EFFECT OF FAMILY HISTORY OF DEMENTIA AND SELF-REPORT OF SLEEP QUALITY ON COGNITIVE PERFORMANCE IN HEALTHY OLDER ADULTS

By

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Abstract

This study sought to identify the effect of family history of dementia and sleep quality on cognitive performance in a cohort of healthy older adults (n=89). Cognitive abilities were assessed using a comprehensive neuropsychological battery. The tested domains included memory, executive function, visuospatial abilities, motor function, processing speed, and language abilities. Subject family history was obtained by self report, and sleep quality was quantified using the Pittsburgh Sleep Quality Index (PSQI). Participants were divided into four groups by family history of dementia and sleep quality. Results indicated no significance effects for memory or executive function, but effects were found in visuospatial and motor tasks. It was observed that subjects without family history of dementia and good quality sleep had better performance on visuospatial tasks, supporting the notion that these factors may have protective functions in cognitive decline.

Introduction

Aging and Cognition

Aging reflects a natural process of many physiological changes, and it has been well established that a general decline in cognitive performance is closely linked with aging. Key effects have been noted in five major cognitive domains—executive function, memory, processing speed, language, and visuospatial function—in healthy older adults (Alexander et al., 2012). It has been established that memory, processing speed, and executive function are the most affected of these domains. Problems arise in memory, particularly in semantic memory retrieval tasks (Nyberg et al., 2003), although preservation of semantic memory itself is relatively stable. Episodic memory, on the other hand, tends to decline with age (Nilsson et al., 2002). Decline in processing speed has also been noted across older age groups. In the executive function domain, age effects have been found in global task switching (Verhaeghen and Cerella, 2002) and proactive interference tasks (Hasher et al., 2007). In other cognitive domains, older adults experience difficulties with language skills, particularly in word retrieval (Kaplan et al., 1983). Additionally, decline in visuospatial function has been closely linked to memory processes that experience age related effects (Moye, 1997).

Effects of Family History of Dementia on Cognitive Decline

While healthy aging is associated with general cognitive decline, other factors may accelerate the process. Genetic susceptibility of dementia and its impact on cognition has been examined, and it has been noted that one's risk of developing dementia is greatly increased if their parents had dementia (Wang et al., 2012). One study

that studied interactions between the genetic risk of dementia and cognitive performance observed significant effects on visuospatial function on subjects with at least one copy of the apolipoprotein ε (APOE) ε4 allele. APOE is a gene that makes the protein apolipoprotein E, and the ε4 allele has been associated with being a significant genetic risk factor for Alzheimer's disease. It has been observed that having one ε4 allele is associated with a three-fold risk of developing Alzheimer's Disease, while having two copies or being homozygous for the ε4 allele is associated with an eight-fold risk of developing Alzheimer's Disease (Jonaitis et al., 2013). Research has also more closely investigated the role of family history of dementia—specifically Alzheimer's disease—in relation to structural brain changes that can reflect cognitive decline. In subjects with family history of dementia, a thinner cortex in the "entorhinal region, subiculum, and adjacent medial temporal lobe subfields" of the hippocampus was observed (Donix et al., 2010). In the brain, the hippocampus is closely linked with memory, and, in turn, any degeneration of the hippocampus may result in cognitive decline in memory. Studies have addressed the decline in memory in elderly adults with family history of dementia—first degree biological relatives of individuals with Alzheimer's disease performed more poorly on memory function tasks than those who did not. Additionally, it has been observed that individuals with family history of dementia tend to rely on immediate memory compared to episodic memory (Donix et al., 2010). Furthermore, research has been done to study other areas of cognitive performance of individuals with family history of dementia. It was found that, compared to subjects without any family history of dementia, subjects with family history of Alzheimer's disease performed significantly

worse—in addition to memory tasks—executive functioning, and processing speed tasks (Donix et al., 2012).

Family history of dementia data can be collected based on self-report. This self-report includes information regarding what blood relatives, if any, had or currently has dementia, as well as the age of onset. First and second degree relatives are included in the self-report, with first degree relatives being parents, siblings, or children. Second degree relatives consist of cousins, aunts, uncles, grandparents, or half siblings.

