 (−0.250, −0.274); 0.930	0.025 (−0.173, 0.222); 0.805	−0.013 (−0.222, 0.196); 0.905

The bold values are statistically significant. Raw regression coefficients and *p*-values were obtained from linear regression models.
Model 1: Adjusted for age.
Model 2: Adjusted for age, sex, physical activity, BMI, race/ethnicity, education, annual income, history of heart attack, diabetes, ApoE4 allele status, place of birth, number of years in the United States, and language at MESA Exam 1.
Model 3: Adjusted for age, sex, physical activity, BMI, race/ethnicity, education, annual income, history of heart attack, diabetes, ApoE4 allele status, place of birth, number of years in the United States, language at MESA Exam 1, and work hours at Exam 5.
Occupational category was not a significant effect modifier.
CI, confidence interval.

Table 4
Association between 10 work hours per week at three examinations and processing speed (DSC) scores among all participants and also stratified by occupational categories.

	n	Exam 1 (2000–2002)	Exam 2 (2002–2004)	Exam 3 (2004–2005)
		β-coeff. (95% CI); *p*-value	β-coeff. (95% CI); *p*-value	β-coeff. (95% CI); *p*-value
All participants	2,497			
Model 1		−0.251 (−0.623, 0.120); 0.185	0.134 0.214, 0.481); 0.451	0.205 (−0.127, 0.538); 0.226
Model 2		0.029 (−0.308, 0.366); 0.865	−0.076 (−0.384, 0.231); 0.626	0.138 (−0.163, 0.440); 0.367
Model 3		−0.001 (−0.339, 0.337); 0.996	−0.122 (−0.432, 0.188); 0.442	0.082 (−0.225, 0.388); 0.602
Management/Professional	1,218			
Model 1		−0.154 (−0.642, 0.334); 0.536	0.081 (−0.382, 0.545); 0.731	0.136 (−0.295, 0.566); 0.537
Model 2		0.207 (−0.292, 0.706); 0.416	−0.017 (−0.476, 0.442); 0.941	0.014 (−0.423, 0.451); 0.950
Model 3		0.170 (−0.335, 0.674); 0.510	−0.075 (−0.545, 0.395); 0.754	−0.043 (−0.491, 0.406); 0.852
Sales/Office	508			
Model 1		**−0.701 (−1.392, −0.010); 0.047**	−0.140 (−0.848, 0.568); 0.698	0.003 (−0.674, 0.680); 0.994
Model 2		−0.344 (−1.049, 0.361); 0.338	−0.111 (−0.809, 0.588); 0.756	0.443 (−0.230, 1.116); 0.196
Model 3		−0.364 (−1.070, 0.341); 0.311	−0.109 (−0.807, 0.589); 0.758	0.394 (−0.286, 1.074); 0.255
Service	369			
Model 1		0.412 (−0.522, 1.346); 0.386	0.623 (−0.229, 1.475); 0.152	0.477 (−0.376, 1.330); 0.273
Model 2		−0.093 (−0.999, 0.813); 0.840	0.061 (−0.728, 0.850); 0.879	0.462 (−0.358, 1.283); 0.268
Model 3		−0.088 (−0.996, 0.821); 0.850	0.071 (−0.724, 0.866); 0.860	0.500 (−0.338, 1.338); 0.241
Blue-collar	364			
Model 1		−0.534 (−1.636, 0.569); 0.342	−0.112 (−0.933, 0.709); 0.789	0.088 (−0.743, 0.919); 0.835
Model 2		−0.091 (−1.064, 0.882); 0.854	−0.705 (−1.428, 0.017); 0.056	−0.415 (−1.183, 0.353); 0.289
Model 3		−0.099 (−1.068, 0.871); 0.841	**−0.798 (−1.522, −0.073); 0.031**	−0.514 (−1.286, 0.258); 0.192

The bold values are statistically significant. Raw regression coefficients and *p*-values were obtained from linear regression models.
Model 1: Adjusted for age.
Model 2: Adjusted for age, sex, physical activity, BMI, race/ethnicity, education, annual income, history of heart attack, diabetes, ApoE4 allele status, place of birth, number of years in the United States, language at MESA Exam 1.
Model 3: Adjusted for age, sex, physical activity, BMI, race/ethnicity, education, annual income, history of heart attack, diabetes, ApoE4 allele status, place of birth, number of years in the United States, language at MESA Exam 1, and work hours at Exam 5.
Effect modification by occupational category: $p = 0.040$ (Model 3).
CI, confidence interval.

observed between work hours and processing speed among any of the other occupational categories. Sex, race/ethnicity, and ApoE did not significantly modify this association.

4. Discussion

In this population-based study, we investigated associations between total hours worked per week and subsequent cognitive function. The analyses used a prospective approach, although we lacked cognitive information at baseline, assessing whether work hours at Exams 1, 2, and 3 were associated with cognitive function 5 to 10 years later at Exam 5.

Our results show that, in the full cohort, hours of work at Exams 1, 2, and 3 were not significantly associated with cognitive function at Exam 5, as measured by the three instruments. However, occupational group significantly modified the associations between (1) work hours and global cognitive function and (2) work hours and processing speed. In occupation-stratified analyses, our results show that persons in the Sales/Office group who worked longer hours at Exam 1 had a lower global cognitive function at Exam 5 compared to those who worked fewer hours. We also observed that blue-collar workers who worked longer hours at Exam 3 had a lower global cognitive function at Exam 5 compared to those who worked fewer hours. However, these results are weak.

