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How do occupational sedentary behavior and occupational cognitive complexity relate to cognitive function?

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Thesis

HOW DO OCCUPATIONAL SEDENTARY BEHAVIOR AND OCCUPATIONAL COGNITIVE COMPLEXITY RELATE TO COGNITIVE FUNCTION?

by

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DEDICATION

I would like to dedicate this work to my umma, the strongest and softest person.

ACKNOWLEDGMENTS

I would like to thank my primary mentor, Dr. Nicole L. Spartano, for her guidance and mentorship throughout this project and my time at Boston University. Thank you for exposing me to the building blocks and influence of epidemiology. Thank you for your continuous support, patience, and belief.

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ABSTRACT

Background: Lower occupational cognitive complexity (OCC) and physical inactivity have been associated with advanced brain aging and cognitive decline in older adulthood. However, sedentary behavior may have a more complex relationship with cognitive function due to cognitively complex occupations often being highly sedentary.

Objectives: This study examined whether occupational sedentary time related to cognitive function. In secondary analysis, we determined whether this relationship was partially explained by higher OCC among those with higher sedentary behavior.

Methods: In this cross-sectional study, data was utilized from the Framingham Heart Study (FHS) Generation 3 based cohorts: Third Generation, New Offspring Spouse (NOS), and Omni 2 cohorts. Our analysis included those who attended exam 2, did not have dementia, and fulfilled the neuropsychology, accelerometry, and occupation assessments (n=1,959). Sedentary time was measured objectively by an omnidirectional accelerometer and questionnaire which asked about the frequency of sitting at work. Three cognitive function assessments were used including logical memory delayed recall (LMD), total raw score from Weschler Adult Intelligence Scale (WAIS) similarities subtest (SIM), time in minutes to finish trail A, subtracted from the time in minutes to finish trail B (TRAILSB-A). Lastly, OCC was measured as substantive cognitive complexity, using data from the U.S. Department of Labor's Occupational Information Network (O*NET). Linear regression analyses were computed to evaluate the association between occupational sedentary time and cognitive function, including models adjusting for age, sex, education, and substantive complexity.

Results: Higher accelerometer-measured sedentary time was associated with higher cognitive performance. When additionally adjusting for education and substantive complexity, sedentary time's association with cognitive performance was attenuated and no longer significant. Participants more likely to sit as work similarly exhibited higher cognitive performance in LMD, including after adjusting for age and sex (0.61 [0.17], p=0.0004). This association was attenuated when additionally adjusting for education (0.33 [0.17], p=0.06), and furthermore when adding adjustment for substantive complexity (0.19 [0.18], p=0.30).

Conclusions: Our findings indicate that the association of higher occupational sedentary time with higher cognitive function was partially explained by higher substantive complexity and education level. Occupations with higher OCC, often requiring more education, may contribute to cognitive resilience.
Keywords: occupational cognitive complexity, occupational sedentary time, occupational physical activity, dementia risk.

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LIST OF ABBREVIATIONS

AD.. Alzheimer's Disease

BMI..Body Mass Index

BU..Boston University

FHS..Framingham Heart Study

I&O..Industry & Occupation

LMD..Logical Memory - Delayed Recall

LS..Least Squares

MVPA...Moderate to Vigorous Physical Activity

NIOCCS.......................... National Industry of Occupation Computerized Coding System

NIOSH ....National Institute for Occupational Safety and Health

NOS.. New Offspring Spouse

OCC ....Occupational Cognitive Complexity

O*NET..Occupational Information Network

RCT.. Randomized Controlled Trial

REGARDS................................ Reasons for Geographic and Racial Differences in Stroke

SIM..Similarities Subtest

SOC..Standard Occupational Classification

TRAILSA.. Time in minutes to finish trail A

TRAILSB..Time in minutes to finish trail B

TRAILSB-A................Time in minutes to finish trail B - Time in minutes to finish trail A

WAIS ....Weschler Adult Intelligence Scale

INTRODUCTION

Dementia

Age related disease risk is a primary subject of concern due to the rise in life expectancy. One major neurocognitive disorder that has consequently become more common from this is dementia. Dementia is an umbrella term that describes a wide range of symptoms causing cognitive impairment that interferes with daily life (Livingston et al., 2017). Alzheimer’s disease (AD) is the most common type of dementia (Cheng, 2016). One in nine Americans over the age of 65 has AD and there is currently no cure (Alzheimer's disease research at the Weizmann Institute of Science, 2020). Further research is needed to assess preventative strategies for cognitive decline due to limited understanding of strategies, despite the rising prevalence.

A growing body of evidence recognizes certain risk factors for dementia including high blood pressure, hearing impairment, smoking and alcohol intake, obesity, depression, diabetes mellitus, low social contact, less education, traumatic brain injury, exposure to air pollution, and physical inactivity (Livingston et al., 2020). These 12 risk factors account for 40% of dementias, globally, which could be targeted as prevention and/or deferment strategies. Interventions that improve education, nutrition, health care, and lifestyle have been associated with decreased incidence of dementia (Livingston et al., 2020). Early life education for instance widely influences cognitive reserve and neuropathological developments. Policy changes such as prioritizing childhood education for all could play a key role in protective measures for brain health and dementia risk.

Physical inactivity and poor education are the two modifiable risk factors that may have the greatest impact on AD risk globally, accounting for 13% and almost 20% of AD prevalence, respectively (Cheng, 2016). In developed countries, such as the United States, low educational attainment is less common and physical inactivity is more common; in these countries, physical inactivity is estimated to account for more than 20% of the prevalence of AD.

Physical activity and dementia

Physical activity is a key element in health promotion and wellbeing. Physical activity has been proven to decline with age and subsequently reduce functional fitness (Milanović et al., 2013). About 50% of adults are not meeting the Physical Activity Guidelines for Americans of at least 150 minutes of moderate-to-vigorous physical activity per week (U.S. Department of Health and Human Services, 2018). The high prevalence of physical inactivity is concerning due to the correlation between age-related physical inactivity and AD risk.

Physical activity preserves cognitive health and neuroplasticity by lessening the likelihood of vascular diseases and improving cerebral perfusion (e.g., plaque deposits in arteries, atherosclerosis, high blood pressure, and stroke) (Sofi et al., 2010). It also improves respiratory function, fuels growth factors such as brain-derived neurotrophic factor (BDNF) and insulin-like growth factor-1, downregulates oxidative stress and inflammatory responses, and lessens the brain's exposure to neurotoxic factors (Cheng, 2016). Gains in brain volume and network connectivity are two main protective features of physical activity. In a randomized controlled trial (RCT) consisting of older adults, conducted by the University of Muenster, Germany, participants in the exercise intervention for 6 months exhibited increased gray matter volume in the prefrontal and the cingulate cortex and increased memory score, compared to those without the exercise intervention (Ruscheweyh et al., 2011).

Physical activity's protective features are also not limited to healthy individuals. Another RCT including those with mild cognitive impairment or dementia presented slowing of age-related decline in gray matter with implementation of physical activity (ten Brinke, L. F., et. al). A meta-analysis including 15 prospective studies presented protection against the occurrence of cognitive decline for all levels of physical activity (Sofi et al., 2010). Another confirmed the modifiable risk factors for AD including improved access to education and effective methods targeting vascular risk factors (physical inactivity, smoking, high blood pressure, overweightness, and diabetes) (Norton et al., 2014). Although there is copious supporting evidence for the beneficial role of physical activity on cognitive function, the evidence linking sedentary behavior with cognitive decline has been more ambiguous.

Sedentary time and dementia

Multiple lines of evidence suggest that increased sedentary behavior may be a risk factor for age-related cognitive decline (Siddarth et al., 2018). In a study including middle-aged and older adults, higher self-reportings of time spent sitting (hours/day) were associated with less thickness in the medial temporal lobe (MTL) substructures on

MRI scans. These outcomes suggest that reducing sedentary behavior may be a potential target for interventions designed to improve and protect cognitive health in older adults (Siddarth et al., 2018).

A meta-analysis including 8 studies examined the association of sedentary behavior with cognitive function (Falck et al., 2016). 75% of the studies reported significant negative associations between sedentary behavior and cognitive function, supporting that partaking in regular moderate-to-vigorous physical activity and reducing sedentary behavior may preserve cognitive health (Falck et al., 2016).

Although much evidence supports the association of sedentary time with cognitive decline, my colleagues recently observed a positive association of sedentary time with *higher* cognitive function in a middle-aged cohort, the Third Generation of the FHS (Spartano et al., 2019). We hypothesize that these results may reflect unmeasured sedentary activities that promote cognitive resilience, such as time spent on a computer, socializing, reading, playing word/number games, as well as sedentary duties in an occupational setting (Fujishiro et al., 2017. Kesse-Guyot et al., 2012. Cheng, 2016). Sedentary occupations have been associated with higher cognitive demand and/or cognitive complexity (Fujishiro et al., 2017). More cognitively complex occupations can contribute diverse attributes such as brain health, environment, income, education, and resources (Cheng, 2016). In this investigation, we assessed if occupational complexity partially explains the association between sedentary time and cognitive function.

Occupational cognitive complexity

Evidence from epidemiological cohort studies has shown that occupational cognitive complexity (OCC) may be a protector of late-life cognition (Fujishiro et al., 2017). OCC is work that in its very substance requires thought and independent judgment. It is the cognitive demand an occupation imposes. Occupations with higher OCC have been associated with higher cognitive function. Many occupations with higher cognitive complexity may also have lower occupational physical activity and higher sedentary time. It is hypothesized that the cognitive demand of these occupations may be a protective feature towards later-life cognitive function.

Interestingly, there are many elements that can influence the relationship between sedentary time and cognitive function. An occupation with more cognitively complex duties, may also be characterized as an enriched environment for cognitive stimulation on a regular basis (Cheng, 2016). This provokes aspects of environmental factors that may influence cognitive reserve and longevity. One series of supporting evidence of the potential role of cognitive stimulation and cognitive reserve in protecting again brain aging are studies proposing that bilingualism may delay clinical AD symptoms through processes affecting neuronal metabolic functions, vascular factors, and myelin structure and neurochemical signaling (Gold, 2015). Speaking more than one language is an intellectual activity thought to strengthen executive control.

Specific sedentary behaviors have also been differentially associated with cognitive function. For example, computer use has been associated with higher cognitive function, whereas television viewing presented the opposite effect (Kesse-Guyot et al., 2012). In a study of older French adults, a negative association was observed between TV viewing and executive functioning, whereas those with higher computer use time displayed better verbal memory and executive functioning. Furthermore, there are other cognitively stimulating sedentary activities that may positively influence cognitive performance such as reading, playing games, or puzzles as a component of the cognitive reserve model (Kesse-Guyot et al., 2012). Better understanding the effects of sedentary behavior on cognitive health is critical given the epidemic of physical inactivity, sedentary lifestyles, and likelihood of cognitive decline with aging.

In this cross-sectional investigation in the FHS, we explored the association of objectively measured sedentary time with cognitive function, examining the role of OCC (also known as substantive complexity) in this relationship. This focus aims to expand the understanding between sedentary and cognitive function and clarify protective factors for brain health and cognitive longevity.

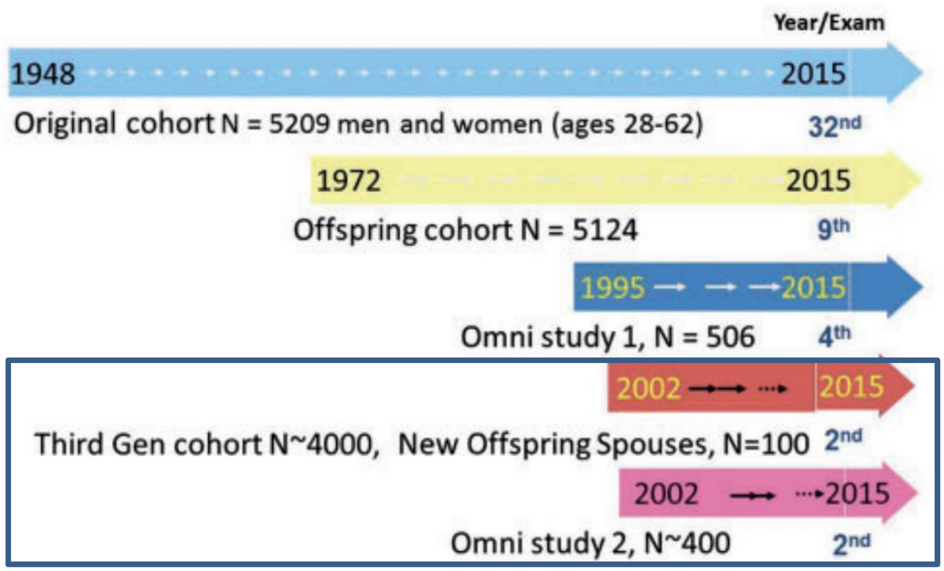
METHODS

Study Design/Population

The FHS was the first large, longitudinally followed cohort to study cardiovascular disease epidemiology in the USA. Paving the way for epidemiological research in preventative medicine, it has become a multigenerational community-based cohort based in Framingham, Massachusetts (Tsao & Vasan, 2015). The Original FHS cohort was enrolled in 1948, enrolling a total of 5209 (Figure 1, n = 2336 men and 2873 women) between the ages of 30-59 years (Tsao & Vasan, 2015). Commencement of the second generation (Offspring) cohort began in 1971, comprised of offspring from the original cohort and spouses of those offspring (n=5124). To increase the ethnic and racial diversity since the first enrollment, the first omni cohort was initiated in 1994. This population included a total of 506 participants, consisting of African American, Hispanic, Asian, Indian, Pacific Islander and Native American descent (Tsao & Vasan, 2015).