Effects of Sleep on Cognitive Decline

Additionally, it is commonly acknowledged that sleep plays a critical role in cognition; particularly in poor quality sleep and its relationship with decreased cognitive performance. Studies have indicated that both total and partial sleep disturbance and sleep loss are associated with deficits in attention, executive function, and memory. (Kronholm et al., 2009). The effects of poor sleep quality are increasingly prevalent in older adults who already experience cognitive decline due to the effects of aging. Increasing age correlates with decreasing sleep quality, including lower overall sleep duration, decreased REM sleep time, and more sleep fragmentation. These effects have been attributed to common sleep disorders in older adults such as insomnia, restless limb syndrome, and sleep disordered breathing (Cochen et al., 2009). In a study examining the impact of sleep problems on 'healthy, dependent, and frail older adults', physiological changes in sleep were found to be the result of an "interaction between a reduction in the homeostatic drive for sleep, and a reduced strength of the circadian signal", both of which are linked to decreased melatonin secretion, that occurs as a result of aging (Cochen et

al., 2009). Additionally, sleep deprivation has been linked with an increase in amyloid-β concentrations, which in turn may result in changes in sleep patterns and overall increased wakefulness. Overall, this can negatively affect cognitive performance (Yaffe et al., 2014).

Sleep quality can be evaluated in several ways, including actigraphy or self-report. Actigraphy is a non-invasive method to track physical movement, which can therefore yield insightful data on how a person sleeps. It is then possible to accurately evaluate one's sleep quality and to clinically observe insomnia, restless leg syndrome, or other sleep disorders. Additionally, sleep quality can be measured and quantified based on self-report, by, for example, the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989). This self-report includes questions regarding one's usual sleep habits, such as the time one usually goes to bed, or whether one has trouble sleeping. Overall, this allows for a comprehensive evaluation of one's sleep quality.

Present Study

It is clear that both the risk of dementia and poor sleep have detrimental effects on normal aging, which in turn, can lead to even greater cognitive decline that occur in otherwise healthy aging. However, what has not been thoroughly explored is the interaction of these two risk factors of family history of dementia and sleep quality in healthy older adults and how that might affect cognitive performance.

Therefore, the purpose of this study is to examine the relationship between family history of dementia, sleep quality, and cognitive performance in older adults. The main

hypothesis tested is that individuals with family history of dementia as well as self reported poor sleep will perform more poorly on cognitive domain tasks of memory, executive function, and processing speed than other groups. I also hypothesize that groups with a family history of dementia and poor sleep quality will each individually show decreasing levels of cognitive function. Examining these relationships and effects of family history of dementia in good and poor quality sleepers on cognitive performance may provide interesting information regarding the impact of these risk factors on cognitive aging, and may also raise awareness in terms of which factors are most important for determining cognitive decline in older adults.

Methods

Participants

For this study, 89 neurologically healthy older adults 60-89 years of age were selected from a cohort of 210 subjects from a healthy aging longitudinal study conducted by the Brain Imaging, Behavior, and Aging Lab at the University of Arizona. All subjects were assessed and screened medically and neurologically, and were excluded if their Mini Mental State Exam (MMSE) (Kurlowicz, et al., 1999) score was below 26 and if they scored higher than a seven on the Hamilton Depression Rating Scale (HDRS) (Hamilton, 1960). All subjects were matched for age, gender, education, and hypertension. Of the 89 subjects (51 females, 38 males) 30 individuals were determined hypertensive by self report.

In order to group the subjects by sleep quality (quantified by the Pittsburgh Sleep Quality Index) and family history of dementia (quantified by self-report), subjects were divided into those with a PSQI score greater than five as being poor sleepers, and those with a PSQI score less than or equal to five as being good sleepers (Buysse et al., 1989). In turn, participants with any first or second-degree relatives with dementia were included in the family history of dementia group. Of the 89 subjects, 44 participants were good sleepers with 19 of these participants having family history of dementia. Of the 45 poor sleepers, 23 individuals self reported family history of dementia. As previously noted, all four groups were matched for age [$F(3, 85) = 0.894$, $p = 0.448$], education [$F(3,85) = 0.780$, $p = 0.508$], gender [Chi-Square = 0.561, $p = 0.454$], and hypertension [Chi-Square = 0.756, $p = 0.385$].

