Complexity of Work and Risk of Alzheimer’s Disease: A Population-Based Study of Swedish Twins

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We examined the association between risk of dementia or Alzheimer’s disease (AD) and occupation by using measures of complexity of work with data, people, and things. The study included 10,079 members of the population-based Swedish Twin Registry who were participants in the HARMONY study. We diagnosed dementia by means of a two-stage procedure—cognitive impairment screening followed by full clinical evaluation. We analyzed data with case-control and cotwin control designs. The cotwin control design provides control over genetic and familial factors. In the case-control study, controlling for age, gender, and level of education, we found that more complex work with people was associated with reduced risk of AD. Greater complexity of work with people and data was protective in twin pairs discordant for AD. Findings suggest that greater complexity of work, and particularly complex work with people, may reduce the risk of AD.

MODIFYING daily activities may be among the simplest ways to affect the course of human aging. Behavioral factors associated with lifestyle choices such as smoking, drinking alcohol, or exercising have long been known to influence the onset of diseases, including cancer or heart disease. Recently, more attention has been paid to the possibility that lifestyle may also play a role in reducing the risk of dementia and Alzheimer’s disease (AD). Because dementia is among the most salient health concerns of older adults (Henig, 1994), knowing whether behavioral factors may modify risk is of great practical interest.

Factors that cannot be amended, such as family history and increasing age, are among the most reliable predictors of dementia (Farrer et al., 1997; Hendrie, 1998). However, there is some evidence that an intellectually stimulating lifestyle may help modify late-life cognitive outcomes (Fratiglioni, Paillard-Borg, & Winblad, 2004; Katzman, 1995; Orrell & Sahakian, 1995; Scarmeas & Stern, 2003). Some researchers have found factors that seem to reflect levels of intellectual stimulation over the course of adulthood, such as education (Gatz et al., 2001; Launer et al., 1999), leisure activity (Crowe, Andel, Gatz, Pedersen, & Johansson, 2003; Fratiglioni, Wang, Ericsson, Maytan, Winblad, 2000; Wilson et al., 2002), and occupation (Smyth et al., 2004; Stern et al., 1995), to be related to reduced risk of dementia. Other researchers (e.g., Salthouse, Berish, & Miles, 2002) have cautioned that empirical support for the possibility that cognitive stimulation affects cognition is still only tentative at best.

Occupation may be particularly interesting with respect to examining the potential association between intellectual stimulation and subsequent dementia, because people generally spend a substantial portion of their adult years at work. Along the lines of the use it or lose it hypothesis (Katzman, 1995; Orrell & Sahakian, 1995), occupations with high mental demands may provide a form of mental exercise that supports brain function further into older adulthood. Mental exercise provided by frequent engagement in intellectually demanding activity at work may facilitate the maintenance of inherent cognitive reserve, leading to more sophisticated cerebral networks in old age (Churchill et al., 2002; Kolb & Whishaw, 1998) and allowing aging individuals to tolerate dementia neuropathology longer into the progression of the disease (Scarmeas & Stern, 2003; Stern et al., 1995).

A similar hypothesis was articulated by Schooler (1984) to explain the effect of complexity of work on cognitive functioning in nondemented older adults. Schooler posited that complex environments that reward cognitive effort and require making decisions motivate individuals to continue to develop their intellectual capacities. To substantiate the environmental complexity hypothesis, Kohn and Schooler (1983) and Schooler, Mulatu, and Oates (1999) derived a factor score from self-reports about complexity of work with data, people, and things, modeled after the Dictionary of Occupational Titles (U.S. Department of Labor, 1965). Results based on this measure suggested that substantive complexity of work facilitates intellectual flexibility and promotes stable cognitive function.

The link between occupation and dementia has generally been explored by use of occupational classifications that reflect occupational status. Lifetime occupations characterized by low socioeconomic status have been found to increase the risk of
dementia in case-control studies such as the Canadian Study of Health and Aging (1994), studies based in Sicily (Azzimondi, D’Alessandro, Pandolfo, & Feruglio, 1998) and Kungsholmen, Sweden (Fratiglioni, Ahlbom, Viitanen, & Winblad, 1993), and studies of incident dementia conducted in East Boston (Evans et al., 1997), New York (Stern et al., 1994), and Kungsholmen (Qui et al., 2003). Potential explanations for this relationship include greater mental demands of high-status occupations (Stern et al.) and a greater likelihood of adverse occupational exposures in low-status occupations (Canadian Study of Health and Aging; Fratiglioni et al.). However, no association between low-status versus high-status occupation and risk of dementia was reported in case-control studies such as the Conselice Study based in Northern Italy (Ravaglia et al., 2002) or in studies of incident dementia such as the French PAQUID project (Personnes Âgées QUID project; Helmer et al., 2001) and a study conducted in the United Kingdom (Paykel et al., 1994), leaving the link between occupation and dementia unclear.