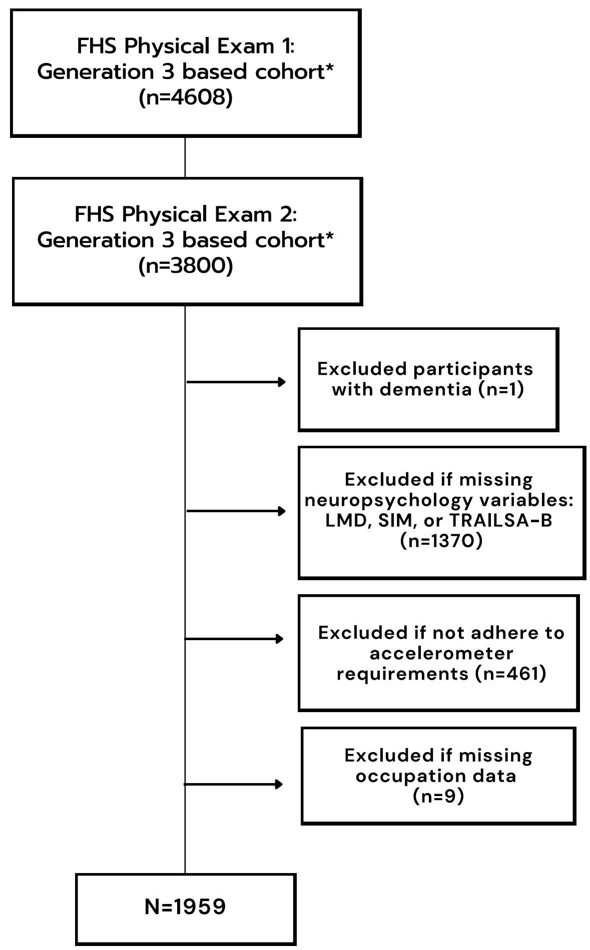
Our investigation focuses on the Third Generation cohort (Generation 3), which was initiated in 2002, consisting of adults of at least 20 years of age, with at least one parent in the Offspring cohort (n=4095). At this time point, 103 parents of Third generation participants who were not formerly enrolled in the Offspring cohort were enrolled as the New Offspring Spouse (NOS) cohort (Figure 1). In 2003, a second Omni cohort began, known as Omni 2, enrolled a total of 410 ethnically and racially diverse adults, some of whom were family members of those in the first Omni cohort. These three Generation 3-based cohorts (Generation 3, NOS, and Omni 2) were initiated near the same timepoint, and consequently followed comparable timelines for follow-up exams.

Figure 1: Enrollment of Framingham Heart Study Cohorts (Tsao & Vasan, 2015).



The Generation 3-based cohort comprised of 3,800 subjects who attended exam 2 (2008-2011). Participants with dementia were first excluded, along with any subjects missing occupation data (n=10). Next, participants were excluded if missing certain neuropsychological variables (n=1370) Participants were lastly excluded if non-adherent to accelerometer requirements for the physical activity assessment (n=461) concluding a sample size of 1,959, as seen in Figure 2. All participants provided written informed consent, and the institutional review board at the Boston University Medical Center approved study protocols.

Figure 2: Participant flowchart, inclusion and exclusion criteria.



Generation 3 based cohort* includes Framingham Heart Study Third Generation, New Offspring Spouse, and Omni 2. LMD, logical memory - delayed recall; SIM, similarities subtest; TRAILSB-A, Time in minutes to finish trail B - Time in minutes to finish trail A.

Neuropsychology assessment

Neuropsychology assessments were conducted during examination 2 (2008-2011) and at subsequent call-back examinations. We included neuropsychology assessments conducted during exam visit and for two years following the conclusion of the exam, until January 2014. Time in minutes to finish trail A (TRAILSA), time in minutes to finish trail B (TRAILSB), total raw score from WAIS similarities subtest (SIM), and logical memory - delayed recall (LMD) variables were included. LMD measured verbal memory and was the primary outcome of cognitive function in our analysis (Au et al., 2004). LMD was assessed as total number of correct story details (verbatim and paraphrased are both worth 1 point) and calculated accordingly within a range from 0-23. WAIS SIM subtest measured abstract reasoning skills on a scale of 0-26 (Au et al., 2004). Participants had to identify the qualitative relationship between pairs of words to score correctly. TrailsA and TrailsB were tests of visual motor and attention (Au et al., 2004). Trails A measured simple attention, whereas Trails B tested cognitive flexibility and a more complex level of attention, scored as completion time to finish their respective trail (Smith Watts et al., 2018). TrailsB-A was log transformed to normalize the distribution and the sign was reversed to make interpretation consistent across cognitive outcome measures. Higher scores for all cognitive outcomes represented higher cognitive function. Duplicates founded were isolated to the earliest dated assessment, and any remaining were removed.

Physical activity and sedentary time assessment

The accelerometer assessment provides an objective measure of sedentary behavior and physical activity intensity and duration. Physical activity was monitored by an omni-directional accelerometer (Actical model #198-0200-00), which is a small (28×27×10 mm), waterproof device weighing 17 grams. It records accelerations in the range of 0.05–2.0 g and is sensitive to movements in the range of 0.35–3.5 Hz. The Actical has an internal time clock and extended memory and can record the magnitude of acceleration and deceleration associated with every movement. The recorded signals are scored as "counts" and "steps," which are summed over a 30-second epoch (Spartano et al., 2022).

During Generation 3 based exam 2, participants were instructed to wear the device 24 hours a day for 8 days on the hip (Spartano et al., 2022). After wearing period, participants returned the activity monitor to the FHS by mail. Sedentary time was defined as any minute with ≤100 counts per minute and standardized to wear time by dividing sedentary time by wear time and multiplying by 18 hours, reported as average hours/day (Spartano et al., 2022).

Sedentary time secondly measured through self-reported likelihood of sitting at work. The categorical variable asked if "at work do you sit?". There were 4 options for response: 0-never, 1-seldom, 2-sometimes, 3-often, 4-always. Sedentary time differs from physical inactivity, which means not doing enough physical activity or not meeting the physical activity guidelines. Participants were excluded if they wore the accelerometer for less than 3 valid days (valid day defined as ≥10 hours wear time/day).

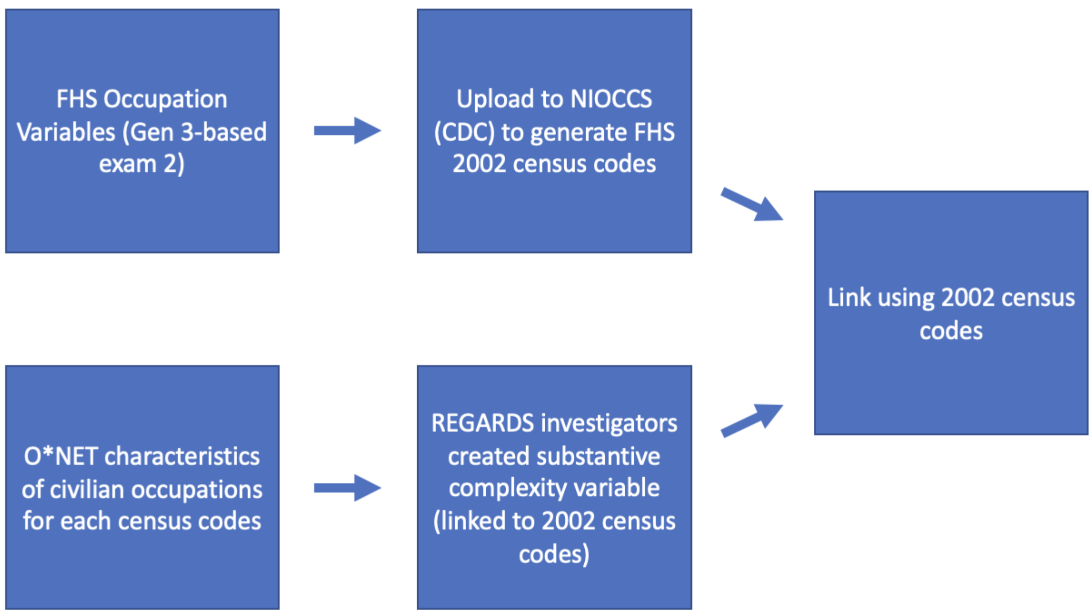
Occupational cognitive complexity assessment

FHS occupation was assessed with an open-ended question: "What is your current occupation?" Participants were also asked to report their occupational industry by answering the multiple-choice question, "which response best describes your occupation?" (See possible options in Figure 4). Using the participants' reported occupations and occupational industries, we developed a new variable called substantive complexity as a measure of OCC, similarly created and used by the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study investigators (Fujishiro et al., 2017). Substantively complex work is defined as work that in its very substance requires thought and independent judgment. It requires decision making involving ill-defined or apparently contradictory contingencies (Schooler et al., 1999).

To create this new variable, FHS occupational data was translated into census codes, using the National institute for occupational safety and health (NIOSH) industry of occupation computerized coding system (NIOCCS). NIOCCS is a free web application, maintained by the Center for Disease Control and used to translate industry and occupation text found in surveys, death certificates, and medical records into standardized codes for data analysis (https://csams.cdc.gov/nioccs/).

To generate census codes in NIOCCS, we completed the following steps (Figure 3). Step 1: Framingham occupational datasets were formatted for industry and occupation (I&O) coding in NIOCCS. The narrative occupational variable was sorted through manually to assure no identifiable information (names of companies, names of personnel, etc.) and eliminate abbreviations. Step 2: We uploaded our cleaned file into NIOCCS I&O processing with the following fields: ID, industry title, and occupation title. The output dataset then contained the census industry code, census industry title, census occupation code (2012), census occupation title, NAICS code, NAICS title, NAICS probability, standard occupational classification (SOC) code, SOC title, SOC probability, and unexpected NAICS/SOC combo. Step 3: Using these variables, this file was then reformatted for crosswalk coding to generate the 2002 census occupation codes.

Figure 3: Flowchart of the FHS occupation dataset and REGARDS substantive complexity variable linkage.



As shown in Figure 3, the FHS 2002 census occupation codes were then linked to the substantive complexity variable created by REGARDS investigators, who used 2002 census occupation codes (Fujishiro et al., 2017). REGARDS investigators created the substantive complexity variable using data from the U.S. Department of Labor's Occupational Information Network (O*NET). O*NET is a public database of detailed characteristics for civilian occupations in the U.S. labor market from a multiyear data collection program to gather information from workers in occupations in the O*NET-SOC occupational structure (https://www.onetonline.org/). O*NET job characteristics are linked to epidemiologic data using compatible standardized occupation codes. Because of its extensive coverage and content, it has been used as a job exposure matrix in epidemiologic investigations (Cifuentes, Boyer, Lombardi, & Punnett, 2010).

Based on Hadden, Kravets, & Muntaner (2004)'s factor analysis findings, REGARDS investigators created the substantive complexity variable using 11 O*NET items: inductive reasoning, deductive reasoning, updating and using relevant knowledge, complex problem solving, active learning, making decisions and solving problems, skill utilization, critical thinking, gathering necessary information, frequent decision making, and freedom to decide on the job (Meyer et al., 2007). The substantive complexity measure was constructed by computing the mean of the 11 variables, with higher scores indicating greater complexity (Fujishiro). This variable aims to umbrella all factors associated with cognitive complexity that an occupation imposes.