Neuropsychological Measures

In order to assess cognitive function, a comprehensive neuropsychological battery was used to evaluate six major cognitive domains consisting of memory, executive function, language, processing speed, visuospatial skills, and motor abilities. Memory tasks employed in this study include the Bushke Selective Reminding Test (BSRT) Sum Recall, BSRT Delayed Recall, BSRT Long Term Retrieval, BSRT Continuous Long Term Retrieval, which assess verbal memory (Buschke, 1973). Additionally, to test visual memory, the Rey Ostrieth Complex Figure Test (RCFT) Delay was used (Meyers, 1955). Executive function tasks included the Paced Auditory Serial Addition Test (PASAT), Stroop Word-Color Interference Test, Trail Making Test (TMT) Part B, and Wechsler Adult Intelligence Scale – IV (WAISIV) Matrix Reasoning (Gronwall, 1977;

Stroop, 1935; Reitan R., 1958; Wechsler, 2008). Tasks that assess processing speed included the Wechsler Adult Intelligence Scale – IV Symbol Search and Coding as well as TMT A and B. Language was measured by the Wechsler Adult Intelligence Scale subtests Similarities, Vocabulary, Information, and Letter Fluency (FAS). Visuospatial function was measured by the WAISIV subtests Block Design and Visual Puzzles. The Finger Tapping test and Grooved Pegboard test with both dominant and non-dominant hands were used to measure motor functionality (Reitan and Wolfson, 1993).

Statistical Analysis

In order to assess the cohort's matching for demographics and clinical variables, chi-squared tests and ANOVAs were used to test subject groups in terms of age, gender, education, hypertension, and IQ. This was to ensure that there were no significant differences between the groups in relation to these variables. In order to examine the influences of sleep quality and family history of dementia on cognitive function, ANOVAs were used to assess the performance of the four subject groups in relationship to the cognitive domain tasks. Main effects and means were compared, and significance differences were observed in the tests of between subjects effects in the PSQI and family history subject groups individually, as well as the interaction between the two groups. If a significant interaction ($p \leq 0.05$) occurred, directionality of performance was assessed by observing the mean results from each of the four groups. To quantitatively evaluate the simple effects for any significant interactions, ANCOVAS were performed between the four subject groups. Covariates included in the ANOVAS were age, gender, education, hypertension, and overall IQ (WAIS-IV FSIQ).

Results

Results of ANOVA indicated a two-way interaction effect that remained significant after covarying age, hypertension, gender, education, and IQ for the WAIS-IV Visual Puzzles test ($F(1, 81) = 5.687$, $p = 0.014$), with good sleepers without family history of dementia performing better than good sleepers with family history of dementia ($F(1,42) = 4.552$, $p = 0.039$) (Figure 1). Additionally, there was a two-way interactive effect of family history of dementia and sleep quality for visuospatial function in the WAIS-IV Block Design ($F(1, 85) = 4.015$, $p = 0.048$) (Figure 6). A simple effect test indicated a trend that poor sleepers with family history of dementia performed better on this task than poor sleepers without family history of dementia ($F(1,43) = 3.968$, $p = 0.053$). However, the addition of covariates resulted in non-significant effects.

Significance was also noted in motor tasks. There was a two-way interaction for family history of dementia and sleep quality of the Finger Tap Dominant Hand task ($F(1,81) = 4.527$, $p = 0.014$) (Figure 2), with poor sleepers with family history of dementia performing better than good sleepers with family history of dementia ($F(1,36) = 6.994$, $p = 0.010$). This result remained significant after covarying age, gender, hypertension, education, and IQ ($F(1,36) = 5.987$, $p = 0.012$). Additionally, a main effect due to family history of dementia was noted for the Grooved Pegboard Dominant Hand task ($F(1,83) = 4.917$, $p = 0.029$), with individuals without family history of dementia performing better than those with family history of dementia ($F(1,84) = 4.512$, $p = 0.038$) (Figure 3). However, this result was not significant after covarying for age ($F(1,83) = 3.891$, $p = 0.047$). While we found these results for visuospatial and motor function, there

was no statistical significance in the performance of subject groups in relation to memory or executive function. There was an trend from interaction that remained consistent despite the addition of covariates for WAIS-IV Matrix Reasoning ($F(1,85) = 3.581$, $p = 0.062$).

Discussion

In this study, we examined the effects of family history of dementia and sleep quality on cognitive function. We hypothesized that those subjects with a family history of dementia and poor sleep quality would perform the most poorly on cognitive domain tasks than subjects without family history of dementia and or with good sleep quality. Additionally, we expected to find that individuals with family history of dementia would perform more poorly on cognitive tasks than individuals without family history of dementia. It was also expected that individuals with poor sleep quality would perform more poorly on cognitive tasks than individuals with good sleep quality. We hypothesized to find that memory and executive function would be most affected by these variables. Results indicated no significant effect of these variables on memory or executive function, therefore not supporting my hypothesis. However, there was a significant trend in the WAIS-IV Matrix Reasoning Task. Notably, there were significant two-way interactive effects of family history of dementia and sleep quality in visuospatial and motor tasks, with an additional main effect of family history of dementia on the Grooved Pegboard Dominant Hand Task. For the two-way interactive effect for WAIS-IV Block Design, the better performing group was the family history of dementia and poor sleep group, which was contrary to my hypothesis. For the two-way interaction on