Two studies conducted by Stern and colleagues (1995) and Smyth and colleagues (2004) have used indicators reflecting occupational demands. In a study of AD patients, Stern and colleagues used factor scores reflecting substantive complexity, interpersonal demands, management requirements, and physical demands—derived from occupational characteristics based on the Dictionary of Occupational Titles (U.S. Department of Labor, 1977)—to explore the association between occupational factors and current cerebral blood flow. They found that, when dementia severity, age, and education were controlled for, patients who had held jobs with high interpersonal and physical demands had relatively greater deficits in cerebral blood flow in the parietal area compared with patients who had held jobs with low demands. High physical and interpersonal demands also accounted for a significant amount of variance when these variables were entered into a covariate-adjusted model in a stepwise fashion. Stern and colleagues interpreted these results as showing a delay in clinical expression of AD that they attributed to the protective effect of occupational demands on the brain. The same study found no differences in cerebral blood flow related to substantive complexity or management requirements. In a case-control study, Smyth and associates derived scores from the Dictionary of Occupational Titles that were collapsed to reflect mental, social, physical, and motor demands. They analyzed types of occupational demands in separate models. They found that, after race, gender, year of birth, and education were controlled for, participants diagnosed with AD had held jobs with lower mental and higher physical occupational demands compared with controls. Moreover, the difference in occupational demands between demented and nondemented participants appeared to be greater for occupations held closer to retirement. In both the Stern and the Smyth studies, as one potential explanation of their findings the authors offered that differences in occupational status probably reflected differences in occupational complexity.

Using data from a population-based twin registry, we explored the association between occupation and risk for all types of dementia and for AD only. We coded each occupation to reflect three types of intellectual demands at work—complexity of work with data, with people, and with things. These measures, called “worker functions,” have been used as basic indicators of complexity (Miller, Treiman, Cain, & Roos, 1980). We expected that high complexity of work, particularly on the dimensions of work with data and people, would be associated with reduced risk of dementia and AD. We expected to find less relevance of complexity of work with things to dementia and AD, because this complexity dimension appears to provide a relatively poor representation of general complexity of work (Kohn & Schooler, 1983; Schooler et al., 1999) and is characterized by lower reliability of measurement (Miller et al.).

We analyzed the data within two designs—case control and cotwin control. The cotwin-control design estimates disease risk in twins who are discordant for the disease (i.e., one twin has the disease whereas the cotwin does not). A cotwin-control study can account for genetic and familial factors better than other types of case-control designs (see Lichtenstein et al., 2002). For example, because twins share their age and gender (for same-sex pairs), control over these covariates is inherent in the design. Because twins are generally reared together, they share their early-life environment, including childhood socioeconomic status. Finally, twins tend to be similar in terms of cognitive abilities (Pedersen, Plomin, Nesselroade, & McClearn, 1992), thus providing some control over cognitive functioning earlier in life. The case-control design compared demented with nondemented individuals while statistically controlling for covariates.

**Methods**

**Participants**

Participants in this study were members of the Swedish Twin Registry (Lichtenstein et al., 2002)—a population-based registry of all twins residing in Sweden—who were 65 years of age or older in 1998. The Swedish Twin Registry was established in the 1960s when all twins in Sweden were identified. In 1961, 1963, and 1967, all same-sex twin pairs born before 1926 were mailed a questionnaire. Nonresponders in 1967 were sent another questionnaire in 1970. All same-sex pairs born between 1926 and 1958 were sent a questionnaire in 1973. Opposite-sex pairs were registered but were not sent questionnaires.