The 2002 census occupation codes were the linking variable between the FHS dataset exported from NIOCCS and the aggregated O*NET substantive complexity file created by REGARDS investigators (Figure 3).

Covariates

In addition to assessing OCC, the present study assessed additional covariates including age, sex, education level, occupation, and employment status Age (years) and substantive complexity are continuous variables. Education level, occupation, and employment status are categorical variables. Education was categorized as: did not graduate high school (0), high school graduate (1), some college (2), college graduate (3), and unknown (.). Occupation was categorized into 34 industry options presented in Table 2, and employment status was categorized into employed (part-time or full-time, unemployed, or retired.

Statistical Analysis

Participant characteristics were reported by mean and standard deviation (SD) or frequency (%) by occupational status (retired, unemployed, employed), with employed participants being further broken down into four OCC categories The associations of OCC (using categories) with objective sedentary time, occupational sedentary time, and cognitive function were analyzed using Least Squares (LS) means.

Linear regression models were used to assess the relationship between sedentary time (independent variable) and cognitive function (dependent variable). All primary linear regression analyses were conducted after excluding participants who were retired (n=57) or unemployed (n=81), as they do not have reliable OCC. Analyses including retired and unemployed participants was presented in the appendix. Sedentary time was assessed by two variables: objective sedentary time and self-reported likelihood of sitting at work. Cognitive function was represented by 3 different forms of cognitive measure: LMD, SIM, and TRAILSB-A. To assess confounding, we determined which factors confounded the relationship between sedentary time and cognitive function where the effect estimate was changed by ~10% or more. Although age and sex did not change the effect estimate by 10%, they were determined potential confounders, a priori.

Linear regression models were computed under 3 different models. Model 1 assessed the association between LMD and sedentary time, adjusting for age and sex. Model 2 includes model 1 covariates, adding the adjustment for education, dichotomized as college graduate or non-college graduate. Lastly, model 3 includes model 1 and 2 covariates, adding adjustment for substantive complexity as the continuous measure of OCC.

RESULTS

Our sample consisted of 1959 participants, with an average age of 48.5 (±) 9.1 years, of whom 47% were men (Table 1). A majority of participants self-identified as white (96%) and were currently employed (86%). A smaller proportion of our participants were retired (n=57, 2.9%) or unemployed (n=81, 4.1%); of those unemployed, 21% were jobless due to disability.

In Table 1, we reported participant characteristics by occupation status and substantive complexity categories. The majority of participants in our study sample were college graduates, n=1212 (61.9%), with over 78% of participants with higher substantively complex (≥65) occupations having graduated college. Men were also over-represented (making up >51%) among participants with higher substantively complex occupations. Participants with the lowest substantive complexity (<60) occupations were slightly older (49.2 years) compared to other occupations, were more likely to be smokers (11.8%), and depressed (9.7%). They were also the most physical activity, achieving >8000 steps/day on average, but a lower average MVPA than those with high substantively complex jobs.

Table 1: Participants baseline characteristics at exam 2 by occupation status and substantive complexity categories.

Variable	Full study sample N=1959	Currently employed (by substantive complexity category) <60 N= 516	60-64 N= 252	65-69 N= 577	70+ N= 476	Unemployed	Retired
Age, mean ± SD, y	48.5 ± 9.1	49.2 ± 8.4	47.7 ± 8.0	46.9 ± 8.8	47.9 ± 8.7	49.9 ± 7.7	65.8 ± 8.5
Men, n (column %)	919 (47)	228 (44.2)	87 (34.5)	295 (51.1)	246 (51.7)	38 (46.9)	25 (43.9)
Household income, n (column %)	N=1893	N = 495	N = 240	N = 564	N = 462	N = 79	N = 53
<$35,000	178 (9.4)	79 (16)	17 (7.1)	18 (3.2)	23 (5)	28 (35.4)	13 (24.5)
$35,000-$100,000	944 (49.9)	318 (64.2)	138 (57.5)	260 (46.1)	165 (35.7)	32 (40.5)	31 (58.5)
>$100,000	771 (40.7)	98 (19.8)	85 (35.4)	286 (50.7)	274 (59.3)	19 (24.1)	9 (17)
Education, n (column %)							
<High school	14 (.71)	5 (0.97)	5 (1.98)	0 (0)	1 (0.2)	2 (2.5)	1 (1.8)
High school grad	275 (14.0)	132 (25.6)	44 (17.5)	43 (7.5)	23 (4.8)	19 (23.5)	14 (24.6)
Some college	458 (23.4)	174 (33.7)	93 (36.9)	82 (14.2)	77 (16.2)	17 (21)	15 (26.3)
College graduate	1212 (61.9)	205 (39.7)	110 (43.7)	452 (78.3)	375 (78.8)	43 (53.1)	27 (47.4)
Race, n (column %)							
Caucasian or white	1890 (96.5)	502 (97.3)	246 (97.6)	553 (95.8)	464 (97.5)	76 (93.8)	49 (86.0)
Hispanic or Latino	36 (1.9)	14 (2.8)	9 (3.7)	6 (1.1)	5 (1.1)	2 (2.5)	0 (0)
African American or Black	26 (1.3)	5 (1.0)	2 (0.8)	6 (1.0)	8 (1.7)	1 (1.2)	4 (7.0)
Asian	34 (1.7)	4 (0.8)	3 (1.2)	19 (3.3)	4 (0.8)	0 (0)	4 (7.0)
Substantive complexity, mean ± SD	63.8 ± 8.1	53.1 ± 5.0	62.9 ± 1.2	66.2 ± 1.3	72.0 ± 2.6	--	--

Current smoker, n (column %)	151 (7.7)	61 (11.8)	25 (9.9)	32 (5.5)	19 (4.0)	13 (16.1)	1 (1.8)
Treated for hypertension, n (%)	327 (16.8)	97 (18.9)	35 (13.9)	70 (12.2)	75 (15.8)	22 (27.2)	28 (50.0)
Treated for diabetes, n (%)	65 (3.3)	17 (3.3)	2 (0.8)	16 (2.8)	17 (3.6)	2 (2.5)	11 (19.3)
Clinical depression, n (%)	148 (7.6)	50 (9.7)	23 (9.1)	33 (5.7)	31 (6.5)	9 (11.1)	2 (3.5)
Mostly sits at work, n (%)	1020 (59.3)	195 (38.6)	74 (46.3)	404 (70.6)	338 (73.3)	8 (44.4)	1 (33.3)
Total steps/day, mean ± SD	8053 ± 3795	8759 ± 4601	8372 ± 3437	7871 ± 3459	7711 ± 3151	6626 ± 3454	6965 ± 4954
MVPA min/day, mean ± SD	21.8 ± 20.2	19.9 ± 20.1	19.8 ± 16.1	23.7 ± 22.4	23.8 ± 17.9	18.1 ± 22.4	16.8 ± 24.9
Standard sedentary time counts/min, mean ± SD	13.6 ± 1.4	13.2 ± 1.5	13.3 ± 1.4	13.8 ± 1.2	13.8 ± 1.2	13.9 ± 1.4	14.5 ± 1.4

Numbers missing demographic variables: smoking status=1, treatment for hypertension status=10, diabetes mellitus status=2, and likelihood of sitting at work=240.

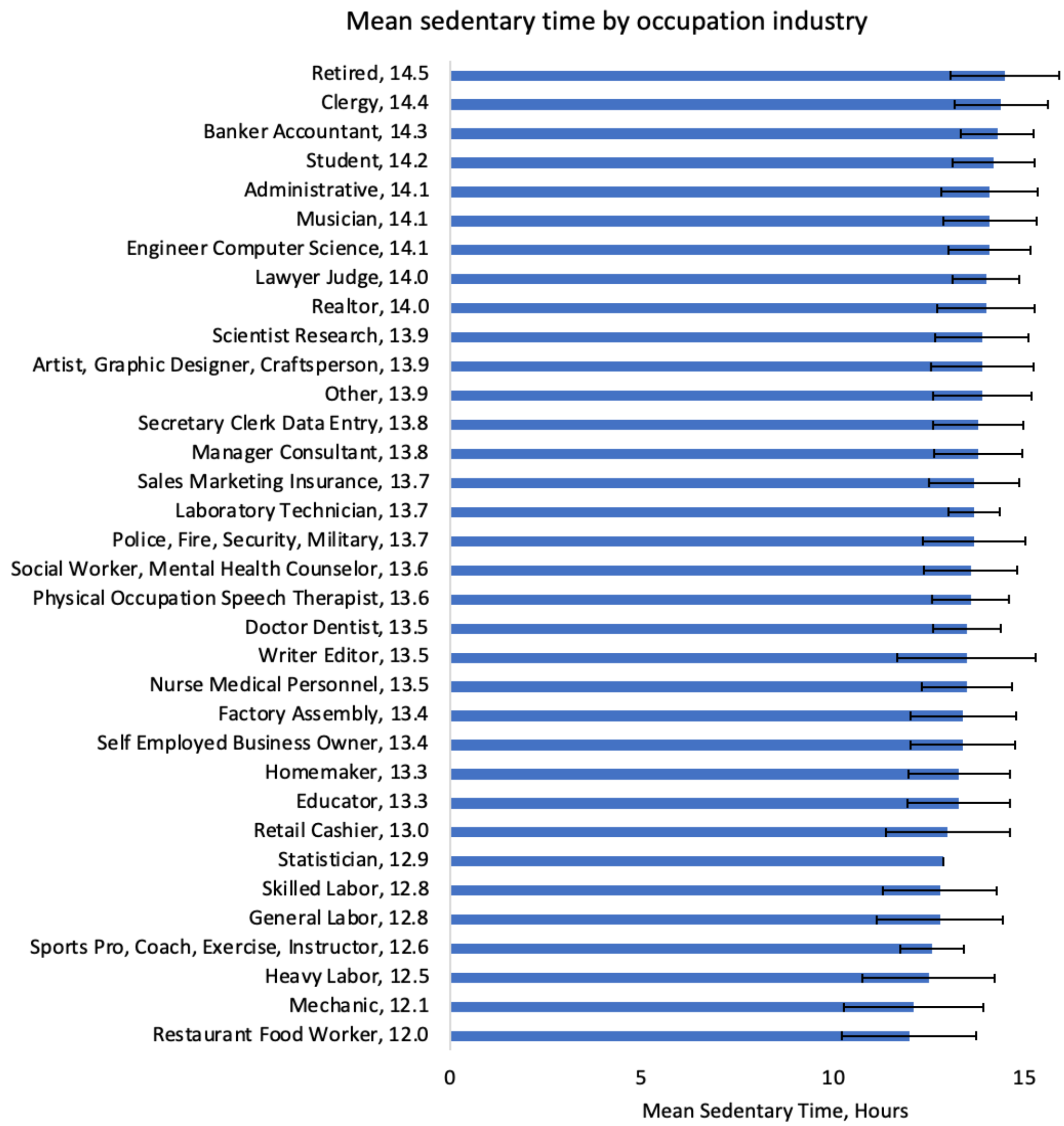
Occupation industries with the highest levels of substantive complexity include lawyer, judge, doctor, dentist, clergy, mental health professional, and social worker (Appendix Figure 11). Students and participants who were retired also categorized into the highest substantive complexity level (70+). On the contrary, industries categorized into the lowest level of substantive complexity (<60) include general or skilled labor, restaurant/food worker, musician, factory assembly, heavy labor, retail cashier, secretary clerk, and mechanic.

We used accelerometers to measure objective sedentary time and presented the distribution by occupation industry among study participants (Figure 4). On average, industries with the highest sedentary time are clergy, banker, accountant, administrative, musician, engineer, and computer science, spending more than 14 hours/day sedentary.

Students and participants who are retired also spend >14 hours/day in sedentary time. In contrast, the industries with the lowest sedentary time were restaurant/food worker, mechanic, heavy labor, sports related work (athlete, coach, instructor), general or skilled labor, and statistician, spending 12-12.9 hours/day sedentary.