the WAIS-IV Visual Puzzles, the best-performing group was subjects without family history and with good sleep, furthermore supporting the main hypothesis. However, poor sleepers appeared to be performing better than good sleepers. These results may be due to possible outliers or other influential variables such as differences in diet and exercise. Additionally, having a small cohort with relatively few severe cases of family history of dementia and poor sleep may have contributed to the lack of significant effects in memory and executive function.

In the case of motor function in the Finger Tap Dominant Hand Task, the best performing group was the family history of dementia and poor sleeper group. Given the hypotheses, this group was expected to perform the most poorly. This may be due to individual differences in the sample. It is possible that some subjects had better fine motor skills, which may need to be assessed further for a more accurate representation of motor skills among the subjects. The main effect of family history of dementia for the Grooved Peg Board task supports the hypothesis that individuals with family history of dementia will have poorer cognitive abilities than those without.

A strength of this study was the extent of data available from this cohort. A smaller sized cohort allowed for more health and neuropsychological measures, which therefore allows for a more comprehensive assessment of cognitive ability. In contrast, epidemiological studies do not allow for such comprehensive and intensive assessments. Although a larger cohort yields a more expansive and general representation of a population, it is more difficult to collect specific and comprehensive data on the subjects. However, this study did have its limitations. Each group in this study contained only about 20 subjects, which is a small sample size due to filtering the groups by age, family

history of dementia, and PSQI. Therefore, the power to observe any significant effects, particularly in memory and executive function, was notably reduced. Additionally, in the original sample of 210 subjects, there were not many severe cases of poor sleep quality and family history of dementia, since participants were selected based on good health from the population. This also may have contributed to the decreased power in finding more significant effects in the cognitive tasks.

For further future research, it may be beneficial to improve the quality of the sleep data collected in terms of accuracy. PSQI sleep quality is based on self report, which may not be very reliable. An alternative option is the use of actigraphy in order to monitor and measure one's physical activity during the day, specifically during sleep. Additionally, because family history of dementia was also a self-report, perhaps it may be beneficial to target genetic risk factors such as APOE E4, which could be documented through DNA samples. The caveat, however, is that while this gene is complementary to family history of dementia, the two variables are not completely separable. Overall, a more accurate representation of sleep quality and family history of dementia could be improved with these measures, which can therefore yield more representative results from this type of study.

While results did not support effects of family history of dementia and sleep quality on memory and executive function, we did find some significant effects in visuospatial and motor function. These findings suggest that family history of dementia and sleep quality may have an important interactive role in understanding individual differences in cognitive aging, but the results were variable across different areas of cognition. These results support the variability of cognitive decline, and how aging can

be an individualistic process that requires extensive research in order to be better understood. The foundation of this study, with improved experimental measures, may help to better represent the process of aging and to allow for the development of preventative measures against cognitive decline in older adults.

Table 1. Subject Characteristics

	Good Sleepers		Poor Sleepers	
	FH-	**FH+**	**FH-**	**FH+**
N	25	19	22	23
Age (yrs)	77.6 (7.3)	76.1 (7.6)	78.9 (8.0)	75.6 (6.7)
Education (yrs)	16.1 (2.4)	16.4 (2.9)	15.3 (2.4)	15.9 (2.5)
Gender (M/F)	13/12	6/13	9/13	10/13
MMSE	28.8 (0.9)	28.5 (1.3)	29.1 (0.8)	29.1 (1.2)
HHTN	10	6	7	7
HDRS	1.1 (1.4)	1.2 (1.1)	1.8 (1.4)	2.6 (2.1)
PSQI	2.8 (1.4)	3.4 (1.2)	8.3 (2.0)	7.6 (2.1)

Table 1. Data represents mean (SD). Groups did not differ in the demographic and cognitive measures. FH = Family History of Dementia, M/F = Male/ Female, MMSE = Mini Mental State Examination, HHTN = hypertension (self-report), HDRS = Hamilton Depression Rating Scale, PSQI = Pittsburgh Sleep Quality Index

