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Job demands and dementia risk among male twin pairs

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Abstract

Background— Job characteristics may influence dementia risk, but some types of job complexity remain to be examined. Twin studies provide a useful methodology to examine job differences between pairs who share many environmental and genetic influences.

Methods— Members of the NAS-NRC Twins Registry of World War II Veterans received a clinical evaluation for dementia and had job ratings from the Dictionary of Occupational Titles.

Results— Cotwin-control models ($n = 220$ pairs) indicated lower dementia risk with greater job demands of reasoning, mathematics, language, and vocational training, with comparable results in case-control models ($n=425$ cases). These effects were significant among twin pairs discordant for 6 or more years, but not among those discordant between 3–5 years. Results were similar for Alzheimer's disease, and main effects were not further explained by zygosity or apolipoprotein E genotype.

Conclusions— Jobs that utilize data, academic skills, and extensive vocational training may protect against dementia; however, in twin pairs these effects only emerged among individuals who remained free of dementia several years after onset in their sibling.

Keywords

Dementia; Alzheimer's disease; Twins; Occupation; Job complexity

1. Introduction

The projected doubling of incident Alzheimer's disease (AD) by the year 2050 [1] has created a compelling interest in identifying factors that may prevent or delay the emergence of this and other dementias. Research suggests that older adults who regularly engage in intellectually stimulating activities maintain better cognitive functioning over their lifespan than those who do not [2], and the principal activity throughout the lives of most adults is their work. Longitudinal studies by Kohn and Schooler found that the substantive complexity of an individual's occupation is positively associated with his or her cognitive functioning, as characterized by performance on measures of intellectual flexibility [3]. Subsequent research found this effect to hold true over a 30-year period, and moreover, that it was stronger among older workers [4]. Studies of the association between work and dementia, however, have had

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mixed results; for instance, several studies based on broad occupational categories have found that manual work is associated with higher dementia risk than non-manual work [5–7], while similar studies have found no such relationship to dementia [8–11]. One reason for these equivocal findings may be that broad occupational categorizations can encompass other factors like socioeconomic attainment or exposure to industrial agents that may also influence cognitive function [12,13]. Broad categories may also obscure the specific work characteristics that are most influential to dementia. Studies of specific work characteristics have found a more consistent association to dementia than those using broader occupational categories, but there are still differences in what specific characteristics most influence disease risk. In one case-control study, AD risk was greater when mental occupational demands were lower and physical occupational demands were higher, with no association to social demands [14]. Another study using a case-control model found that social demands were associated with reduced risk of AD, but that intellectual demands were not [15]. Intellectual demands in the workplace may not be a unitary construct, however, and it is important to examine how specific types of job characteristics may relate to dementia outcome.

Explanations of the relationship between job characteristics and dementia often focus on the idea of cognitive reserve. Cognitive reserve theory asserts that some individuals have greater capacity than others to function effectively in the context of brain injury or pathology due to advantageous biological mechanisms or methods of compensation [16]. Factors like occupational complexity may promote cognitive reserve by strengthening or diversifying neural pathways, or by facilitating more adaptive use of cognitive processing mechanisms. In theory, higher levels of cognitive reserve enable some individuals to avoid clinical manifestations of dementia longer than others even though the extent of their underlying brain pathology may be similar. For instance, one study that examined the relationship between occupational characteristics and dementia found that individuals with greater lifetime job demands of intellectual complexity and interpersonal skills demonstrated less clinical manifestation of dementia relative to a neuroimaging-based marker of AD pathology [17]. Intellectual complexity, however, did not remain significant after controlling for education level, which suggests that some effects may not be independent of education. Studies have also found that individuals with higher occupational complexity and higher education show a more rapid decline in memory and general cognitive status after clinical manifestation of AD, which is believed to occur as diminishing cognitive reserve results in neurocognitive performance that is more reflective of underlying dementia pathology [18,19].

Twin studies provide a useful methodology for examining how differences in factors like occupation or education may influence the clinical manifestation of dementia between two individuals who share many environmental and genetic influences. When considering a condition like dementia that may be influenced by multiple genetic and non-genetic factors that occur throughout the lifespan, twins provide a unique control for both known and unknown influences. Monozygotic (MZ, identical) twins share all of their genetic material, whereas dizygotic (DZ, fraternal) twins on average share 50% of their genes. Differences in a predictor or outcome between genetically identical pairs are presumed to reflect an environmental influence; both identical and fraternal twin pairs are most likely similar for early life influences such as socioeconomic status or upbringing that can affect later life outcomes like occupation and cognition. Cotwin-control analysis compares how differences within twin pairs on a particular variable contribute to differences within pairs on an outcome of interest, such as dementia. One twin study has examined the relationship between occupational complexity and dementia and found that twins with higher complexity of work with people and data were at less risk of dementia and AD specifically than their co-twins with lower scores in these job domains [15]. The effect of complexity with people remained significant in analysis of MZ twins only, which suggests that this beneficial effect of interpersonal complexity in work was not due to genetic factors.