We did not find significant associations for hours worked (at any of the three examinations) with attention/working memory or processing speed at Exam 5 among the entire cohort. However, we did observe a weak, inverse, and statistically significant association between hours of work at Exam 2 and processing speed among blue-collar workers.

According to the Bureau of Labor Statistics, most workers classified in the Sales/Office category sell retail merchandise and perform clerical duties (although this category also includes a variety of positions, with some being more prestigious than others) [29]. In the lower level jobs of this occupational category, the job turnover rate can be high. The same can be said for blue-collar workers. It is also possible that persons in the Sales/Office and blue-collar groups may experience higher levels of dissatisfaction and job strain. Job strain may influence decline in cognitive performance [30].

A search of the peer-reviewed literature identified very few studies that investigated relationships between long working hours and cognitive function. Virtanen et al [15] conducted a prospective cohort study to investigate this question at baseline and at follow-up. Compared with working a maximum of 40 hours per week, they found that working more than 55 hours per week was associated with lower scores in the vocabulary tests (at baseline and follow-up examinations) and predicted worse performance on the reasoning test over a 5-year follow-up period, even after adjustment for several potential confounding and risk factors. In Virtanen et al, participants were almost exclusively white-collar civil servants and had a mean age of 52.1 years at baseline, and 77% were male. The sample size was 2,214, which is comparable to ours ($n = 2{,}497$). In another study, increased overtime work (>8 hours a day or >5 days in the 7 days before examination) predicted poorer performance on tests measuring attention and executive function among automotive workers [31].

4.1. Biological mechanisms

There is sufficient evidence for a plausible biological mechanism whereby longer working hours may be associated with cognitive function. Results from previous studies show that persons who worked longer hours per week were more likely to have shorter sleep duration, CVD, and were at higher risk of developing depressive symptoms and anxiety [8,32,33]. All the above outcomes are associated with cognitive impairment [34–37]. It has been well documented that good quality sleep is essential for various cognitive functions and that inadequate sleep duration and poor sleep quality are harmful to cognitive function, even after adjusting for several confounders and factors known to increase cognitive impairment [34,35]. Park and Moghaddam [36] reviewed

animal and human studies, which showed that anxiety affects the prefrontal cortex to impair cognitive flexibility. Shimada et al [37] investigated the associations between depressive symptoms (or depression), cognitive function, serum brain-derived neurotrophic factor, and volumetric MRI measurements in adults aged ≥65 years. Their results showed that individuals with depressive symptoms or depression had lower serum brain-derived neurotrophic factor concentrations and greater atrophy of the right medial temporal lobe than those who did not have depressive symptoms. Moreover, working long hours may take away from time that could be spent in leisurely physical activity, another factor known to be protective of cognitive ability especially among older persons [38].

4.2. Limitations and strengths

One of the limitations of this study is that, because of the unavailability of the cognitive function information at Exam 1, we were unable to control for cognitive performance levels at that time. The absence of data on sleep duration and sleep quality at Exam 1 is another limitation. It has been suggested that sleep disturbances (e.g., short sleep duration, sleep fragmentation, and sleep-disordered breathing) might increase the risk of cognitive impairment [39,40]. Because of the unavailability of sleep data, we were unable to adjust for confounding or assess for effect modification by these variables. We cannot rule out uncontrolled confounding. Also, it is possible that participants may have changed jobs over time and we were not able to model changing occupational status. Because the categories of Sales/Office and blue-collar include a wide variety of positions, it would have been useful to be able to sub-categorize these groups into more homogeneous categories to determine which jobs were affected. However, we did not have details on the jobs included in these categories. In addition, use of self-reported work hours as opposed to a more objective measure may have resulted in information bias, although that is not expected to be substantial. If information bias did exist, the impact would be expected to be nondifferential and therefore likely to have minimized any associations observed. Finally, given the number of tests or multiple comparisons performed (4 tests in Table 2 and 8 tests in Table 4), it is possible that the probability of at least one of those tests is a false positive (i.e., declaring a significant result when in fact there is not one) could be higher than 5%. Therefore, the inflation of the Type I error rate is an additional limitation that should be considered when interpreting the significance of a test. Because of the study design, we cannot conclude that working long hours is a risk factor for cognitive impairment.

One of the strengths of this study is the use of standardized and valid measures of cognitive performance [41] administered by trained and certified examiners. Other strengths include the large sample size, the demographic and occupational diversity of the participants, and the standardization of all measurements.

Studies investigating potentially modifiable occupational risk factors for cognitive impairment are important because of the increasing incidence of dementia and increased mortality occurring in all major industrialized nations, and the lack of well-established preventive approaches [42–44]. In situations where working long hours is unavoidable, the risk of cognitive impairment may be mitigated by better overall cardiovascular health habits [45,46] and the incorporation of healthier lifestyle choices [47–51]. Additional studies investigating associations of long working hours and other occupational exposures with cognitive function are needed. Such studies may be improved by using a prospective design.

In summary, our study found that longer work hours were weakly associated with poorer global cognitive function and slower processing speed among Sales/Office and blue-collar workers. It is important to replicate these findings and if replicated, to identify the factors that explain these findings.

Author contributions

Dr Charles designed the study, searched and reviewed the literature, and wrote the manuscript. Dr Fekedulegn conducted data analysis. All authors reviewed the manuscript for important intellectual content, provided interpretation of the data, and approved the final version.

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Ethics approval and informed consent

All participants signed written informed consent.

Disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention.

Conflicts of interest

All authors have no conflicts of interest to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.shaw.2020.02.004.

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