Table 2. Neuropsychological Test Performance

	Mean (SD)				p - values		
	Good Sleepers		Poor Sleepers		Main Effect:	Main Effect:	FH x
Visuospatial	**FH-**	**FH+**	**FH-**	**FH+**	**FH**	**PSQI**	**PSQI**
WAIS-IV BD*	33.12 (10.7)	31.17 (8.6)	29.64 (8.9)	35.61 (11.1)	0.422	0.717	0.048
WAIS-IV VP*	12.16 (3.6)	10.05 (2.7)	10.55 (3.0)	12.13 (4.2)	0.725	0.755	0.014
Motor							
Finger Tap DH*	39.992 (10.2)	35.347 (7.1)	36.591 (8.3)	40.552 (5.5)	0.806	0.441	0.014
Grooved Pegboard DH**	110.8 (24.7)	99.4 (29.0)	115.8 (36.3)	99.31 (26.7)	0.029	0.697	0.720
Executive							
WAIS-IV DS*	25.92 (5.0)	28.47 (4.4)	26.59 (5.4)	26.57 (3.6)	0.489	0.824	0.026
WAIS-IV MR	15.4 (4.7)	12.89 (5.1)	13.91 (4.7)	15.22 (4.3)	0.554	0.681	0.062
FAS Total	45.62 (13.5)	43.19 (12.4)	47.59 (12.3)	45.73 (13.7)	0.087	0.873	0.886
Stroop WC	32.84 (9.3)	35.61 (8.6)	33.73 (7.9)	34.22 (9.7)	0.895	0.967	0.546
Memory							
BSRT Sum Recall	103.9 (20.3)	108.5 (21.2)	95.97 (18.9)	102.8 (19.1)	0.650	0.794	0.502
BSRT Del Recall	8.01 (2.9)	8.35 (2.8)	7.44 (2.5)	8.37 (2.3)	0.921	0.975	0.384
RCFT Delay	15.61 (6.6)	17.08 (7.4)	12.45 (5.7)	13.83 (6.3)	0.698	0.486	0.923
Processing Speed							
WAIS-IV SS	25.24 (7.5)	27.89 (8.5)	23.14 (6.6)	24.78 (6.3)	0.527	0.098	0.675
TMT A	36.34 (11.3)	37.36 (18.2)	35.62 (10.3)	37.11 (14.0)	0.245	0.774	0.98
TMT B	76.14 (27.2)	84.31 (50.8)	87.38 (29.8)	88.59 (39.3)	0.250	0.421	0.73
Language							
WAIS-IV SI	26.76 (3.7)	26.22 (4.7)	26.45 (3.3)	27.04 (4.6)	0.468	0.608	0.576
WAIS-IV VC	44.80 (7.5)	45.50 (6.9)	45.59 (6.6)	44.26 (8.6)	0.446	0.912	0.614

Table 2. (A) Results for measures of cognitive performance between participants with (FH+) and without (FH-) family history of dementia and good and poor sleepers after controlling for gender, education, hypertension, and IQ. (B) (*) Indicates significance for the interactive effect of Family History and PSQI Total. (**) indicates significance for the main effect of family history. (C) To note: significant interactive effect was only present for WAIS-IV BD without covariates. Significant interactive effect was only present for WAIS-IV DS after covarying for IQ. WAIS-IV MR only showed a trend for an interactive effect after controlling for all covariates. All other main effects and interactions were not significant.