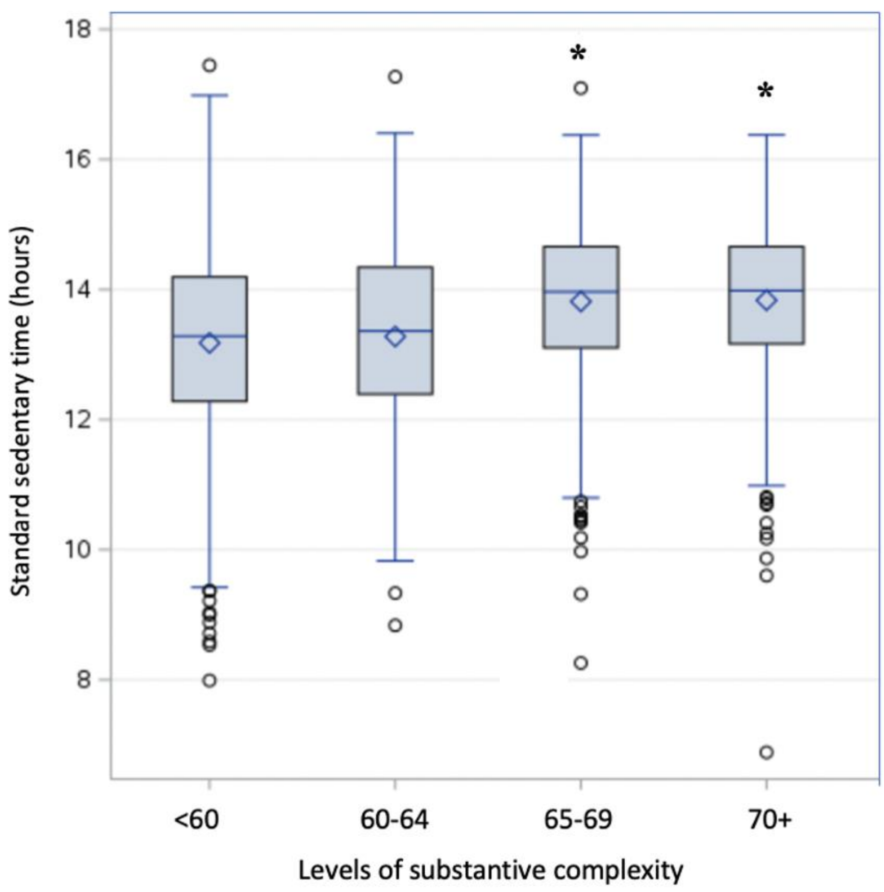
Certain industries overlap, categorizing in both the highest level of substantive complexity and highest level of sedentary time such as clergy; as well as categorizing in the lowest level of substantive complexity and lowest level of sedentary time such as general or skilled labor and restaurant/food worker.

Figure 4: Mean sedentary time across industry categories.



Excluding retired and unemployed participants, we observed a positive association of substantive complexity with sedentary time (Figure 5). Unemployed, retired, and substantive complexity levels ≥ 65 presented significantly higher sedentary times from the reference group, <60 (Appendix Figure 12). Greater than 78% of participants with occupations that have substantive complexity ≥65 were college graduates, whereas participants with occupations with substantive complexity <65, less than 45% graduated college (Appendix Figure 13).

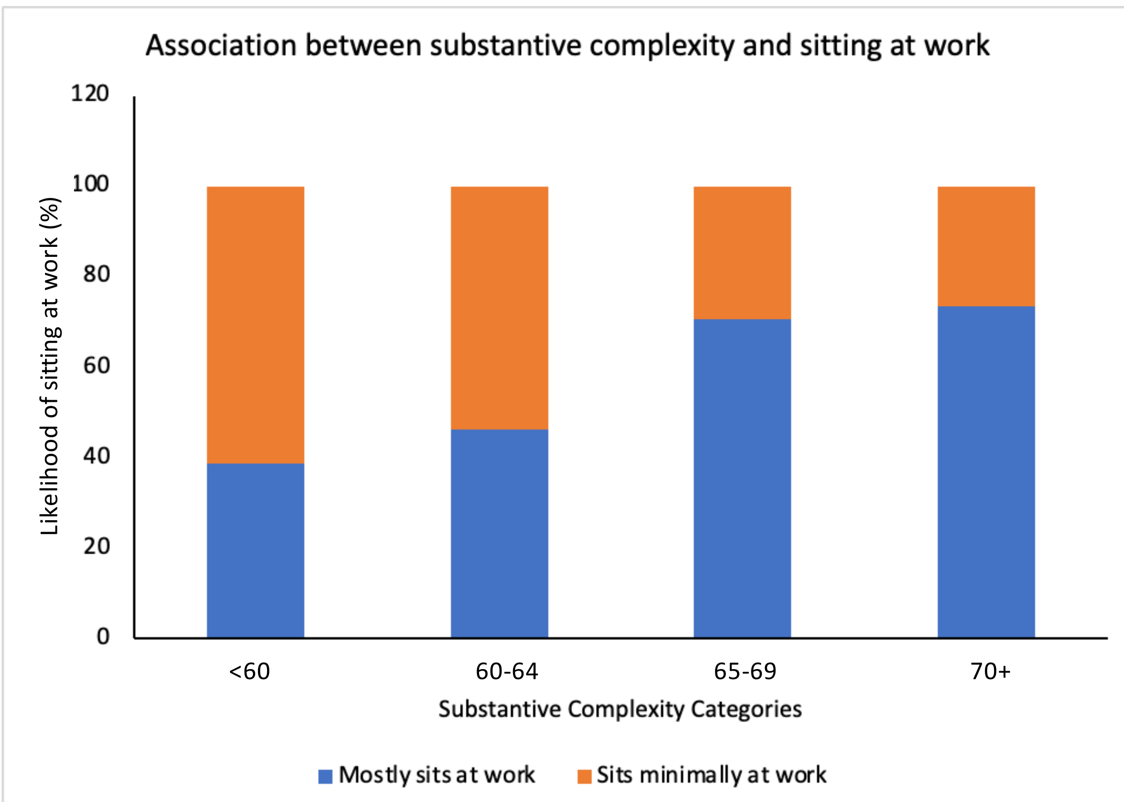
Figure 5: Least square means of objective sedentary time across categories of occupational substantive complexity in the currently employed (n=1821).



Adjusted for age, sex, and education. Education grouped into 2 categories: Did not graduate college (0-2) and college graduate (3) (0- high school did not graduate, 1- high school graduate, 2- some college, 3- college graduate). *Significantly different from reference substantive complexity <60 ($p<0.05$).

Occupational sedentary time was measured through a categorical variable, which asked "at work do you sit?" Excluding retired and unemployed participants, those with substantive complexity ≥65, over 70% reported mostly sitting at work (Figure 6). Whereas substantive complexity <65, presented below 50% of participants mostly sitting at work (38.6% and 46.3% respectively). This may indicate that more substantively complex occupations are more likely to be associated with sitting positions and/or higher sedentary time.

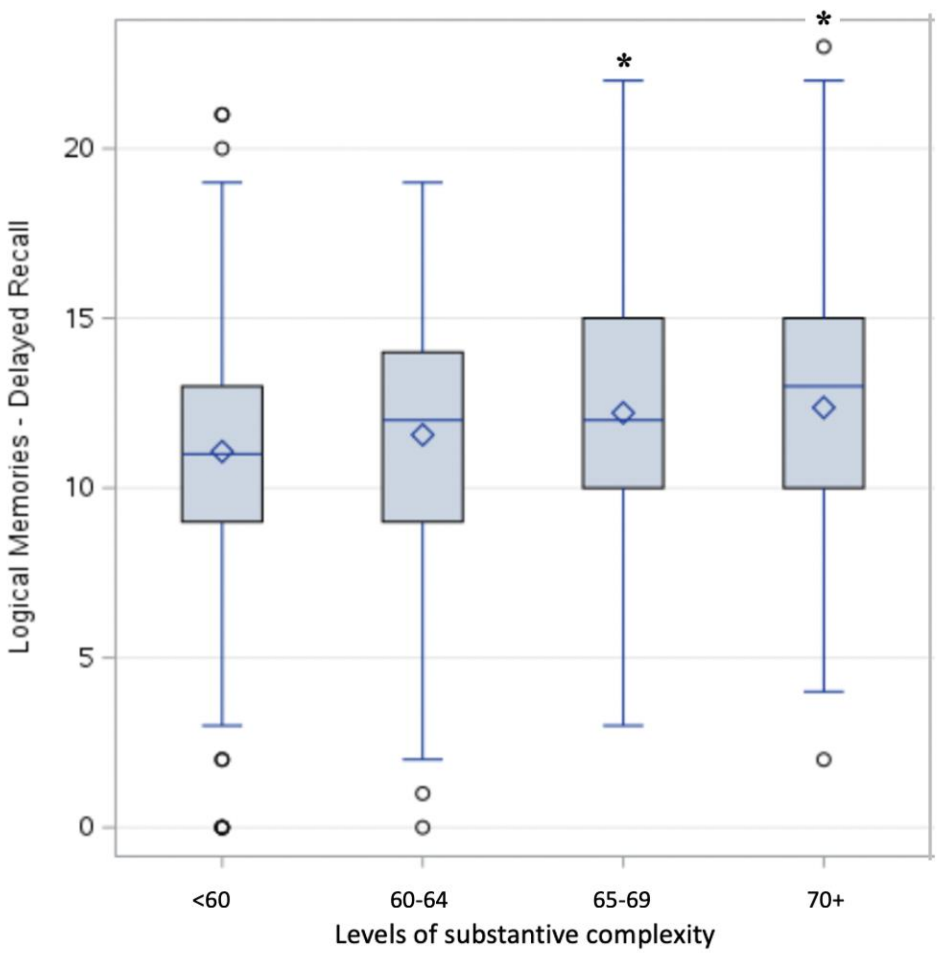
Figure 6: Likelihood of sitting at work across categories of occupational substantive complexity in the currently employed (n=1821).



Self-reported sitting at work grouped into 2 categories: unlikely to sit at work (0-2) and likely to sit at work (3-4) (0- never, 1- seldom, 2- sometimes, 3- often, 4- always).

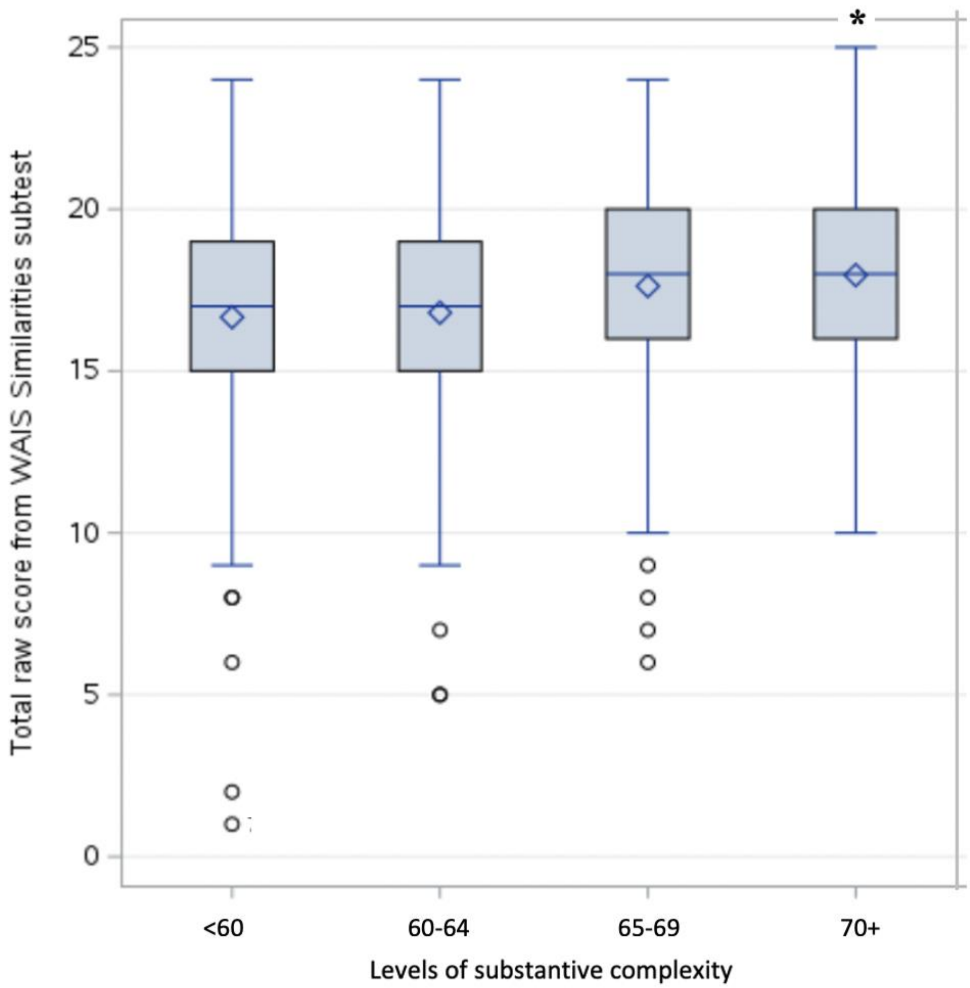
Excluding unemployed and retired participants, we observed a positive association of substantive complexity level with cognitive outcomes LMD, SIM, and TrailsB-A, after adjusting for age, sex, and education (Figure 7, 8, and 9). The higher the level of substantive complexity, the higher the cognitive outcomes of LMD, SIM, and TrailsB-A. Participants with substantive complexity levels ≥ 65, presented significantly higher LMD and TrailsB-A (higher memory and executive function) compared to the reference group <60 (p<0.05, Figures 7 and 9). Substantive complexity <65 did not present significantly different LMD or TrailsB-A results from the referent. Only substantive complexity ≥70 presented higher SIM (verbal comprehension) outcomes from the reference group (<60) (p=0.001, Figure 8). Retired participants only presented significantly different cognitive outcome LMD compared to reference group <60 (p=0.01). Unemployed participants only presented significantly different cognitive outcome TRAILSB-A compared to reference group <60 (p=0.04) (Appendix Figure 15, 16, and 17).

