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The Effect of Occupational Cognitive Complexity on the Risk of Alzheimer's Disease Mortality
in the State of Georgia

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Rollins School of Public Health of Emory University
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Abstract

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By Tavia Binger

The cognitive reserve hypothesis suggests that working in occupations of higher complexity may increase an individual's resistance to the onset of Alzheimer's disease (AD). Using death records coded via the National Occupational Mortality Surveillance (NOMS), we examined the relationship between usual lifetime occupational complexity and mortality due to AD among deaths of workers age 60 and older in the state of Georgia. Three components of complexity (data, people, and things) were obtained for each occupation, and the sum of these was used to create a fourth overall complexity index (OCC). Covariate-adjusted logistic regression models assessed the relationship between four OCC indices and AD mortality. Low complexity of work with things was significantly associated with mortality due to AD in the study population. These findings suggest that the physical and mental stimulation provided by complexity of worker functions with things may contribute to cognitive reserve, and may ultimately be a modifiable risk factor in the development of AD.

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INTRODUCTION

Alzheimer's Disease (AD) is a progressive, neurodegenerative illness that is characterized by loss of memory and decline in cognitive ability, as well as anxiety, depression, and apathy (Mielke, Vemuri, & Rocca, 2014). An estimated 47 million people currently suffer from dementia globally. Alzheimer's disease is the most common cause of dementia, accounting for approximately two-thirds of cases (Henderson, 2014). In the US alone, one in nine people age 65 and older are diagnosed with AD (Mielke et al., 2014), and with the increasing age of population it is estimated that 13.8 million Americans will be diagnosed by the year 2050 (Miller & Boeve, 2017). This places a significant burden on society in the form of the direct medical care costs, loss from the workforce, reduced quality of life, as well as the burden placed on families and caretakers of patients.

Diagnosis and Symptoms

Dementia is an umbrella term that describes several diseases and conditions that develop when nerve cells in the brain either die or do not function properly. The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV), provides a definition of dementia commonly used by physicians in making diagnoses. According to the DSM-IV criteria, symptoms of dementia must include a decline in memory and at least one of the following cognitive abilities:

1. The ability to speak coherently or understand spoken or written language
2. The ability to recognize or identify objects, assuming intact sensory function
3. The ability to perform motor activities, assuming intact motor abilities and sensory function and comprehension of the required task

4. The ability to think abstractly, make sound judgements, and plan and carry out complex tasks

The decline in cognitive abilities must also be severe enough to interfere with daily life (Alzheimer's, 2013). The various types of dementia also have their own unique symptoms and brain abnormalities.

The National Institute of Aging and the Alzheimer's Association proposed new guidelines to describe and diagnose AD in 2012. According to these guidelines, there are three stages of AD. The first is the preclinical AD stage, in which patients may have measurable changes in the brain, but clinical symptoms such as memory loss are not yet present. This stage is estimated to begin up to 20 years or more before symptoms occur. The second stage is mild cognitive impairment (MCI) due to AD. Symptoms of MCI may include changes in cognitive abilities that are noticeable, perhaps to an individual's family members and friends, but do not interfere with their ability to carry out every day activities. The final stage is dementia due to AD, which occurs when memory, cognitive, and behavioral symptoms impair an individual's ability to perform everyday tasks (Alzheimer's, 2013).

Mortality

AD is the fifth leading cause of death in the United States (Alzheimer's, 2013). In the state of Georgia, the annual mortality rate due to AD was 21.5 per 100,000 in the year 2010 (Alzheimer's, 2013). However, it is estimated that AD causes more deaths than is recorded. Severe forms of dementia can lead to several other hazardous conditions that can cause death, such as immobility, pneumonia, malnutrition, and swallowing disorders. In these cases, the acute condition that leads to death of a person with AD is often listed on the death certificate

instead of AD. The true number of deaths due to AD is therefore likely somewhere between the official estimated numbers, as indicated by death certificates, and the number of those dying after developing AD (Alzheimer's, 2013).

Risk Factors

While the exact underlying pathological mechanisms of Alzheimer's Disease are still unclear, it is well known that it has a complex multifactorial etiology and is also modulated by various risk factors (Mistridis, 2017). Epidemiologic studies have demonstrated that advancing age is a primary risk factor for the development of AD (Miller & Boeve, 2017). The presence of genetic mutations has also been identified as a risk factor for early-onset AD, however this only comprises 5-10% of cases (Davanipour, Tseng, Lee, & Sobel, 2007). Symptoms among individuals who develop AD due to genetic mutation typically develop before age 65. However, the changes that occur in the brain for early-onset AD cases can also be present in patients who develop the disease later on in life (Alzheimer's, 2013).

Both increasing age and genetic predispositions represent unmodifiable risk factors for the disease, however observational studies have shown that there are also potentially modifiable risk factors for AD. These include cardiovascular factors, such as hypertension, high blood glucose, obesity, and abnormal blood cholesterol levels (Alzheimer's, 2013). Lifestyle and psychosocial factors, such as education, cognitive activity, and social engagement are also thought to reduce the risk of AD and dementia, although the exact mechanism for some of these are still unknown (Alzheimer's, 2013; Harrison et al., 2015). Further research is needed to understand how these risk factors affect AD, and could provide useful preventative strategies against the development of the disease.