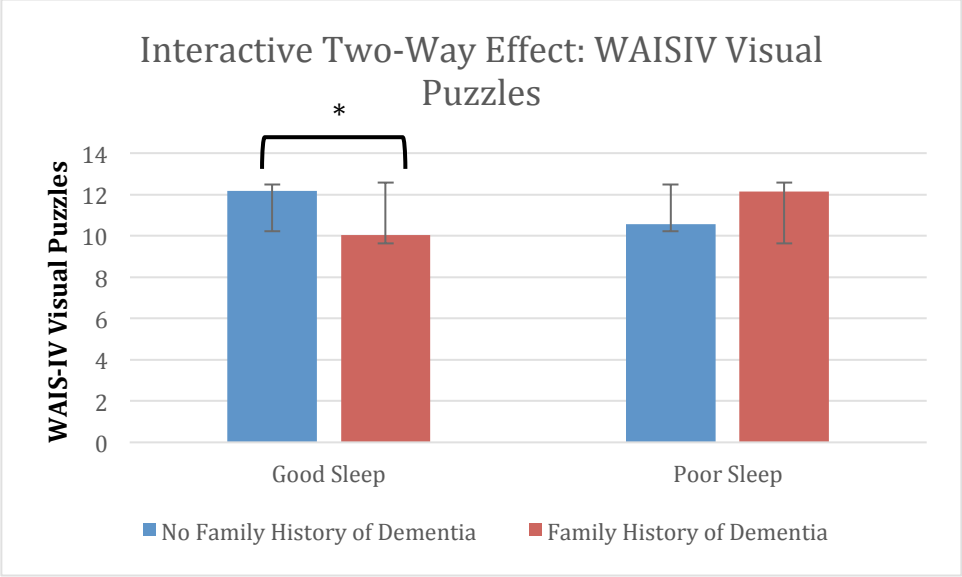

Figure 1. Interactive effects of family history of dementia and sleep quality on performance on the Wechsler Adult Intelligence Scale-IV Visual Puzzles after controlling for gender, education, hypertension, and IQ (p=0.048). Good sleepers without family history of dementia performed better than good sleepers with family history of dementia (p=0.039)

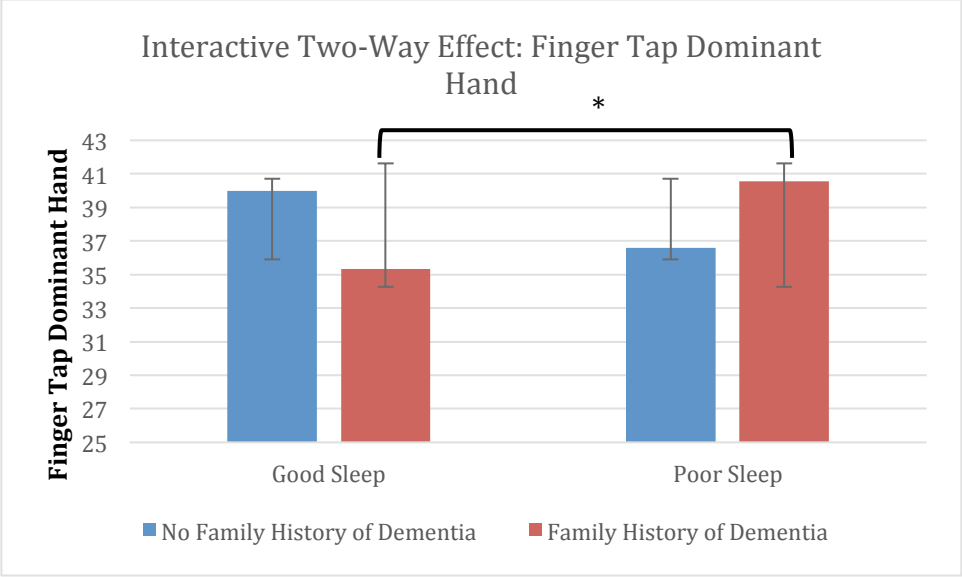

Figure 2. Interactive effects of family history of dementia and sleep quality on performance on the Finger Tap Dominant Hand after controlling for gender, education, hypertension and IQ (p=0.014). Poor sleepers with family history of dementia performed better than good sleepers with family history of dementia (p=0.010)