In 1998, the HARMONY study began a follow-up of all twins from both same- and opposite-sex twin pairs who were at least 65 years of age. A random sample of twins was selected for contact by telephone each month. The cognitive screening used the previously validated TELE instrument (Gatz et al., 1995; Gatz, Reynolds, Nikolic, Lowe, & Karel, 2002). Individuals who screened positive for cognitive dysfunction and their co-twins were contacted for an in-person clinical diagnostic evaluation for dementia. Clinical diagnoses of dementia followed the diagnostic criteria set forth in the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV; American Psychiatric Association, 1994). Differential diagnoses were made according to National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer’s Disease and Related Disorders Association (NINCDS–ADRDA) criteria for AD (McKhann et al., 1984), National Institute of Neurological Disorders and Stroke–Association Internationale pour la et l’Enseignement en Neurosciences (NINDS–AIREN) criteria for
vascular dementia (Roman et al., 1993), Lund and Manchester criteria for frontotemporal dementia (Lund and Manchester Groups, 1994; Neary et al., 1998), and consensus criteria for dementia with Lewy bodies (McKeith et al., 1996). A complete discussion of the study design can be found in Gatz and colleagues (2005). In the HARMONY study, 20,269 participants were eligible for screening. The response rate for telephone screening was 71.5%; the response rate for those eligible for the clinical phase was 70.2%. The same telephone screening also included questions about demographic factors, health and behavioral information, and main lifetime occupation (Lichtenstein et al., 2002). For those who responded to the telephone screening, 85.4% supplied data about lifetime occupation. This information was obtained from self-reports for 93% of the participants and from reports by knowledgeable informants for 7% of participants.

Overall, 10,168 individuals aged 65 and older had both complete data for cognitive status and main lifetime occupation. Of these, 314 individuals were classified as dementia cases and 9,854 individuals were classified as controls. Among cases, informant reports about occupation were available for 225, while 89 had self-reports only, potentially introducing a recall bias. Therefore, we excluded these 89 cases from the analyses. Among controls, 325 had only informant reports as a result of various health reasons other than cognitive impairment and were kept in the dataset. Thus, we included 10,079 participants. Complete data for cognitive status and main lifetime occupation. This information was obtained from self-reports for 93% of the participants and from reports by knowledgeable informants for 7% of participants.

We were able to identify 55 complete twin pairs discordant for dementia, of which 28 pairs were discordant for AD. The zygosity and gender of twins that we included in our cotwin-control analyses are shown in Table 2. In analyses with twin pairs discordant for all types of dementia, twin cases included 29 men and 26 women, and cotwin controls included 26 men and 29 women. In analyses with twin pairs discordant for AD only, there were 14 men and 14 women among twin cases and 15 men and 13 women among cotwin controls.
Table 3. Proportion of Participants With Main Lifetime Occupations in Each Level of Occupational Complexity (N = 10,079)

<table>
<thead>
<tr>
<th>Dimension</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data</td>
<td></td>
</tr>
<tr>
<td>Synthesizing</td>
<td>0.5</td>
</tr>
<tr>
<td>Coordinating</td>
<td>6.9</td>
</tr>
<tr>
<td>Analyzing</td>
<td>25.5</td>
</tr>
<tr>
<td>Compiling</td>
<td>16.0</td>
</tr>
<tr>
<td>Computing</td>
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</tr>
<tr>
<td>Copying</td>
<td>6.2</td>
</tr>
<tr>
<td>Comparing</td>
<td>17.2</td>
</tr>
<tr>
<td>M</td>
<td>3.0</td>
</tr>
<tr>
<td>SD</td>
<td>1.6</td>
</tr>
<tr>
<td>People</td>
<td></td>
</tr>
<tr>
<td>Mentoring</td>
<td>0.4</td>
</tr>
<tr>
<td>Negotiating</td>
<td>0.7</td>
</tr>
<tr>
<td>Instructing</td>
<td>3.0</td>
</tr>
<tr>
<td>Supervising</td>
<td>3.3</td>
</tr>
<tr>
<td>Diverting</td>
<td>0.7</td>
</tr>
<tr>
<td>Persuading</td>
<td>2.5</td>
</tr>
<tr>
<td>Speaking or signaling</td>
<td>22.6</td>
</tr>
<tr>
<td>Serving</td>
<td>34.6</td>
</tr>
<tr>
<td>Taking instructions</td>
<td>32.2</td>
</tr>
<tr>
<td>M</td>
<td>6.3</td>
</tr>
<tr>
<td>SD</td>
<td>1.6</td>
</tr>
<tr>
<td>Things</td>
<td></td>
</tr>
<tr>
<td>Setting up</td>
<td>0.0</td>
</tr>
<tr>
<td>Precision work</td>
<td>1.7</td>
</tr>
<tr>
<td>Operating</td>
<td>23.1</td>
</tr>
<tr>
<td>Driving and operating</td>
<td>11.8</td>
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<tr>
<td>Manipulating</td>
<td>16.5</td>
</tr>
<tr>
<td>Tending</td>
<td>11.0</td>
</tr>
<tr>
<td>Feeding or offbearing</td>
<td>3.8</td>
</tr>
<tr>
<td>Handling</td>
<td>32.1</td>
</tr>
<tr>
<td>M</td>
<td>4.1</td>
</tr>
<tr>
<td>SD</td>
<td>2.2</td>
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complexity of work with people, and .46 for complexity of work with things.