Cognitive Reserve Hypothesis

The cognitive reserve hypothesis suggests that a lifestyle of high cognitive activity is protective against cognitive decline, and therefore may delay the onset of clinical signs of dementia and AD, despite significant neuropathology (Boots et al., 2015; Mistridis, 2017). Cognitive reserve has been defined as the amount of brain damage an individual can tolerate before reaching a clinical threshold for impairment (Andel, Vigen, Mack, Clark, & Gatz, 2006).

High educational attainment is thought to provide cognitive reserve by increasing the connections between neurons in the brain and using alternate neuron-to-neuron communication routes, which compensate for the early changes in the brain caused by AD (Alzheimer's, 2013). High levels of leisure activity and social engagement are also thought to help provide cognitive reserve. Leisure activities can include activities that are mentally, socially, or physically stimulating, that are performed on a regular basis. Social engagement is essentially the strength of the social network of an individual, and can be measured by marital status, living alone, and relationships with children or friends.

Occupational attainment has also been investigated as a source of cognitive reserve. However, the way that occupation has been defined in previous studies has varied and may contribute to the inconsistency found in results. Occupational complexity (OCC) quantifies the cognitive processes and skills required to perform various occupations (Boots et al., 2015). A systematic review examining the cognitive reserve hypothesis found occupation, high educational attainment, and regular participation in social activities to be associated with a decreased risk of dementia (Harrison et al., 2015).

In 1995, Stern et al. determined that occupational experience may provide cognitive reserve and influence the clinical expression of AD. Patients who had lifetime occupations that

required higher complexity had greater deficits of parietal blood flow, after matching for clinical disease severity. This provided indication that the underlying disease progression was more advanced for these patients. In addition, occupation was determined to contribute significantly to this relationship even after controlling for education, suggesting that it may still be a significant contributor of cognitive reserve above that provided by education (Stern et al., 1995).

Similarly, in a 2015 study of middle-aged adults at risk for AD, higher occupational complexity was significantly associated with decreased hippocampal volume and increased whole-brain atrophy among participants that were matched on cognitive function. Those with worse AD neuropathology in comparison to their matched counterparts, but higher OCC, were able to sustain similar levels of cognitive performance due to the delay in the clinical expression of symptoms of the disease (i.e. memory loss). These findings are in alignment with the cognitive reserve hypothesis and suggest that OCC may provide cognitive reserve and may be a modifiable protective factor against cognitive decline (Boots et al., 2015).

The concept of cognitive reserve is still under development and has been debated and critiqued by some researchers. Since there is currently no established standard definition, further research is needed in order to understand which factors contribute to cognitive reserve.

Purpose

The purpose of this study is to investigate the relationship between the cognitive complexity of pre-retirement occupations and mortality due to Alzheimer's Disease among adults age 60 and older in the state of Georgia, using death certificate data. OCC will be used as a proxy to measure cognitive reserve. Based on previous findings, it is hypothesized that lower levels of OCC will be associated with an increased odds of AD mortality.

METHODS

Data Source and Study Population

The data for this study were obtained from the Georgia Department of Public Health's death certificate records for the years 2011 - 2013. Death records during this time period were coded under the National Occupational Mortality Surveillance (NOMS) system of industry/occupation codes. NOMS is a state-based program developed by the National Institute of Occupational Safety and Health (NIOSH), which provides surveillance of acute and chronic disease mortality of US workers. Through NOMS, each subjects' usual lifetime occupation was coded according to the 2000 Census Occupational and Industrial Classification System.

The study population included an initial total of 167,847 death certificate records. Age was restricted to deaths at age 60 and over in order to exclude cases who developed early-onset AD. Occupations that were recorded as homemaker, disabled, unknown, retired, student, or missing, were excluded from the analysis, as the DOT did not have an occupational complexity score for these. In addition, subjects who had other types of dementia not classified as AD were excluded from the comparison group in order to focus exclusively on AD.

Occupational Complexity Classification

The Dictionary of Occupational Titles (DOT) was used to classify each occupation in terms of complexity of work with data, people, and things. The DOT is a source of standardized occupational information provided by the U.S. Department of Labor, and has been used as a classification tool in previous studies. Each occupation in the DOT is classified according to a 9-digit numeric system. Each set of digits in the occupational code number corresponds to a specific purpose and meaning. The fourth, fifth, and sixth digits of the DOT code indicate

worker functions, which are ratings of the tasks performed in each occupation, arranged to reflect a scale of simple to complex tasks. Each level of worker functions includes those that are simpler and excludes those that are more complex. It should be noted that these are general assignments, and therefore may be more applicable for some occupations than others.