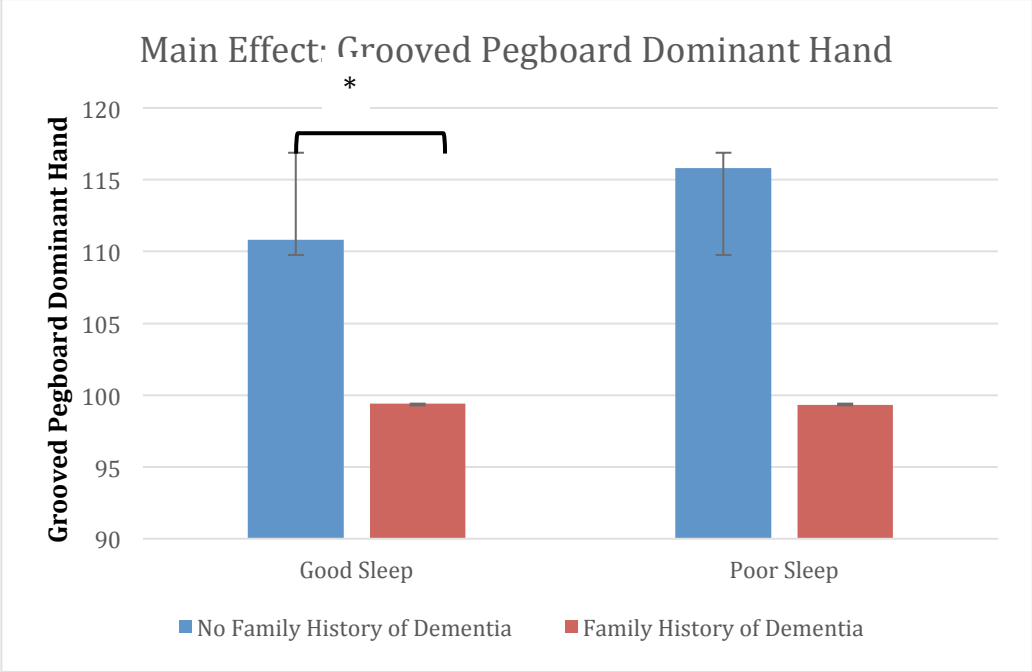

Figure 3. Main effect of family history of dementia on performance on the Grooved Peg Dominant Hand after controlling for gender, education, hypertension and IQ (p=0.029). Subjects without family history of dementia performed better than subjects with family history of dementia (p=0.038)

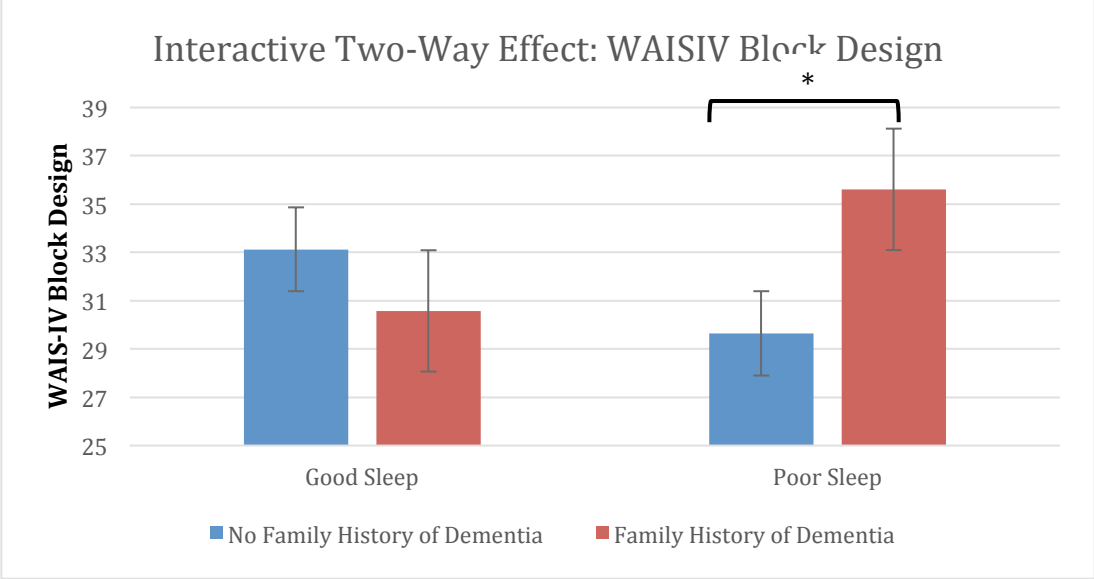

Figure 4. Interactive effects of family history of dementia and sleep quality on performance on the Wechsler Adult Intelligence Scale-IV Block Design without controlling for covariates (p=0.048). Trend: poor sleepers with family history of dementia performed better than poor sleepers without family history of dementia (p=0.053)