One approach to better understanding the effects of work characteristics on dementia is to examine their strength among twin pairs that remain discordant for dementia for different lengths of time. The longer a protective effect holds, the more influential it will be in preventing dementia. We included several work characteristics directly available in the Dictionary of Occupational Titles [20], and were particularly interested in those that reflect application of prior educational and vocational training, which have not been specifically examined in previous studies.

2. Methods

The procedures described below were approved by the Institutional Review Board at Duke University Medical Center.

2.1. Participants

Participants were enrolled in the Duke Twins Study of Memory in Aging, and were members of the National Academy of Sciences-National Research Council (NAS-NRC) Registry of World War II veteran male twins, born from 1917 to 1927. As part of the study, surviving and consenting twin pairs were administered a cognitive status measure every 3 to 4 years beginning in 1990 as part of a screening and assessment protocol for dementia. Occupational history was collected by trained interviewers during telephone interviews at either Wave 3 (1996–98) or Wave 4 (2000–2001) for all nondemented pairs and for those pairs in which a member was identified as demented in Waves 3 or 4. For individuals who were identified as demented prior to Wave 3 (and their cotwins), the occupational history was collected during follow-up phone interviews administered by trained interviewers. This information was obtained directly from the participant in most cases, and from a proxy informant if the participant was unable to complete the interview.

2.1.1. Sample composition: Case-control analysis—A total of 6473 eligible nondemented control participants completed an occupational history at either Wave 3 or 4. The difference in the final sample of 6075 was due to: 1) individuals with unknown cognitive status because all targeted phases were not completed, or 2) missing information on education or date of birth. We excluded potential control participants who did not complete targeted telephone cognitive screening interviews or in-person clinical assessments in order to avoid including individuals with possible dementia who were not fully assessed for this condition.

The sample for dementia cases included 425 individuals diagnosed with dementia based on the screening and assessment protocol described below, and 295 of these cases were diagnosed as AD.

2.1.2. Sample composition: Cotwin-control analysis—Twin pairs were included in cotwin-control analyses if they were discordant for any diagnosis of dementia; that is, one twin has a dementia diagnosis (proband) and the other (cotwin) either does not carry a current diagnosis of dementia or was nondemented at time of death. To account for the insidious onset of dementia symptoms and thus the imprecision in estimating an age of onset, we required that the cotwin remain alive and non-demented for at least three years after dementia onset in the proband. Of the total of 408 twin pairs in which one or both twins were demented, 130 pairs were excluded due to concordance for dementia or because the unaffected cotwin had not been followed for at least three years after the age the onset in the twin with dementia; others were excluded because occupational information was not available ($n = 37$), the cognitive status of the cotwin was not known ($n = 16$), or zygosity was unknown ($n = 5$). This resulted in a sample 220 twin pairs, of which 112 pairs were MZ. Zygosity was determined from DNA samples in 92 pairs and from the best available information from questionnaire responses, fingerprint

analysis, and anthropometric data from military records [21,22] for the remainder of the pairs. Cross-validation has found these methods of establishing zygoty to be 97% correct [23]. Availability of APOE data was comparable between demented (MZ = 87%, DZ = 73%) and nondemented (MZ = 87%, DZ = 74%) groups.

2.2. Dementia assessment and diagnosis

The diagnosis of dementia was determined based on the outcome of a multi-step screening and assessment protocol that has been described previously [24]. All individuals in the study were screened for possible cognitive impairment with the modified Telephone Interview for Cognitive Status (TICS-m) [25] during at least one wave of data collection. A minority of individuals who were unable to complete the TICS-m were screened by proxy with the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) [26] or another brief proxy interview. Proxy informants were individuals who knew the study participant well enough to provide reliable ratings of their cognitive and functional abilities, usually the spouse or an adult child. For study participants who scored below a predetermined score on the TICS-m or by proxy screening, the Dementia Questionnaire (DQ) [27] was then administered to a knowledgeable proxy informant. Individuals whose DQ indicated possible dementia were scheduled for an in-home evaluation by a research nurse and a neuropsychology technician, which included both direct assessment of the participant and data gathering from a knowledgeable informant. As part of the evaluation, the participants completed: 1) a battery of neuropsychological measures, 2) a standardized neurological examination, 3) blood pressure readings, 4) collection of blood or buccal DNA samples for determination of zygoty and apolipoprotein E (APOE) genotyping, and 5) a brief videotaped segment of cognitive status items and the neurological examination. Information collected from the informant included: 1) a chronological history of cognitive function, 2) medical history and current medications, 3) current neuropsychiatric symptoms, 4) history of memory problems in first-degree relatives, and 5) measures assessing severity of cognitive and functional symptoms. When possible, we attempted to obtain medical records for neuroimaging and laboratory results that might be relevant to diagnosis.

Each participant who completed an in-home assessment was reviewed at case conferences using all available information. Case conferences were attended by geropsychiatrists, neurologists, neuropsychologists, cognitive neuroscientists, nurses, and neuropsychology technicians. The purpose of the case conferences was to assign a preliminary research diagnosis to each individual based on their cognitive and functional status. Final diagnoses were assigned by an expert consensus panel of invited neuropsychologists, neurologists, and psychiatrists with expertise in dementia.