Based on the DOT occupational codes, there were three components used to measure OCC: complexity of work with Data, complexity of work with People, and complexity of work with Things. A fourth index measured the sum of these parameters to obtain an overall summary occupational complexity score. The Data component of complexity ranged from 0 to 6, with 0 being most complex and 6 being least complex. Data are intangible and include numbers, words, symbols, ideas, concepts, and oral verbalization. Complexity of work with People ranged from 0 to 8, with 0 being most complex and 8 being the least complex. People are defined as human beings, or animals dealt with on an individual basis as if they were human. Complexity of work with Things ranged from 0 to 7, with 0 being the most complex and 7 being the least complex. Things are defined as inanimate objects as distinguished from human beings, and have a tangible shape and form. A complete description of each level of each complexity component is provided in the Appendix.

Outcome Classification

ICD-10 codes in the mortality data were used to analyze cause of death. Cases were identified from death certificates for which there was any mention of Alzheimer's disease, including cause, underlying cause, or contributing condition of death. Other types of dementia that were not included in the analysis were: Creutzfeldt-Jakob disease, vascular dementia,

Huntington's disease, Parkinson's disease, frontotemporal dementia, and other degenerative diseases of the nervous system, specified or unspecified.

Cause of death is defined as the morbid condition or disease process, abnormality, injury or poisoning, if any, that gave rise to the immediate cause of death. The underlying cause of death is defined as the disease or injury that initiated the train of morbid events, which led directly to death, or the circumstance of the accident or violence which produced the fatal injury. Contributing condition is defined as other significant diseases or conditions that contributed to death, but did not result in the underlying cause of death.

Statistical Analysis

Descriptive statistics were used to summarize the demographic attributes of the study population as well as the relationship between the complexity components of Data, People, and Things. Preliminary exploration revealed that age was a significant predictor of AD mortality, with risk increasing monotonically with age. Therefore, age was used as a continuous variable in further analyses.

Complexity of work with Data, People, and Things were each dichotomized for their respective initial analyses, following earlier work (Andel et al., 2006). OCC scores of 0-2 for Data (synthesizing, coordinating, and analyzing) were assigned to high complexity as the reference group, while scores of 3-6 were assigned low complexity (compiling, computing, copying, and comparing). For complexity of work with People, OCC scores of 0 – 6 (mentoring, negotiating, instructing, supervising, diverting, persuading, speaking/signaling) were assigned to high complexity, while scores of 7 and 8 (serving, taking instructions/helping) were assigned to low complexity. High complexity for Things were scores of 0 – 4 (setting up, precision working,

operating, controlling, driving/operating, and manipulating). Low complexity with Things were scores of 5 – 7 (tending, feeding/off bearing, and handling).

Statistical analyses assessed the relationship between the OCC parameters and AD mortality using logistic regression modeling to produce mortality odds ratios. Model 1 of the analysis assessed the relationship between quartiles of the summary OCC index and AD mortality, while controlling for age, sex, education level, and race. Models 2, 3, and 4 assessed the relationship between complexity of work with Data, People, and Things, respectively, while also controlling for the same three predictors as Model 1. Tests for effect modification in each of the models indicated that there was no statistically significant interaction between OCC and either age, sex, education, or race in any of the AD analyses.

In subsequent analyses, complexity scores for Data, People, and Things were segmented into quartiles based on the distribution of the population. Logistic regression was used to evaluate the relationship between quartiles of complexity and AD mortality, while controlling for age, sex, education level, and race. To calculate a test for trend, a score was assigned to each quartile by taking a weighted average of the scores within the quartile, where the weights were the number of subjects with those scores.

Finally, complexity of work with data, people, and things, were entered into the same model, adjusting for age, sex, education level, and race. A test for trend was again performed for each complexity component by assigning a weighted-average complexity score within each quartile.

RESULTS

The original sample contained a total of 167,847 records for the years 2011 – 2013 among deaths occurring in the state of Georgia of people age 60 years and older. Occupations that were recorded as homemaker, disabled, unknown, retired, student, or missing, were excluded from the analysis, as the DOT did not have an occupational complexity score for these. 37,273 records fit this description, resulting in a sub-total of 130,574 deaths. Subjects who did not have a record of AD, but did have any of the other types of dementia were excluded from the comparison group. As a result, the final sample for the analysis included data from 115,777 records.

Table 1 lists some of the demographic and other characteristics of the final sample of death records. The average age at death of the final sample was 77 years old (SD=10.06). Prior to dropping records, women made up 53% of the population, however in the final sample women composed only 42.2% of the population. The demographic clusters indicating socio-economic status were created using EASI demographics data at the census block level, which classify people into four major categories based on several variables related to income, housing, education, and employment.

Deaths attributed to any mention of AD on the death certificate composed 4.3% of the study population. Of these, 3.2% were classified as Alzheimer's disease with late onset (usually after the age of 65), and 96.8% were classified as unspecified AD. Of records with any mention of AD, 79.24% were classified as the underlying cause of death.

The summary index for Total OCC was normally distributed with a mean of 13.03 and standard deviation of 4.07. The component of OCC that indicated the highest complexity level

was complexity of work with Data, with an average score of 2.74. Records had an average complexity of work with People and Things of 5.63 and 4.66, respectively.

Table 2 lists the same characteristics of the study population, stratified by AD and non-AD deaths. The average age at death among those who died due to AD was 85, and among those who died due to other causes was 77. There was also a higher proportion of women among AD deaths (61%) than among non-AD deaths (41%).