Figure 7: Least square means of cognitive outcome LMD across categories of occupational substantive complexity in the currently employed (n=1821).



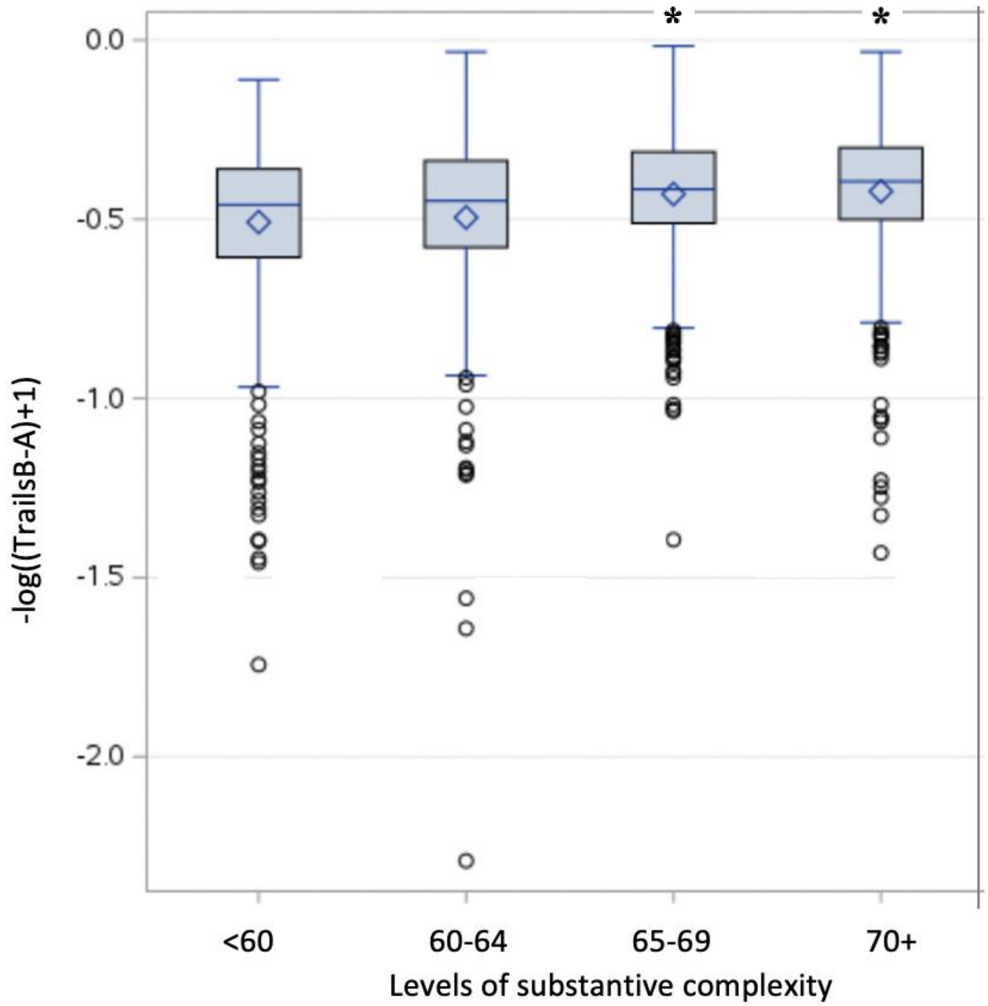
Adjusted for age, sex, and education. Education grouped into 2 categories: Did not graduate college (0-2) and college graduate (3) (0- high school did not graduate, 1- high school graduate, 2- some college, 3- college graduate). *Significantly different from reference substantive complexity <60 ($p<0.05$).

Figure 8: Least square means of cognitive outcome SIM across categories of occupational substantive complexity in the currently employed (n=1821).



Adjusted for age, sex, and education. Education grouped into 2 categories: Did not graduate college (0-2) and college graduate (3) (0- high school did not graduate, 1- high school graduate, 2- some college, 3- college graduate). *Significantly different from reference substantive complexity <60 (p<0.05).

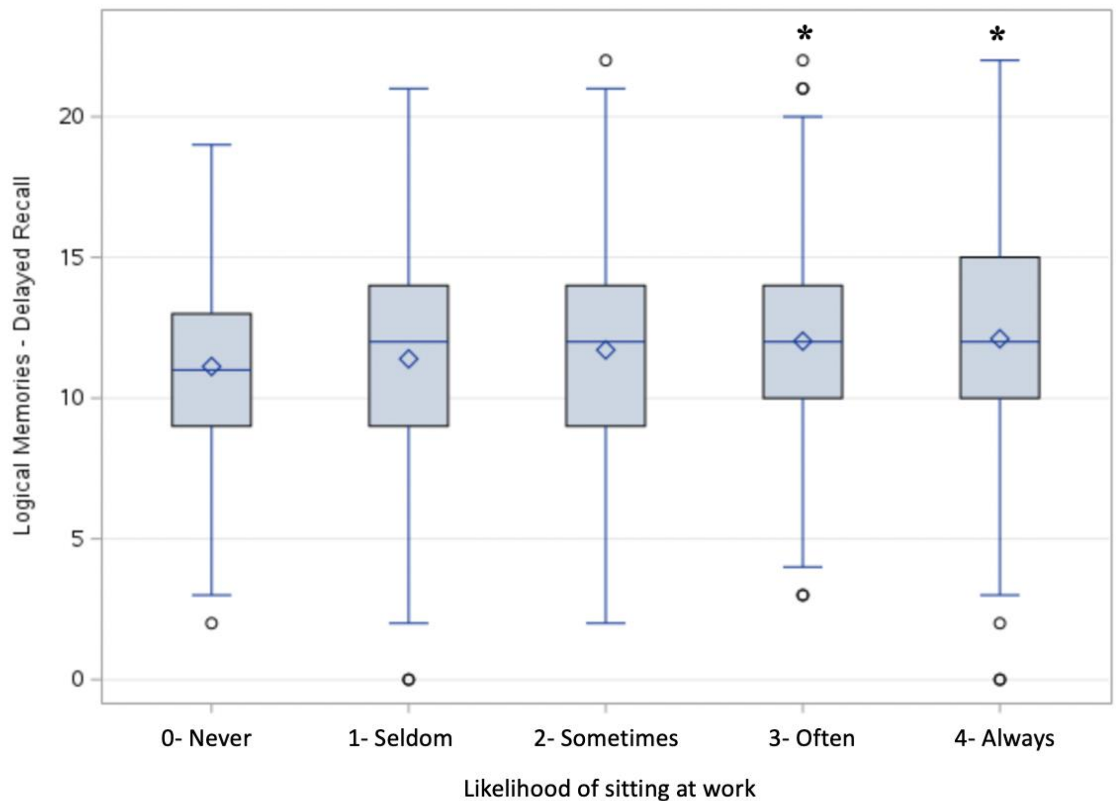
Figure 9: Least square means of cognitive outcome TrailsB-A across categories of occupational substantive complexity in the currently employed (n=1821).



N=1820. Adjusted for age, sex, and education. Education grouped into 2 categories: Did not graduate college (0-2) and college graduate (3) (0- high school did not graduate, 1- high school graduate, 2- some college, 3- college graduate). *Significantly different from reference substantive complexity <60 (p<0.05).

After excluding retired and unemployed participants, participants who reported that they were more likely to sit at work presented a higher mean LMD than those who were less likely to sit (Figure 10). Those who reported sitting at work often or always (3 and 4) had higher LMD compared to the referent group (0, never), p-values= 0.01, after adjusting for age, sex, and education.

Figure 10: Least square means of cognitive outcome LMD across categories of sitting at work in the currently employed (n=1821).



Excluding unemployed and retired participants. Adjusted for age, sex, and education. Education grouped into 2 categories: Did not graduate college (0-2) and college graduate (3) (0- high school did not graduate, 1- high school graduate, 2- some college, 3- college graduate). *Significantly different from reference likelihood of sitting at work, 0-never ($p<0.05$).

Excluding retired and unemployed participants, there was a positive association of self-reporting a higher likelihood of sitting at work and objective sedentary time with cognitive outcomes LMD, SIM, and TRAILSB-A, after adjusting for age and sex (Table

2, p<0.01). When additionally adjusting for education, the associations of self-reported sitting at work with LMD and SIM were attenuated (for SIM, the beta-estimate went from 0.48 [0.15], p=0.001 to beta=0.12 [0.15], p=0.4), but LMD remained borderline significant (the beta-estimate went from 0.061 [0.17], p=0.004 to beta=0.033 [0.017], p=0.06). After further adjustment for substantive complexity, the association with LMD was further attenuated and was no longer statistically significant (beta= 0.19 [0.18], p=0.3). The association of sitting at work with TRAILSB-A was slightly attenuated under model 3 conditions but remained significant (p= 0.002).

The association between objective sedentary time and all cognitive outcomes LMD, SIM, and TRAILSB-A were attenuated, but remained borderline statistically significant after adjusting for age, sex, and education in model 2 (beta-estimates were 0.11 [0.06], 0.09 [0.05], and 0.01 [0.004] for LMD, SIM, and TRAILSB-A respectively) (all p-values 0.05-0.1). These associations were fully attenuated after further adjusting for substantive complexity (beta-estimates were 0.06 [0.06], 0.05 [0.05], 0.003 [0.004] for LMD, SIM, and TRAILSB-A respectively) (all with p-values≥ 0.3). Sedentary time was slightly higher among college graduates (13.7 hours/day compared to 13.5 hours/day among those with a lower education level), but these differences were not large and had a similar range of 7 to 17.5 hours/day (Appendix Figure 14).

Including retired and unemployed participants, a positive association was observed between self-reporting a higher likelihood of sitting at work and objective sedentary time with cognitive outcome LMD when adjusting for age and sex (Tables 5 and 6) (beta estimates were 0.59 [0.17] and 0.16 [0.06] respectively) (p-values$\leq$ 0.01). When additionally adjusting for education and substantive complexity, the associations of self-reported sitting at work and objective sedentary time with LMD were attenuated and no longer statistically significant (beta estimates were 0.16 [0.18] and 0.08 [0.06] respectively) (p-values 0.2-0.4).

Table 2: Linear regression of self-reported likelihood of sitting at work and cognitive outcome (Learning Memory-delayed recall, SIM, and TrailsB-A) in the currently employed (n=1821).