The scores range from 0.0 to 6.0 for complexity of work with data, 0.0 to 8.0 for the complexity of work with people, and 0.0 to 7.0 for the complexity of work with things. The codes are constructed so that lower scores reflect higher complexity and higher scores reflect lower complexity. Using one occupation as an example, “Radio and TV Mechanic” is assigned scores of 2.0 for complexity of work with data, 7.7 for people, and 1.2 for things, indicating that the occupation mostly involves “analyzing” data, “taking instructions–helping” people, and “precision working” with things. Occupation “Telephone Operator” is assigned scores of 4.8 for complexity of work with data, 5.8 for people, and 2.3 for things, indicating that the occupation involves “copying” data, “speaking–signaling” people, and “operating–controlling” things.

Table 3 summarizes the distribution of participants in the present study across complexity levels. Average complexity was 3.0 (± 1.6) for complexity of work with data, 6.3 (± 1.6) for people, and 4.1 (± 2.2) for things. In comparison, the averages for the same variables were 3.3 (± 1.9), 6.2 (± 2.0), and 4.5 (± 2.6) in a sample of the U.S. labor force in 1971 (Cain & Treiman, 1981). Score distribution for complexity of work with people was more skewed than score distributions for complexity of work with data or things, which corresponds with findings reported in Miller and associates (1980) and Cain and Treiman (1981). In our study, skewness was .19 for complexity of work with data, −1.77 for complexity of work with people, and .09 for complexity of work with things.

We observed significant intercorrelations for all three measures of occupational complexity. Complexity of work with data was positively correlated with complexity of work with people (r = .54, p < .05) and things (r = .19, p < .05). There was an inverse correlation between complexity of work with people and things (r = −.34, p < .05). The correlations for the U.S. labor force in 1971 were .56 for complexity of work with data and with people, −.04 for complexity of work with data and with things, and −.32 for complexity of work with people and with things (Cain & Treiman, 1981).

Other measures.—We considered age, gender, and level of education to be the main covariates in this study, as these have been identified as risk factors for dementia in a number of research reviews (e.g., Cummings, Vinters, Cole, & Khachaturian, 1998; Hendrie, 1998; Launer et al., 1999). In case-control analyses, participants were on average 72.7 years old (range 65–103 years). Women accounted for 52% of the sample. Table 1 shows tests of the association of each covariate with dementia and with AD. Higher age, female gender, and low educational attainment were risk factors for all types of dementia and for AD. Correlation coefficients between level of education and occupational complexity were .34 for data, .36 people, and −.04 for things (p < .05 for all reported correlations).

In our cotwin control analyses, the average age of participants was 80 years (range 66–92 years), and 50% of the sample were female. Differences between twin cases and cotwin controls on gender and on education were not significant.

For the purposes of data analysis, we measured education as basic versus more than basic. Participants described their highest level of education attained, that is, basic education, gymnasium, vocational high school, or university. Basic education corresponded to 6 years or, later, 7 years of school, and it reflected the level of education that was mandatory in Sweden during the first part of the 20th century. In this sample, 55% of the individuals attained this level of basic education, whereas 42% attained more than basic education.

Statistical Analyses

In our case-control analyses, we used logistic regression models to assess the association between complexity of lifetime occupation and risk of AD and all dementias. We used the LOGISTIC procedure in SAS (version 8.2; SAS Institute, Inc., Cary, NC). Because we included members of complete twin pairs in the analyses in the same way as individual participants, we corrected confidence intervals with robust standard errors for having two members from the same family included, using a program developed for this purpose and described by Moradi and associates (2002). Zygosity did not explain a significant amount of variance in any of the models (p > .30 in all models), and it did not influence the relationship between occupational complexity and risk of dementia or AD only. Therefore, we excluded it from final models. Results show the odds that participants with high levels of occupational complexity in their...
main lifetime occupation would be at a reduced risk of all types of dementia and AD only later in life. We calculated the odds while sequentially controlling for age and gender, level of education, and other types of complexity.