The mean age at death within each quartile of the total occupational complexity index (Table 3) was slightly lower in quartile 4, which had a younger average age at death than the total sample. In regards to the proportion of gender in each quartile, men were more likely to work in the most complex and least complex occupations. The percentage of people who attended some college or higher tended to increase as the level of total occupational complexity increased. This is expected, as more years of education are typically required to perform jobs that demand advanced skills and techniques, and overall higher levels of complexity. The proportion of people of higher socio-economic status was highest in quartile 1 and decreased as complexity decreased.

As shown in Table 4, scores for complexity of work with Data were positively correlated with complexity of work with People ($r = 0.593$). Complexity of work with Things had a moderate, negative correlation with People OCC ($r = -0.315$), and a weak correlation with Data OCC ($r = -0.095$).

Table 5 displays results of the analysis for AD mortality after controlling for age, sex, education level, and race. In Model 4, complexity of work with Things showed a statistically significant association with an adjusted MOR of 1.11 (95% CI=1.05, 1.18). In each model, tests

for potential effect measure modification between the exposure and age, sex, education level, and race showed that there was no significant interaction between OCC and either covariate.

Table 6 displays the results of three separate logistic regression models using quartiles of each OCC component (Data, People, and Things) as predictors. Quartile 4 of low complexity of work with Things was significantly associated with AD mortality (MOR=1.13, 95% CI=1.04, 1.23). In addition, the test for trend showed a significant increase in AD mortality with decreasing complexity ($\beta=0.021$, p-value = 0.0004). Complexity of work with Data and People both showed insignificant tests for trend with regression coefficients of 0.005 (p-value=0.5933) and -0.009 (p-value=0.1832), respectively.

Results from the model of quartiles of OCC, adjusting for other OCC components are presented in Table 7. Quartile 4 of low complexity of work with Things remained significantly associated with AD mortality (MOR=1.11, 95% CI = 1.01, 1.21), even after controlling for Data and People OCC, in addition to sex, education level, age, and race. In the test for trend, complexity of work with Things remained consistent with a significant increase in AD mortality with decreasing complexity ($\beta=0.021$, p-value=0.0009). Trend results for complexity of work with Data and People remained insignificant, with an increasing trend for Data OCC ($\beta=0.011$, p-value=0.2321) and a decreasing trend for People OCC ($\beta=-0.006$, p-value=0.4987).

DISCUSSION

In this study of mortality in the state of Georgia, there was no evidence of increased mortality due to Alzheimer's disease among individuals whose usual lifetime occupation had lower overall complexity compared with individuals who worked in occupations of higher overall complexity, after controlling for age, sex, education level, and race. While there was no evidence of an increased odds of mortality due to Alzheimer's disease associated with low complexity of work with either data or people, there was a statistically significant association observed between complexity of work with things and mortality due to AD. The odds of mortality due to Alzheimer's disease among individuals with usual lifetime occupations of low complexity with things was 11% higher than among workers in occupations with high complexity of work with things. In the analysis of quartiles of OCC components in separate regression models, complexity of work with things was significantly associated with AD mortality in the fourth quartile, even after adjusting for the two other complexity components. The tests for trend also support these findings, and again are significant even after controlling for other components of OCC.

Given that in our data there is a significantly protective effect of increased complexity with things, but slight trends in the opposite direction for people and data, it is not surprising that we find no significant results for OCC, which is a sum of things, people, and data.

The results for complexity of work with things in this study provide evidence in support of the cognitive reserve hypothesis, in the sense that work with high complexity of things provides a cognitive reserve protecting against cognitive decline. Based on these findings, low complexity of work with things in occupational functions may have an adverse effect on the risk of AD mortality. This indicates that occupational work with things could be a potentially

modifiable risk factor in the development of the disease. The association between overall occupational complexity and AD mortality produced inconclusive findings in this analysis. However, this does not disprove increased occupational complexity as a measure of cognitive reserve, as there has been more decisive evidence in the literature in support of this.

The worker functions that have the most complex scores for things involve precision working and setting up/installation of various machinery, tools, and materials. As such, occupations that involve superior levels of manual and operational responsibilities may require less complex duties in regards to working with data or people. Thus, the observed negative correlation between complexity of work with people and things does seem plausible, as does the positive correlation between people and data. In order to account for the relationship between levels of complexity within each component, all three OCC components were entered into the same regression model. When controlling for the other components of complexity the effects of things OCC observed in the model were persistent in showing a statistically significant association. In addition, adjusting for complexity of work with things appears to reduce the negative trend seen for complexity of work with people when complexity of work with things was not in the model, making the trend for complexity of work with people non-significant.

The results of this study differ from previous findings in that overall occupational complexity did not have a significant association with AD mortality. Furthermore, the only component of OCC that was significantly associated with AD mortality was complexity of work with things, whereas Boots et al found that only complexity of work with people was significantly associated with brain atrophy in AD patients. The current findings, however, demonstrate that complexity of work with things may also contribute positively to cognitive reserve.