		LMD		SIM		TRAILSB-A	
		Beta-estimate (SE)	p-value	Beta-estimate (SE)	p-value	Beta-estimate (SE)	p-value
Model 1	Self-reported likelihood of sitting at work	0.61 (0.17)	0.0004	0.48 (0.15)	0.001	0.06 (0.01)	<.0001
	Age	-0.05 (0.01)	<.0001	-0.01 (0.01)	0.126	-0.004 (0.001)	<.0001
	Sex	1.39 (0.17)	<.0001	-0.33 (0.15)	0.023	0.04 (0.01)	<.0001
Model 2	Self-reported likelihood of sitting at work	0.33 (0.17)	0.06	0.12 (0.15)	0.425	0.04 (0.01)	<.0001
	Age	-0.04 (0.01)	0.0002	-0.001 (0.01)	0.9	-0.003 (0.001)	<.0001
	Sex	1.37 (0.17)	<.0001	-0.36 (0.14)	0.012	0.04 (0.01)	<.0001
	Education	1.27 (0.18)	<.0001	1.63 (0.15)	<.0001	0.06 (0.01)	<.0001
Model 3	Self-reported likelihood of sitting at work	0.19 (0.18)	0.295	-0.03 (0.15)	0.861	0.03 (0.01)	0.002
	Age	-0.03 (0.01)	0.0005	0.001 (0.01)	0.901	-0.003 (0.001)	<.0001
	Sex	1.38 (0.16)	<.0001	-0.35 (0.14)	0.013	0.04 (0.01)	<.0001
	Education	1.08 (0.19)	<.0001	1.43 (0.16)	<.0001	0.05 (0.01)	<.0001
	Substantive complexity	0.04 (0.01)	0.001	0.04 (0.01)	<.0001	0.003 (0.001)	<.0001

Linear regression excluding unemployed and retired participants (n=1821) (TrailsB-A n=1820).
Model 1: adjusted for age and sex. Model 2 includes model 1 covariates, adding adjustment for education. Model 3 includes model 1 and 2 covariates, adding adjustment for substantive complexity.
Association estimates from regression models were considered significant at P<.05 level.
Education grouped into 2 categories: Did not graduate college (0-2) and college graduate (3) (0- high school did not graduate, 1- high school graduate, 2- some college, 3- college graduate).
Self-reported sitting at work grouped into 2 categories: unlikely to sit at work (0-2) and likely to sit at work (3-4) (0- never, 1- seldom, 2- sometimes, 3- often, 4- always).

Table 3: Linear regression of objective sedentary time and cognitive outcomes (Learning Memory-delayed recall, SIM, and TrailsB-A) in the currently employed (n=1821).

		LMD		SIM		TRAILSB-A	
		Beta-estimate (SE)	p-value	Beta-estimate (SE)	p-value	Beta-estimate (SE)	p-value
Model 1	Sedentary time	0.16 (0.06)	0.007	0.15 (0.05)	0.004	0.01 (0.004)	0.007
	Age	-0.04 (0.01)	<.0001	-0.02 (0.01)	0.07	-0.005 (0.001)	<.0001
	Sex	1.33 (0.16)	<.0001	-0.34 (0.14)	0.017	0.04 (0.01)	0.0002
Model 2	Sedentary time	0.11 (0.06)	0.068	0.09 (0.05)	0.087	0.01 (0.004)	0.066
	Age	-0.03 (0.01)	0.002	-0.002 (0.01)	0.784	-0.004 (0.001)	<.0001
	Sex	1.34 (0.16)	<.0001	-0.33 (0.14)	0.019	0.04 (0.01)	0.0001
	Education	1.32 (0.17)	<.0001	1.65 (0.15)	<.0001	0.08 (0.01)	<.0001
Model 3	Sedentary time	0.06 (0.06)	0.291	0.05 (0.05)	0.346	0.003 (0.004)	0.333
	Age	-0.03 (0.01)	0.003	-0.0004 (0.01)	0.962	-0.004 (0.001)	<.0001
	Sex	1.35 (0.16)	<.0001	-0.31 (0.14)	0.024	0.04 (0.01)	<.0001
	Education	1.1 (0.18)	<.0001	1.44 (0.15)	<.0001	0.06 (0.01)	<.0001
	Substantive complexity	0.04 (0.01)	0.0001	0.04 (0.01)	0.0001	0.003 (0.001)	<.0001

Education grouped into 2 categories: Did not graduate college (0-2) and college graduate (3) (0- high school did not graduate, 1- high school graduate, 2- some college, 3- college graduate).

DISCUSSION

It was recently reported in FHS that higher sedentary time was associated with higher cognitive function (Spartano et al., 2019). In the current investigation, we examined whether the relationship can be explained by higher substantive complexity among those that have higher sedentary behavior. We presented evidence suggesting that both education and substantive complexity partially explain the positive association observed between sedentary time and cognitive function in middle-aged adults.

The relationship between sedentary time and cognitive function, when adjusting for substantive complexity, can be understood through multiple aspects. We first observed trends of specific occupations correlating with higher or lower average sedentary time. These trends help initiate our reflection on the relationships between occupational sedentary time and substantive complexity. For example, the industry "banker" presented a higher mean sedentary time compared to others, indicating that a banker requires more sedentary time to fulfill their occupational duties. During that time of sedentary behavior, we can also consider their responsibilities. They are likely dealing with clients, managing accounts, and overseeing transactions, indicating a relative sense of cognitive demand or substantive complexity required by this occupation. On the contrary, food worker achieved a lower mean sedentary time compared to other industries. Food workers responsibilities may include prepping tables, taking and serving orders, and issuing bills and payments, duties that require less sedentary behavior and different levels of cognitive demand. These occupational responsibilities and demands contribute to where they fall on the sedentary time spectrum and are necessary to be mindful of when exploring this topic.

As shown in Figures 5 and 6, substantive complexity presented a positive association with sedentary time and sitting at work. We observed that more substantively complex jobs were more likely to have higher sedentary time; some examples include lawyer, judge, doctor, and dentist. This could be due to a variety of reasons such as more substantively complex jobs requiring more sedentary activities such as computer usage (administrative), consulting or counseling (banker), listening (judge), or tool usage such as a microscope (scientist). This helps understand why higher substantively complex jobs may require more sedentary behavior, influencing the cognitive effects of generalized sedentary behavior.

In support, prior studies have founded a positive association between education and late-life cognition (Fujishiro et al., 2017). In Figure 11, we can see that substantive complexity presented a positive association with education. Jobs with higher substantive complexity were more likely to have higher educational status. This is likely due to the demand, job requirements, and educational requirements of higher cognitively complex occupations. This helps further clarify the relationship between substantive complexity and sedentary time.

Sequentially, we observed a positive association between substantive complexity and cognitive outcomes LMD, SIM, and TRAILSB-A. Occupations with higher levels of substantive complexity were more likely to have higher cognitive outcomes, measured by LMD, SIM, and TRAILSB-A. Prior studies have confirmed the mentally protective features of specific cognitive stimuli; like a muscle, brain power is strengthened by usage (Kesse-Guyot et al., 2012). Consequently, higher cognitively demanding occupations presented higher memory outcomes possibly due to the cognitive lifestyle these occupations instill.

In this investigation, we also found that participants more likely to sit at work were more likely to have higher logical memory (LMD) than those who were less likely to sit at work. This reinforces that more sedentary-based positions may require more cognitive demand, leading to stronger cognitive reserve and outcomes. Although physical activity plays a key role in both brain and overall health by increasing blood flow, increasing molecular targets such as brain-derived neurotrophic factor, decreasing the number of stress receptors, and more, OCC may be an undermined factor in regard to cognitive longevity.

Occupation is a powerful choice that influences numerous aspects of people's lives, including income, insurance, food access, location, physical activity, education, children, interests, and more. It is said that one-third of your life is spent at work; the average person will spend 90,000 hours at work over a lifetime. Solely based on time, we are consciously and subconsciously influenced by everything that is encompassed by one's occupation. In this study, we challenge the stigmas around sedentary behavior and the significance of occupation. Sedentary behavior has been associated with negative inference, possibly due to the overpromotion of physical activity. In this study we expand the understanding of sedentary time in relationship with health and lifestyle, and how it is influenced by multiple factors, one being OCC.

Substantive complexity or OCC, spearheaded by the REGARDS investigators, explores the long-term effects of intellectually engaging environments and activities throughout adulthood. This focus has been understudied possibly due to the complexity encompassed in the variable itself, low demand of exploring sedentary behavior and health outcomes, focus of physical activity and health outcomes, and newer awareness of occupational and sedentary activities long-term effects. OCC has been founded to be a protector of later life cognitive function and may be a key factor to consider in future research, health prevention, and health policy.

Prior studies revolved around sedentary behavior and cognitive function support our findings. Prior studies founded how occupational complexity mediates the relationship between education and late-life cognition, as well as how physical activity at levels lower than the current PA guidelines were associated with better cognitive function (Fujishiro et al., 2017) (Spartano et al., 2019). Although this topic of investigation is still upcoming, it has initiated a sect of research for many future pursuits involved with sedentary behavior, health outcomes, and education policy.

Strengths and Limitations

A major strength of our study is both our primary exposure and outcome variables, sedentary time and memory, were objectively measured. Self-reported variables may introduce substantial misclassification. Few studies also assess sedentary behavior due to limited and difficulty in methods of measure, and priority of physical activity measure. Our Generation 3-based cohort at exam 2 were instructed to wear the accelerometer device 24 hours a day. Although this provides a more accurate method of measure, there are some sources of challenge due to difficulty in distinguishing between sleep time and sedentary time, and standing versus times when the device was not being worn.

A primary limitation is the cross-sectional nature of our investigation, where both the exposure and outcome were simultaneously assessed. Due to this study design, it is not possible to determine causation and a bidirectional relationship is likely. There is also limited generalizability across the study sample, as the Generation 3 based cohort included a small portion of ethnically and racially diverse adults.

Conclusion

Our findings indicate that the association of higher occupational sedentary time with higher cognitive function was partially explained by higher substantive complexity and education level in a cohort of middle-aged individuals. Occupations with higher OCC, often requiring higher education status, may contribute to cognitive resilience. Future research may be necessary to confirm that this resilience extends into older age.

APPENDIX

Figure 11: Mean substantive complexity across industry categories.

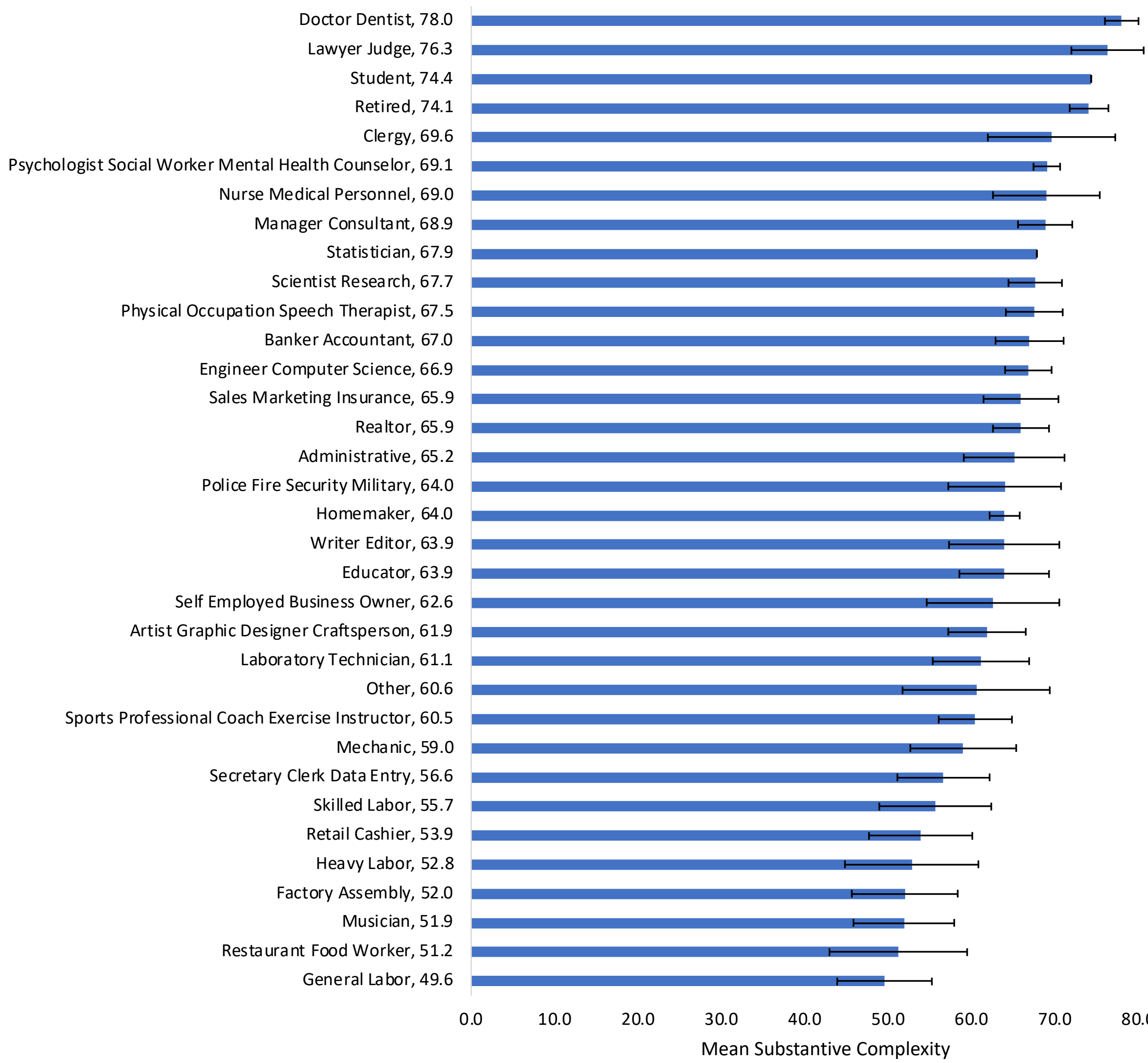
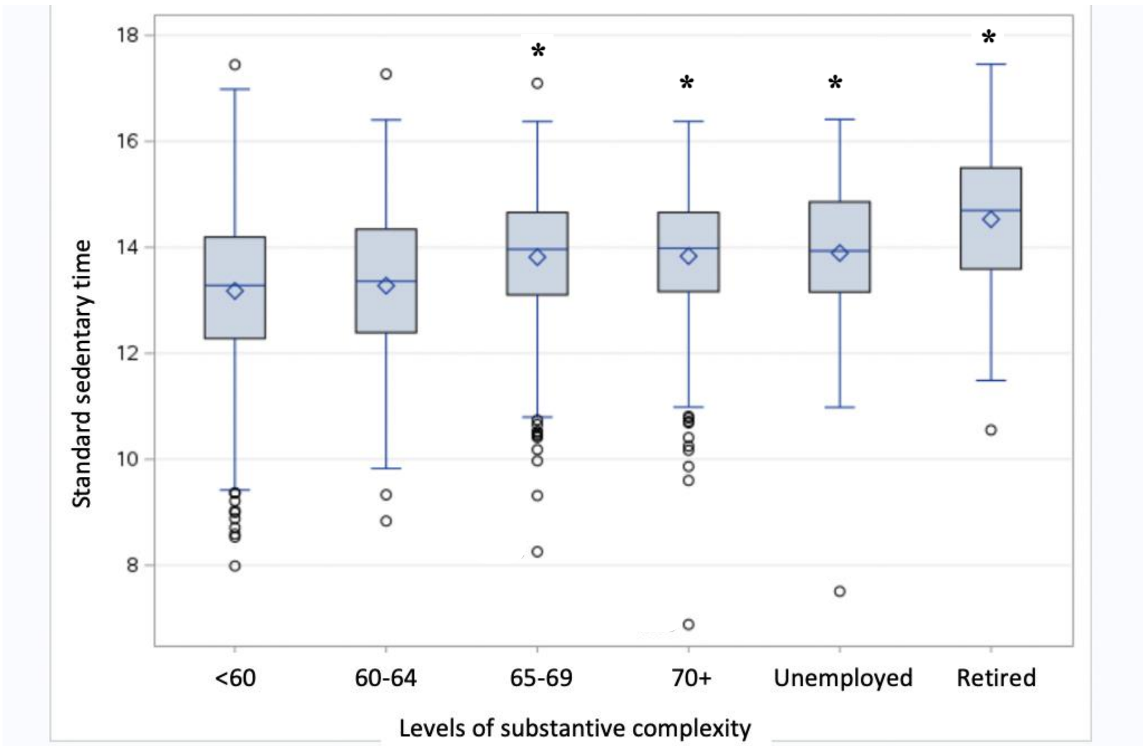