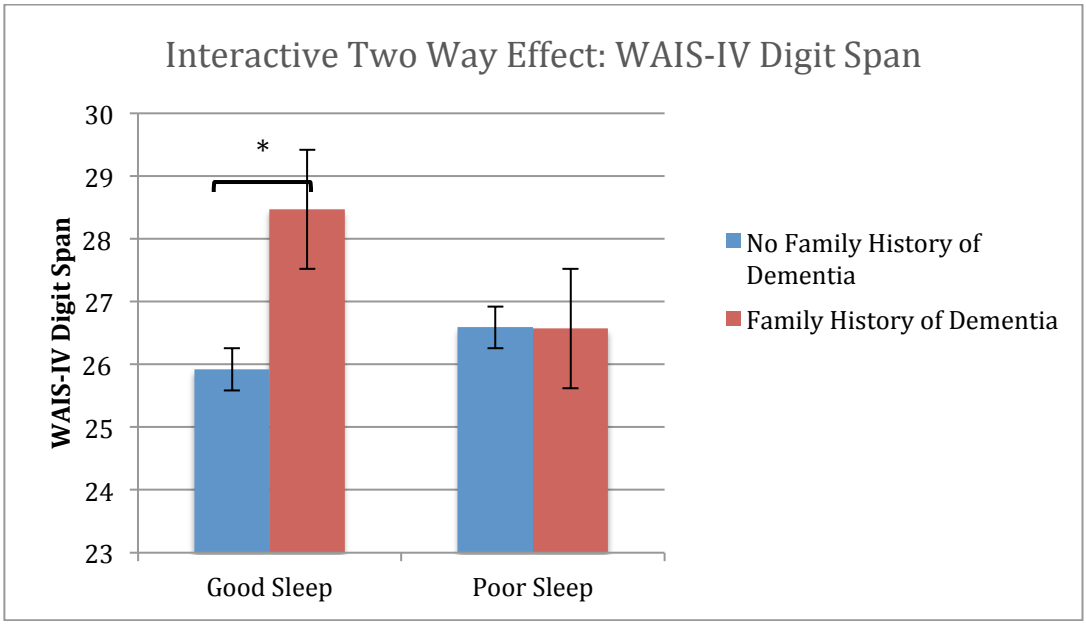

Figure 5. Interactive effects of family history of dementia and sleep quality on performance on the Wechsler Adult Intelligence Scale-IV Digit Span after controlling for IQ (p=0.026). Good sleepers with family history of dementia performed better than good sleepers without family history of dementia (p=0.042)

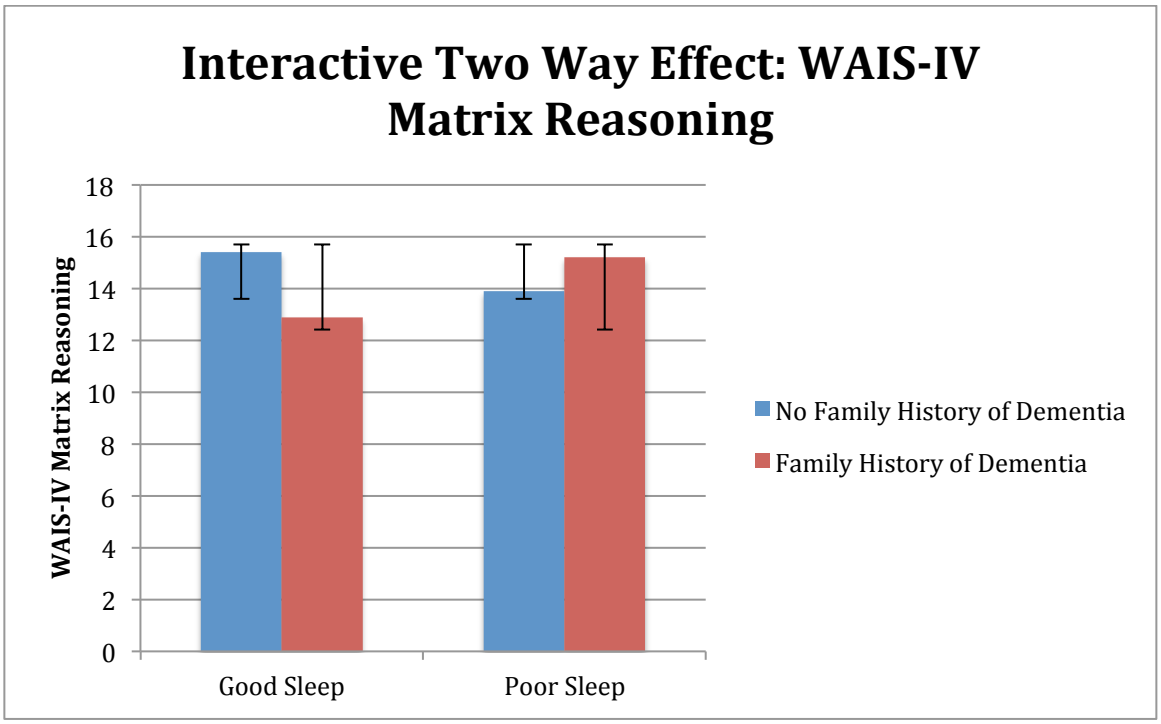

Figure 6. Trend: interactive effects of family history of dementia and sleep quality on performance on the WAIS-IV Matrix Reasoning without controlling for covariates (p=0.062). There were no significant difference between groups.

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