Limitations

This study had several limitations. Many of the present limitations are those that typically accompany the use of death certificate data for quantitative analysis. In the United States, Blacks have an increased prevalence of about 2.0 of AD and other dementias compared to Whites (Alzheimer's, 2013). In addition, other data show that blacks have 1.6 times the incidence of AD compared to whites (Steenland, MacNeil, Vega, & Levey, 2009). However, mortality for whites based on death certificate data is notably higher than for non-whites in the US, suggesting substantial under-reporting of AD among non-Whites on death certificates (Steenland et al., 2009). In the present data, crude analyses indicated that there was a decrease in the odds of AD mortality among non-Whites compared to Whites. In general, non-differential (the same for both more complex and less complex occupations) misclassification of outcome would bias our findings to the null. Furthermore, since non-whites have lower complexity scores than whites, under-reporting of AD on death certificates by non-whites may also suggest under-reporting of AD among those with less job complexity (differential misclassification), which would also tend to bias our findings to the null.

The use of mortality data as opposed to incident data of AD diagnoses also creates less reliability in the measurement of outcome in the analysis. It has been hypothesized in previous literature that high cognitive reserve may actually lead to a steeper decline in AD once symptoms become clinically manifested, due to the increased pathological accumulation (Mistridis, 2017). The observable influence of cognitive reserve on AD therefore may be diminished by the use of mortality data.

Another limitation of this study was the use of death records for obtaining occupational information. While “usual lifetime occupation” is requested, there is a possibility for error in the

record of occupation due to lack of knowledge or memory of the next of kin. Verification of occupation would not be possible in this instance. In addition, certain information such as duration of employment is unattainable in this circumstance.

The use of the Dictionary of Occupational Titles classification system also introduced limitations into the study. Every job requires a worker to function in relation with data, people, and things, and a separate digit in the DOT code is assigned to reflect that relationship. The assignment of the worker function code generally indicates the broadest level of responsibility and judgement needed to perform a particular job, where more complex responsibilities are assigned lower numbers and less complex functions are assigned higher numbers. However, it is also assumed that the worker can perform any less complex function within that component of complexity for a given occupation. As a result, the distinction of the complexity score rating from the DOT may be more accurate for certain occupations and workers than for others.

In addition, the DOT does not have an assigned occupational complexity score for homemakers, as a result these records were not included in the analysis. Homemakers composed a considerable proportion of the original data set, at 17%. The complexity of work of a homemaker would expectedly vary between households and persons, and unfortunately there is no way to capture this. This also affected the balance of sex in the study sample.

CONCLUSION

The current evidence of this study suggests that occupational complexity of work with things may supply cognitive reserve and offer a protective effect against the risk of mortality due to AD. Further research is needed to determine the importance of other components such as overall occupational complexity, complexity of work with data and complexity of work with people, which may also be indicators of cognitive reserve. A fuller understanding of cognitive reserve and its indicators could help provide new strategies in reducing the risk and incidence of dementia and AD.

REFERENCES

- Alzheimer's, A. (2013). 2013 Alzheimer's disease facts and figures. *Alzheimers Dement*, 9(2), 208-245. doi:10.1016/j.jalz.2013.02.003
- Andel, R., Vigen, C., Mack, W. J., Clark, L. J., & Gatz, M. (2006). The effect of education and occupational complexity on rate of cognitive decline in Alzheimer's patients. *J Int Neuropsychol Soc*, 12(1), 147-152. doi:10.1017/S1355617706060206
- Boots, E. A., Schultz, S. A., Almeida, R. P., Oh, J. M., Kosciak, R. L., Dowling, M. N., . . . Okonkwo, O. C. (2015). Occupational Complexity and Cognitive Reserve in a Middle-Aged Cohort at Risk for Alzheimer's Disease. *Arch Clin Neuropsychol*, 30(7), 634-642. doi:10.1093/arclin/acv041
- Davanipour, Z., Tseng, C. C., Lee, P. J., & Sobel, E. (2007). A case-control study of occupational magnetic field exposure and Alzheimer's disease: results from the California Alzheimer's Disease Diagnosis and Treatment Centers. *BMC Neurol*, 7, 13. doi:10.1186/1471-2377-7-13
- Harrison, S. L., Sajjad, A., Bramer, W. M., Ikram, M. A., Tiemeier, H., & Stephan, B. C. (2015). Exploring strategies to operationalize cognitive reserve: A systematic review of reviews. *J Clin Exp Neuropsychol*, 37(3), 253-264. doi:10.1080/13803395.2014.1002759
- Henderson, V. W. (2014). Three midlife strategies to prevent cognitive impairment due to Alzheimer's disease. *Climacteric*, 17 Suppl 2, 38-46. doi:10.3109/13697137.2014.929650
- Mielke, M. M., Vemuri, P., & Rocca, W. A. (2014). Clinical epidemiology of Alzheimer's disease: assessing sex and gender differences. *Clin Epidemiol*, 6, 37-48. doi:10.2147/CLEP.S37929
- Miller, B. L., & Boeve, B. F. (2017). *The behavioral neurology of dementia* (Second edition. ed.). Cambridge, United Kingdom ; New York, NY, USA: University Printing House, Cambridge University Press.
- Mistridis, P. (2017). Use it or lose it! Cognitive activity as a protective factor for cognitive decline associated with Alzheimer's disease. *Swiss Medical Weekly*, 147(0910). doi:10.4414/smw.2017.14407
- Steenland, K., MacNeil, J., Vega, I., & Levey, A. (2009). Recent trends in Alzheimer disease mortality in the United States, 1999 to 2004. *Alzheimer Dis Assoc Disord*, 23(2), 165-170.
- Stern, Y., Alexander, G. E., Prohovnik, I., Stricks, L., Link, B., Lennon, M. C., & Mayeux, R. (1995). Relationship between lifetime occupation and parietal flow: implications for a reserve against Alzheimer's disease pathology. *Neurology*, 45(1), 55-60.