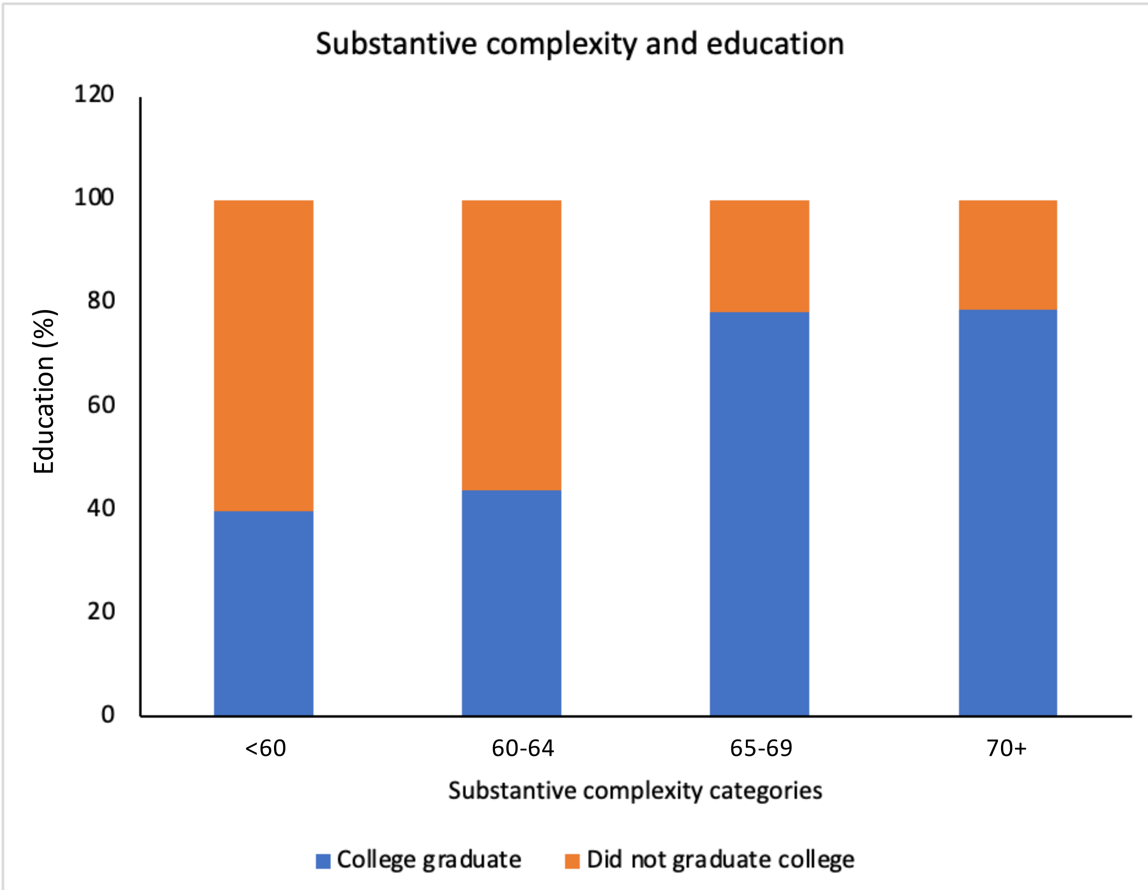
Figure 12: Least square means of sedentary time across categories of occupational substantive complexity in total study sample (employed, unemployed, and retired) (n=1959).



Level of Substantive_complexity_cat	N	stndrdsedtime1		AGE		SEX		EDUCGCAT	
		Mean	Std Dev	Mean	Std Dev	Mean	Std Dev	Mean	Std Dev
0,<60	516	13.1787717	1.52074145	49.2170543	8.43221860	1.55813953	0.49709020	1.39728682	0.48981114
1,60-64	252	13.2775345	1.43934585	47.6547619	8.00422306	1.65476190	0.47639201	1.43650794	0.49693935
2,65-69	577	13.8166968	1.21435631	46.9289428	8.82862361	1.48873484	0.50030681	1.78336222	0.41231115
3,70+	476	13.8352227	1.18961484	47.9117647	8.72724640	1.48319328	0.50024320	1.78781513	0.40928520
4,Unemployed	81	13.8937264	1.40317900	49.9259259	7.67427159	1.53086420	0.50215585	1.53086420	0.50215585
5,Retired	57	14.5299246	1.42382899	65.8070175	8.54700991	1.56140351	0.50062617	1.47368421	0.50374537

Adjusted for age, sex, and education. Education grouped into 2 categories: Did not graduate college (0-2) and college graduate (3) (0- high school did not graduate, 1- high school graduate, 2- some college, 3- college graduate). *Significantly different from reference substantive complexity <60 (p<0.05).

Figure 13: Education across categories of occupational substantive complexity.

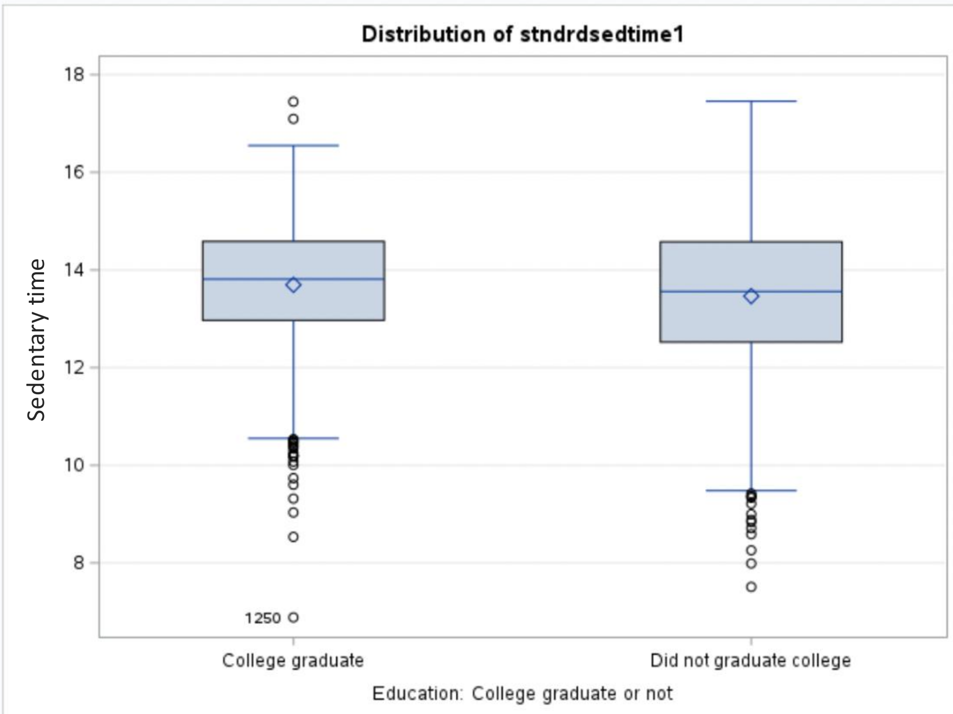


Education grouped into 2 categories: Did not graduate college (0-2) and college graduate (3) (0-high school did not graduate, 1- high school graduate, 2- some college, 3- college graduate).

Figure 14: Least square means of sedentary time across categories of education level in total study sample (employed, unemployed, and retired) (n=1959).

Assessing education and sedentary time, adjusted for age and sex

The GLM Procedure



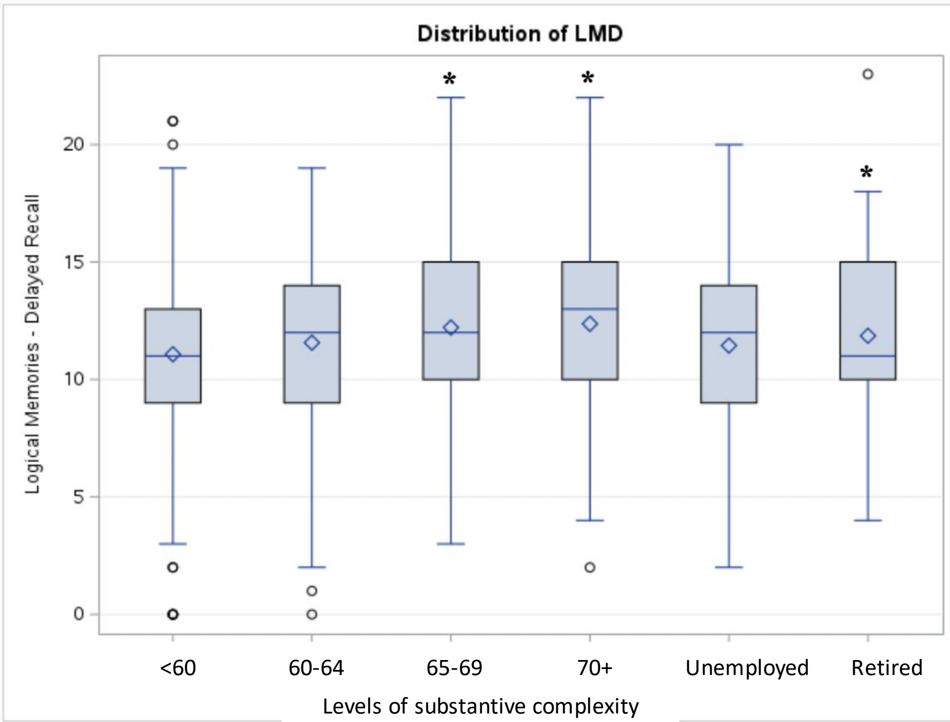
Level of EDUCGCAT	N	stndrdsedtime1		AGE		SEX	
		Mean	Std Dev	Mean	Std Dev	Mean	Std Dev
College graduate	1212	13.6955116	1.26438426	47.5057756	9.16330237	1.53052805	0.49927318
Did not graduate college	747	13.4653580	1.54058666	50.2101740	8.72440743	1.53145917	0.49934368

Adjusted for age and sex. Education grouped into 2 categories: Did not graduate college (0-2) and college graduate (3) (0- high school did not graduate, 1- high school graduate, 2- some college, 3- college graduate).