In our cotwin control analyses, we used conditional logistic regression models in the SAS procedure PHREG. Results show the odds that the twin with a relatively higher complexity of main lifetime occupation is at a reduced risk of dementia or AD compared with the cotwin with a relatively lower complexity. We explored the associations between occupational complexity and risk of dementia in all discordant twin pairs and in discordant monozygotic twin pairs alone. We calculated crude odds ratios and odds ratios controlling for other complexity dimensions. We did not control gender and level of education within these analyses because we had established that twins did not differ significantly on these variables. Most twin pairs were of the same sex. Among opposite-sex pairs, the chances of being demented were equivalent for men and women. Twins also did not differ on age, by definition, and therefore no control for age was warranted.

In all analyses, we used a two-tailed level of significance set at \( p = .05 \).

### RESULTS

#### Case-Control Analyses

Results for the association between dimensions of occupational complexity and risk of dementia and AD only are summarized in Table 4. We found that, when we took age, gender, and level of education into account, higher complexity of work with people in main lifetime occupation was associated with a reduced risk of all types of dementia and AD only. Controlling for age, gender, and level of education, we found that the association between lower complexity of work with things and a reduced risk of dementia was marginally significant \( (p = .05) \) but not significant for AD only. When we added complexity of work with data and things into the same model, higher complexity of work with people was protective against AD only (odds ratio or OR = 0.78; 95% confidence interval or CI = 0.63, 0.98). The result for complexity of work with people and risk of all types of dementia was only marginal \( (OR = 0.84; 95\% \ CI = 0.71, 1.00; p = .05) \), and other complexity dimensions showed no significant associations. No significant findings for complexity of work with data emerged in the case-control analyses.

Because the measure of complexity of work with people was skewed, we also conducted the same analyses by using log-transformed complexity measures. The results remained unchanged.

#### Cotwin Control Analyses

Results of conditional logistic regression analyses for twins discordant for dementia and those discordant for AD only are summarized in Table 5. Twins with higher scores for complexity of work with people were at a lower risk of dementia and AD only than their cotwins, and twins with higher scores for complexity of work with data were at a lower risk of AD. When we entered all complexity dimensions into one model, higher complexity of work with people between twins was associated with lower risk dementia \( (\text{OR} = 0.44; 95\% \ CI = 0.20, 0.97) \). We could not perform the parallel analyses with twins discordant for AD because of the small sample size. No other significant results emerged in these analyses. When we considered only monozygotic twin pairs, twins with higher complexity of work with people were at a lower risk of dementia \( (\text{crude OR} = 0.27; 95\% \ CI = 0.08, 0.98) \). No other results were significant. Results remained unchanged when we added level of education into the models.

#### DISCUSSION

Our aim in this study was to examine the association between specific types of occupational complexity and risk of all types of dementia and AD only in a population-based sample of twins. Although most adults spend substantial portions of their lives in activities commonly performed at work, not enough is known about how these work-related activities influence risk of
dementia later in life. We examined the association between three specific types of intellectual demands encountered at work—complexity of work with data, people, and things—and the risk of dementia and AD. To our knowledge, this is the first study to explore these specific types of occupational complexity in relation to risk of dementia and AD. As far as we know, it is also the first study to use two designs within one study—case control and cotwin control—to examine the occupation–dementia association. Finding similar results in the cotwin-control study suggests that results from the case-control study cannot be explained by genetic or familial confounding.

Our principal finding was that a higher complexity of work with people in the main lifetime occupation was associated with a reduced risk of AD and all types of dementia combined later in life, independent of age, gender, and level of education. The effect was sustained when we also controlled complexity of work with data and things, and when we analyzed data in a cotwin-control design that partially accounted for unmeasured genetic and familial factors shared by twins. In addition, a higher complexity of work with things was associated with a marginal increase in risk of dementia in case-control analyses; furthermore, in cotwin-control analyses, twins with a higher complexity of work with data were at a lower risk of AD than their cotwins.