TABLES AND FIGURES

Table 1. Characteristics of Workers Age 60 and Older Who Died During 2011-2013 in the State of Georgia^a	
Value^b	
Demographics	
Age at death (years)	77.20 (10.06)
Women (%)	42.2
Education	
Some college or higher (%)	35.29
Completed high school or GED (%)	37.73
Less than 12 year of education (%)	26.99
Race	
White (%)	74.9
Black or African American (%)	24.01
Marital Status	
Married (%)	42.86
Divorced (%)	16.07
Widowed (%)	35.31
SES	
Higher SES (%)	29.35
Middle SES (%)	5.91
Lower Middle SES (%)	37.88
Lower SES (%)	22.98
Year of Death	
2011 (%)	32.52
2012 (%)	33.23
2013 (%)	34.25
Occupational Complexity	
Total OCC	13.03 (4.07)
Complexity with Data	2.74 (1.98)
Complexity with People	5.63 (2.32)
Complexity with Things	4.66 (2.52)
Cause of death	
Alzheimer's disease (%)	4.3
Dementia (%)	15.6
Notes: OCC=occupational complexity; SES=socio-economic status ^a Excluding workers with occupation listed on death certificate as homemaker, disabled, unknown, retired, student, or missing ^b Data are given as mean (SD) unless otherwise noted	

Table 2. Characteristics of Workers Age 60 and Older Who Died During 2011-2013 in the State of Georgia According to Cause of Mortality^a

	Value^b			
	Non-AD Deaths		AD Deaths	
Total, <i>n</i>	110,147		5,630	
Demographics				
Age at death (years)	76.81	(10.01)	84.93	(7.49)
Women (%)	41.23		61.08	
Education				
Some college or higher (%)	35.43		32.35	
Completed high school or GED (%)	37.67		38.85	
Less than 12 year of education (%)	26.9		28.80	
Race				
White (%)	74.57		81.26	
Black or African American (%)	24.31		18.10	
Marital Status				
Married (%)	43.46		31.26	
Divorced (%)	16.39		9.80	
Widowed (%)	34.28		55.38	
SES				
Higher SES (%)	29.41		28.28	
Middle SES (%)	5.93		5.51	
Lower Middle SES (%)	37.66		42.13	
Lower SES (%)	23.08		21.15	
Year of Death				
2011 (%)	32.32		36.43	
2012 (%)	33.29		32.01	
2013 (%)	34.39		31.56	
Occupational Complexity				
Total OCC	13.03	(4.08)	13.02	(3.91)
Complexity with Data	2.75	(1.99)	2.65	(1.90)
Complexity with People	5.64	(2.32)	5.49	(2.32)
Complexity with Things	4.65	(2.53)	4.88	(2.48)
Notes: OCC=occupational complexity; SES=socio-economic status				
^a Excluding workers with occupation listed on death certificate as homemaker, disabled, unknown, retired, student, or missing				
^b Data are given as mean (SD) unless otherwise noted				

Table 3. Characteristics of the Study Population According to Quartiles of the Summary Occupational Complexity Index Score

	Total Occupational Complexity Index ^a				Total Sample ^f
	Quartile 1 ^b (Most Complex Occupations)	Quartile 2 ^c	Quartile 3 ^d	Quartile 4 ^e (Least Complex Occupations)	
Total <i>n</i> (%)	28,977 (25.03)	26,134 (22.57)	30,610 (26.44)	30,056 (25.96)	115,777
Age at death, years (mean)	77.6	77.5	77.8	76.0	77.2
Male (%)	71.24	44.88	52.52	61.46	57.8
Some college or higher (%)	58.70	35.18	35.92	11.52	35.29
White (%)	83.85	73.77	79.65	62.40	74.9
Married (%)	52.99	38.04	42.22	37.95	42.86
Higher SES (%)	38.03	29.67	33.54	21.06	30.54
Percent AD Underlying (%) ^g	78.36	81.09	79.30	78.08	78.36

Notes: SES=socio-economic status

^a Calculated as the sum of complexity of work with data, people, and things, according to the Dictionary of Occupational Titles occupational code classifications

^b Summary OCC score of 0-9

^c Summary OCC score of 10-13

^d Summary OCC score of 14-15

^e Summary OCC score of 16-21

^f Excluding workers with occupation listed on death certificate as homemaker, disabled, unknown, retired, student, or missing