Figure 15: Least square means of logical memory across categories of occupational substantive complexity in total study sample (employed, unemployed, and retired) (n=1959).

Assessing substantive complexity and memory, adjusting for age sex and education

The GLM Procedure



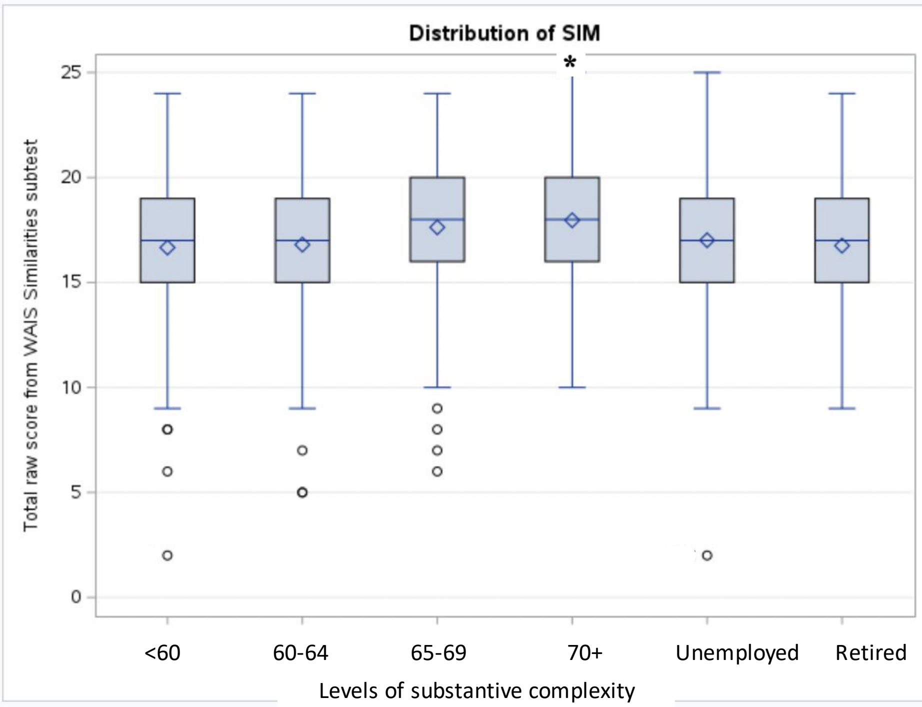
Level of Substantive_complexity_cat	N	LMD		AGE		SEX		EDUCG	
		Mean	Std Dev	Mean	Std Dev	Mean	Std Dev	Mean	Std Dev
0,<60	516	11.0736434	3.63990866	49.2170543	8.43221860	1.55813953	0.49709020	2.12209302	0.82357042
1,60-64	252	11.5674603	3.45826176	47.6547619	8.00422306	1.65476190	0.47639201	2.22222222	0.80227653
2,65-69	577	12.2131716	3.48029670	46.9289428	8.82862361	1.48873484	0.50030681	2.70883882	0.59669943
3,70+	476	12.3697479	3.44732524	47.9117647	8.72724640	1.48319328	0.50024320	2.73529412	0.55183342
4,Unemployed	81	11.4444444	3.96547601	49.9259259	7.67427159	1.53086420	0.50215585	2.24691358	0.90181573
5,Retired	57	11.8596491	3.80525293	65.8070175	8.54700991	1.56140351	0.50062617	2.19298246	0.87502238

Adjusted for age, sex, and education. Education grouped into 2 categories: Did not graduate college (0-2) and college graduate (3) (0- high school did not graduate, 1- high school graduate, 2- some college, 3- college graduate). *Significantly different from reference substantive complexity <60 (p<0.05).

Figure 16: Least square means of SIM across categories of occupational substantive complexity in total study sample (employed, unemployed, and retired) (n=1959).

Assessing substantive complexity and memory, adjusting for age sex and education

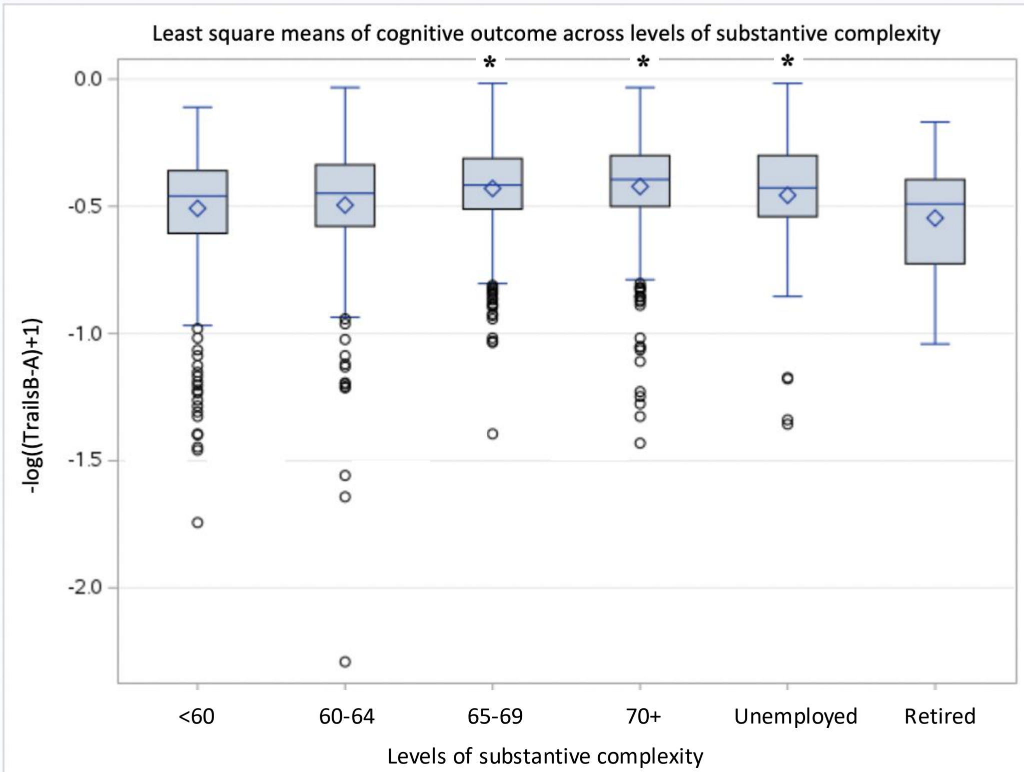
The GLM Procedure



Level of Substantive_complexity_cat	N	SIM		AGE		SEX		EDUCG	
		Mean	Std Dev	Mean	Std Dev	Mean	Std Dev	Mean	Std Dev
0,<60	516	16.6627907	3.18349066	49.2170543	8.43221860	1.55813953	0.49709020	2.12209302	0.82357042
1,60-64	252	16.8015873	3.40615763	47.6547619	8.00422306	1.65476190	0.47639201	2.22222222	0.80227653
2,65-69	577	17.6256499	2.87745679	46.9289428	8.82862361	1.48873484	0.50030681	2.70883882	0.59669943
3,70+	476	17.9621849	2.81698582	47.9117647	8.72724640	1.48319328	0.50024320	2.73529412	0.55183342
4,Unemployed	81	17.0123457	3.87134934	49.9259259	7.67427159	1.53086420	0.50215585	2.24691358	0.90181573
5,Retired	57	16.7543860	3.23640399	65.8070175	8.54700991	1.56140351	0.50062617	2.19298246	0.87502238

Adjusted for age, sex, and education. Education grouped into 2 categories: Did not graduate college (0-2) and college graduate (3) (0- high school did not graduate, 1- high school graduate, 2- some college, 3- college graduate). *Significantly different from reference substantive complexity <60 ($p<0.05$).

Figure 17: Least square means of TrailsB-A across categories of occupational substantive complexity in total study sample (employed, unemployed, and retired) (n=1959).



Level of Substantive_complexity_cat	N	trailsbma1L		AGE		SEX		EDUCG	
		Mean	Std Dev	Mean	Std Dev	Mean	Std Dev	Mean	Std Dev
0,<60	516	-0.50802055	0.23621498	49.2170543	8.43221860	1.55813953	0.49709020	2.12209302	0.82357042
1,60-64	252	-0.49498029	0.25263625	47.6547619	8.00422306	1.65476190	0.47639201	2.22222222	0.80227653
2,65-69	576	-0.42976061	0.16924519	46.9392361	8.83283137	1.48958333	0.50032598	2.70833333	0.59709441
3,70+	476	-0.42206877	0.19082735	47.9117647	8.72724640	1.48319328	0.50024320	2.73529412	0.55183342
4,Unemployed	81	-0.45662706	0.25632013	49.9259259	7.67427159	1.53086420	0.50215585	2.24691358	0.90181573
5,Retired	57	-0.54618990	0.22712500	65.8070175	8.54700991	1.56140351	0.50062617	2.19298246	0.87502238

Adjusted for age, sex, and education. Education grouped into 2 categories: Did not graduate college (0-2) and college graduate (3) (0- high school did not graduate, 1- high school graduate, 2- some college, 3- college graduate). *Significantly different from reference substantive complexity <60 ($p<0.05$).

Table 5: Linear regression of self-reported likelihood of sitting at work with cognitive outcome LMD in total study sample (employed, unemployed, and retired) (n=1959).

		Beta-estimate (SE)	p-value
Model 1	Self-reported likelihood of sitting at work	0.59 (0.17)	0.0005
	Age	-0.05 (0.01)	<0.0001
	Sex	1.40 (0.17)	<0.0001
Model 2	Self-reported likelihood of sitting at work	0.31 (0.17)	0.072
	Age	-0.04 (0.01)	0.0002
	Sex	1.38 (0.16)	<0.0001
	Education	1.24 (0.18)	<0.0001
Model 3	Self-reported likelihood of sitting at work	0.16 (0.18)	0.354
	Age	-0.03 (0.01)	0.0004
	Sex	1.38 (0.16)	<0.0001
	Education	1.04 (0.18)	<0.0001
	Substantive complexity	0.04 (0.01)	0.0007

Includes total study sample (1959). Model 1: adjusted for age and sex. Model 2 includes model 1 covariates, including adjustment for education. Model 3 includes model 1 and 2 covariates, adding adjustment for substantive complexity.
Association estimates from regression models were considered significant at P<.05 level.
Education grouped into 2 categories: Did not graduate college (0-2) and college graduate (3) (0- high school did not graduate, 1- high school graduate, 2- some college, 3- college graduate).
Self-reported sitting at work grouped into 2 categories: unlikely to sit at work (0-2) and likely to sit at work (3-4) (0- never, 1- seldom, 2- sometimes, 3- often, 4- always).

Table 6: Linear regression of sedentary time with cognitive outcome LMD in total study sample (employed, unemployed, and retired) (n=1959).

		Beta-estimate (SE)	p-value
Model 1	Sedentary time	0.16 (0.06)	0.005
	Age	-0.04 (0.01)	<0.0001
	Sex	1.35 (0.16)	<0.0001
Model 2	Sedentary time	0.12 (0.06)	0.043
	Age	-0.03 (0.01)	0.0006
	Sex	1.37 (0.16)	<0.0001
	Education	1.31 (0.16)	<0.0001
Model 3	Sedentary time	0.08 (0.06)	0.198
	Age	-0.03 (0.01)	0.0004
	Sex	1.37 (0.16)	<0.0001
	Education	1.10 (0.17)	<0.0001
	Substantive complexity	0.04 (0.01)	0.0002

Linear regression includes total study sample (1959). Model 1: adjusted for age and sex. Model 2 includes model 1 covariates, including adjustment for education. Model 3 includes model 1 and 2 covariates, adding adjustment for substantive complexity.
Association estimates from regression models were considered significant at P<.05 level.
Education grouped into 2 categories: Did not graduate college (0-2) and college graduate (3) (0-high school did not graduate, 1- high school graduate, 2- some college, 3- college graduate).

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