Our findings for complexity of work with people are consistent with those of Stern and associates (1995), who found that interpersonal demands of main lifetime occupation may delay the onset of AD. Smyth and colleagues (2004) did not find significant results for social demands. However, they found significantly higher scores for AD cases compared with control individuals on a factor representing mental occupational demands. Our finding that twins with greater complexity of work with data than their cotwins were at a reduced risk of AD complements this finding. Comparing across studies, however, is somewhat constrained by the use of different occupational variables by different research groups. For example, complexity of work with people in our study includes mental demands related to organizing tasks as well as social demands related to negotiating and supervising.

The finding that occupation may influence risk of dementia and AD complements findings from studies with nondemented older adults. Schooler and colleagues (1999, 2004) suggested that exposure to complex environments at work affects the level of intellectual flexibility across the life course. The findings are also consistent with the use or lose it hypothesis, in which frequent engagement in “mental practice” is hypothesized to reduce risk of AD and other types of dementia (Katzman, 1995; Orrell & Sahakian, 1995).

Further research is needed to discern why occupations that require complex work with people appear to provide a buffer against dementia. Stern and colleagues (1995) attributed their finding of delayed AD onset for occupations with high demands on interpersonal skills to some unknown, unique life experience associated with working at such a job. Another possibility is that work that involves a person socially, regardless of how complex the work is in other respects, may be protective. In the Kungsholmen study, with a case-control design and using incident dementia cases and social network measured at baseline, Fratiglioni and associates (2000) found that having a larger social network was associated with a lower risk of dementia. In a Japanese case-control sample, Kondo, Niino, and Shido (1994) found that reported low social engagement was a risk factor for dementia. Crowe and colleagues (2003) found that intellectual or cultural leisure activities, such as social visits and going to the theater or cinema, reduced risk of dementia in a cotwin-control study. Another possibility may be that greater occupational complexity represents higher occupational status, which would be related to higher income, less exposure to workplace toxins, and better health-related resources. However, it is unlikely that differences among jobs that differ on complexity of work with people reflect differences in exposure to workplace toxins. Our finding that higher complexity of work with things may increase risk of dementia may be more conducive to such an inference.

Several limitations should be noted. First, this study is a study of prevalent dementia cases. The use of prevalent dementia cases exposes the results to a potential confounding effect of differential survival as a competing explanation for the association between occupational complexity and the risk of dementia. For example, occupations with a lower degree of substantive complexity (Moore & Hayward, 1990) have been found to be associated with higher mortality. However, if less complex occupations are associated with mortality, odds ratios observed in this study would probably underestimate the strength of the association between complex occupations and the risk of dementia.

Second, the sample of twins discordant for dementia included only 17 monozygotic twin pairs, limiting our ability to observe within-twin pair differences. The statistical power to detect significant findings at a $p = .05$ level of significance was 60% or less for the cotwin-control analyses. The fact that we did find significant results in the cotwin-control sample gives credence to the possibility that complex work influences risk of dementia and AD. A post hoc analysis found that the control groups from the case-control analyses and the cotwin-control analyses did not differ significantly on any of the three complexity measures ($p > .05$), adding confidence to the conclusion that results were parallel across the two designs.

Third, even the case-control sample had a relatively small number of cases, which can result in insufficient power and greater risk of Type II error. The power to observe significant results was between 70% and 90%. Fourth, the use of complexity scores from the 1970 U.S. Census for occupations in the 1980 Swedish Census may have resulted in some inaccuracies caused by cross-national differences in occupations.

Fifth, informants were used for participants who could not provide information about main lifetime occupation because they were cognitively impaired. Although the use of informant data for cases and some controls (3%) may lead to bias, the bias of using informant-report data has been found to be minimal in previous studies (Demissie et al., 2001; Rocca et al., 1986). This may be particularly true for a very objective variable such as main lifetime occupation. Finally, some members of the HARMONY study could not be interviewed as a result of illness and absence of an informed proxy. Therefore, information about main lifetime occupation of these participants could not be obtained during the telephone screening. Although these individuals were later reached in person or a proxy was interviewed for purposes of clinical diagnosis, they were not included in this study.
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In conclusion, using a population-based sample of twins within case-control and cotwin-control study designs, we found that complexity of work, and particularly complex work with people, can influence risk of dementia and AD later in life, even when age, gender, and level of education were controlled in case-control analyses and when unmeasured factors shared by twins were controlled in cotwin-control analyses.

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