^gPercent of AD deaths classified as underlying cause of death

Table 4. Correlations Between Each Component of OCC in the Study Population

	Things	Data	People
Things	1.000	-0.095	-0.315
Data	-0.095	1.000	0.593
People	-0.315	0.593	1.000

Notes: OCC = occupational complexity
Data presented are Pearson correlation coefficient

Table 5. Adjusted Associations Between OCC and AD Mortality Among Workers Age 60 and Older Who Died During 2011-2013 in the State of Georgia		
Level of Complexity	Mortality Odds Ratio	
	MOR	95% CI
Model 1: Overall complexity ^{a,b}		
Quartile 1	Reference	
Quartile 2	1.01	(0.93, 1.10)
Quartile 3	1.01	(0.93, 1.10)
Quartile 4	1.05	(0.96, 1.15)
Women	1.75	(1.64, 1.85)
Those with less education ^c	1.07	(0.99, 1.16)
Age	1.08	(1.08, 1.09)
Non-whites	0.76	(0.71, 0.82)
Model 2: Complexity with Data ^{a,d}		
High complexity	Reference	
Low complexity	1.02	(0.95, 1.08)
Model 3: Complexity with People ^{a,e}		
High complexity	Reference	
Low complexity	1.02	(0.95, 1.09)
Model 4: Complexity with Things ^{a,f}		
High complexity	Reference	
Low complexity	1.11	(1.05, 1.18)
OCC = occupational complexity; AD = Alzheimer's disease CI = confidence interval		
^a Controlling for age, sex, education level, and race		
^b Comparing quartiles of the summary OCC index, where Quartile 1 is most complex and Quartile 4 is least complex Quartile 1: 0-9; Quartile 2: 10-13; Quartile 3: 14-15; Quartile 4: 16-21		
^c Twelve years or less		
^d Data dichotomized at 0-2 (high complexity) vs 3-6 (low complexity)		
^e People is dichotomized at 0-6 (high complexity) vs 7-8 (low complexity)		
^f Things is dichotomized at 0-4 (high complexity) vs 5-7 (low complexity)		

Table 6. Adjusted Associations Between Quartiles of OCC^a and AD Mortality Among Workers Age 60 and Older Who Died During 2011-2013 in the State of Georgia					
Level of Complexity	n	Mortality Odds Ratio		β (SE)^b	p trend
		MOR	95% CI		
Complexity with Data^{c,d}					
Quartile 1	47,444	Reference	--		
Quartile 2	12,837	0.95	(0.86, 1.04)		
Quartile 3	28,738	0.99	(0.92, 1.07)		
Quartile 4	26,758	1.02	(0.94, 1.11)	0.005 (0.009)	0.5933
Complexity with People^{c,e}					
Quartile 1	19,400	Reference	--		
Quartile 2	14,010	0.94	(0.85, 1.04)		
Quartile 3	40,996	0.91	(0.84, 0.99)		
Quartile 4	41,371	0.95	(0.87, 1.04)	-0.009 (0.007)	0.1832
Complexity with Things^{c,f}					
Quartile 1	21,043	Reference	--		
Quartile 2	21,781	1.02	(0.92, 1.12)		
Quartile 3	15,168	1.03	(0.92, 1.15)		
Quartile 4	57,785	1.13	(1.04, 1.23)	0.021 (0.006)	0.0004
Notes: OCC = occupational complexity; AD = Alzheimer's disease; CI = confidence interval; SE = standard error; MOR=mortality odds ratio					
^a Comparing quartiles of OCC, where Quartile 1 is most complex and Quartile 4 is least complex					
^b P trend, regression coefficient, and SE obtained from the population-weighted logistic model					
^c Controlling for age, sex, education level, and race					
^d Data OCC categorized as follows: Quartile 1: 0-1; Quartile 2: 2; Quartile 3: 3-4; Quartile 4: 5-6					
^e People OCC categorized as follows: Quartile 1: 0-2; Quartile 2: 3-5; Quartile 3: 6; Quartile 4: 7-					
^f Things OCC categorized as follows: Quartiles 1: 0-1; Quartile 2: 2-3; Quartile 3: 4-5; Quartile 4:					

Table 7: Adjusted Associations Between Quartiles of OCC^a and AD Mortality Among Workers Age 60 and Older Who Died During 2011-2013 in the State of Georgia Controlling for Other OCC Components

Level of Complexity	Mortality Odds Ratio		β (SE) ^b	p trend
	MOR	95% CI		
Data ^{c,d}				
Quartile 1	Reference			
Quartile 2	0.92	(0.84, 1.02)		
Quartile 3	1.04	(0.95, 1.13)		
Quartile 4	1.05	(0.94, 1.18)	0.011 (0.009)	0.2321
People ^{c,d}				
Quartile 1	Reference			
Quartile 2	0.92	(0.82, 1.02)		
Quartile 3	0.91	(0.83, 0.99)		
Quartile 4	0.96	(0.85, 1.08)	-0.006 (0.008)	0.4987
Things ^{c,d}				
Quartile 1	Reference			
Quartile 2	0.98	(0.89, 1.10)		
Quartile 3	0.97	(0.86, 1.09)		
Quartile 4	1.11	(1.01, 1.21)	0.021 (0.006)	0.0009

Notes: OCC = occupational complexity; AD = Alzheimer's disease; CI = confidence interval; SE = standard error; MOR=mortality odds ratio

^a Comparing quartiles of OCC, where Quartile 1 is most complex and Quartile 4 is least complex

^b P trend, regression coefficient, and SE obtained from the population-weighted logistic model

^c Controlling for age, sex, education level, and race

^d Data OCC categorized as follows: Quartile 1: 0-1; Quartile 2: 2; Quartile 3: 3-4; Quartile 4: 5-6

^e People OCC categorized as follows: Quartile 1: 0-2; Quartile 2: 3-5; Quartile 3: 6; Quartile 4: 7-8

^f Things OCC categorized as follows: Quartiles 1: 0-1; Quartile 2: 2-3; Quartile 3: 4-5; Quartile 4: 6-7

APPENDIX

Definitions of Worker Functions for Occupational Complexity	
	Description
<i>Complexity Score with Data</i>	
0 Synthesizing	Integrating analyses of data to discover facts and/or develop knowledge concepts or interpretations.
1 Coordinating	Determining time, place, and sequence of operations or action to be taken on the basis of analysis of data
2 Analyzing	Examining and evaluating data. Presenting alternative actions in relation to the evaluation is frequently involved
3 Compiling	Gathering, collating, or classifying information about data, people, or things
4 Computing	Performing arithmetic operations and reporting on and/or carrying out a prescribed action in relation to them
5 Copying	Transcribing, entering, or posting data
6 Comparing	Judging the readily observable functional, structural, or compositional characteristics of data, people, or things.
<i>Complexity Score with People</i>	
0 Mentoring	Dealing with individuals in terms of their total personality in order to advise, counsel, and/or guide them with regard to problems that may be resolved by legal, scientific, clinical, spiritual, and/or other professional principles
1 Negotiating	Exchanging ideas, information, and opinions with others to formulate policies and programs and/or arrive jointly at decisions, conclusions, or solutions.
2 Instructing	Teaching subject matter to others, or training others (including animals) through explanation, demonstration, and supervised practice; or making recommendations on the basis of technical disciplines

3	Supervising	Determining or interpreting work procedures for a group of workers, assigning specific duties to them, maintaining harmonious relations among them, and promoting efficiency.
4	Diverting	Amusing others, usually through the medium of stage, screen, television, or radio
5	Persuading	Influencing others in favor of a product, service, or point of view.
6	Speaking	Talking with and/or signaling people to convey or exchange information. Includes giving assignments and/or directions to helpers or assistants
7	Serving	Attending to the needs or requests of people or animals or the expressed or implicit wishes of people. Immediate response is involved.
8	Taking Instructions	Attending to the work assignment instructions or orders of supervisor. (No immediate response required unless clarification of instructions or orders is needed.)

Complexity Score with Things

0	Setting Up	Preparing machines (or equipment) for operation by planning order of successive machine operations, installing and adjusting tools and other machine components, adjusting the position of work piece or material, setting controls, and verifying accuracy of machine capabilities, properties of materials, and shop practices. Uses tools, equipment, and work aids, such as precision gauges and measuring instruments.
1	Precision Working	Using body members and/or tools or work aids to work, move, guide, or place objects or materials in situations where ultimate responsibility for the attainment of standards occurs and selection of appropriate tools, objects, or materials, and the adjustment of the tool to the task require exercise of considerable judgment.
2	Operating-Controlling	Starting, stopping, controlling, and adjusting the progress of machines or equipment. Operating machines involves setting up and adjusting the machine or material(s) as the work progresses. Controlling involves observing gauges, dials, etc., and turning valves and other devices to regulate factors such as temperature, pressure, flow of liquids, speed of pumps, and reactions of materials.

3 Driving-Operating

Starting, stopping, and controlling the actions of machines or equipment for which a course must be steered or which must be guided to control the movement of things or people for a variety of purposes. Involves such activities as observing gauges and dials, estimating distances and determining speed and direction of other objects, turning cranks and wheels, and pushing or pulling gear lifts or levers. Includes such machines as cranes, conveyor systems, tractors, furnace-charging machines, paving machines, and hoisting machines.

4 Manipulating

Using body members, tools, or special devices to work, move, guide, or place objects or materials. Involves some latitude for judgment with regard to precision attained and selecting appropriate tool, object, or material, although this is readily manifest.

5 Tending

Starting, stopping, and observing the functioning of machines and equipment. Involves adjusting materials or controls of the machine, such as changing guides, adjusting timers and temperature gauges, turning valves to allow flow of materials, and flipping switches in response to lights. Little judgment is involved in making these adjustments.

6 Feeding-Offbearing

Inserting, throwing, dumping, or placing materials in or removing them from machines or equipment which are automatic or tended or operated by other workers.

7 Handling

Using body members, hand tools, and/or special devices to work, move, or carry objects or materials. Involves little or no latitude for judgment with regard to attainment of standards or in selecting appropriate tool, object, or materials