Dementia was diagnosed based on guidelines from DSM-III-R [28], and AD was diagnosed based on NINCDS-ADRDA criteria [29]. Diagnosis of vascular dementia [30], frontal lobe dementia [31], dementia with Lewy Bodies [32], and other dementias were based on standard criteria. Additional details of the methodology for dementia assessment and diagnosis are described elsewhere [24]. Age of onset for dementia was assigned as part of the case conference diagnosis based on the age at which an individual unambiguously met DSM-III-R criteria for dementia. This methodology of assessment and diagnosis has been successfully used in several other epidemiological studies of dementia, and has resulted in good agreement between clinical and neuropathological diagnoses [33].

2.3. Measures

2.3.1. Occupational coding methodology—Occupational information was collected from a series of questions administered during telephone interviews. Questions included: 1) longest-held job, 2) job title, 3) specific job duties, 4) type of industry, and 5) beginning and

ending year for the job. Specific occupational classifications were then assigned based on these responses. Job classification was based on the Dictionary of Occupational Titles (DOT), 4th edition [20], which contains descriptions of 12,740 occupations. DOT codes were assigned by one of two psychometricians trained in accordance with written procedures and decision rules to ensure coding reliability. A sample of 449 occupations independently coded by both technicians indicated moderately high interrater reliability [34] ranging from 0.85 to 0.90 for the eight specific DOT work characteristics used in this study. These characteristics included: 1) complexity of work with Data, 2) complexity of work with People, 3) complexity of work with Things, 4) Mathematical Development, 5) Language Development, 6) Reasoning Development, 7) Specific Vocational Preparation (SVP), and 8) Strength. The Data, People, and Things ratings were used in previous research on dementia [15], and the remaining five characteristics were selected to include a broader range of relative job demands, including educational and vocational elements. In addition, each of these characteristics is directly accessible from either the numeric code for the DOT occupation (Data, People, Things) or as ratings accompanying the individual job descriptions. Job characteristics in the DOT are based on the work of trained job analysts who rated jobs based on a number of defined criteria [20, 35].

2.3.2. Data, People, and Things—Work with Data is coded from 0–6, ranging from synthesizing and coordinating to copying and comparing. Work with People is coded 0–8, ranging from mentoring and negotiating to taking instructions-helping. Work with Things is coded 0–7, ranging from set-up and precision work to basic handling tasks. The Data, People, and Things ratings are structured such that the lower scores reflect the higher levels of complexity.

2.3.3. Mathematical Development, Language Development, and Reasoning Development—These variables reflect aspects of both formal and informal education that are required of a worker for satisfactory job performance. Mathematical Development is coded from 1 (basic math, working with basic units of measurement) to 6 (advanced mathematics and statistics). Language Development is coded from 1 (simple word reading, basic sentence writing) to 5 (reading and writing of scientific, technical, journalistic, legal, and financial reports, as well as creative writing). Reasoning Development is coded from 1 (using commonsense to execute simple instructions) to 6 (apply principles of logical or scientific thinking to “apprehend the most abstruse classes of concepts”) [20] (pg. 1009). For each of these variables, the highest rating reflects the highest level of complexity.

2.3.4. SVP—The SVP variable represents “the amount of lapsed time required by a typical worker to learn the techniques, acquire the information, and develop the facility needed for average performance in a specific job-worker situation.” [20] (pg. 1009). SVP includes several forms of training that include: 1) specific vocationally relevant coursework in high school and college, 2) apprenticeship training, 3) employer-organized classwork, 4) on-the-job training, 5) and experience in lower grade positions necessary to qualify for higher grade positions. This training time is coded 1–9, ranging from “short demonstration only” to greater than 10 years of preparation. Higher levels of the SVP variable reflect greater amounts of time spent in vocational preparation.

2.3.5. Strength—The strength rating is based on the strength requirements deemed important for satisfactory performance of the specific job. This characteristic is expressed in terms of five discrete levels: Sedentary, Light, Medium, Heavy, and Very Heavy. In the current study, Strength was recoded as a numeric ordinal variable ranging from 1–5, with higher values reflecting greater strength requirements.

2.4. Statistical methods

Case-control analyses used regression in the form of Cox proportional hazards models. We modeled each of the job characteristics separately as a predictor variable with education level as a covariate, and with years to onset of dementia diagnosis as the outcome variable. We then ran the same regression models with the dependent variable limited to AD. In the case-control analyses, we adjusted the covariance matrix of the beta coefficients to partially account for the dependencies between members of a twin pair, utilizing a previously published SAS macro [36]. For cotwin-control analyses, we used similar Cox proportional hazards models that were additionally dependent on twin pairing. We modeled each of the job characteristics separately as predictor variables and with years to dementia onset as the outcome. Following our hypothesis, we then ran similar regression models after stratifying the sample based on the number of years the cotwin has been discordant for dementia. For a twin pair to be discordant for AD, we required that the current age or age at death of the unaffected co-twin be at least three years greater than the age of onset of the proband, which was to account for the imprecision in estimating age of onset of dementia. We separated the groups based on discordance for dementia between 3–5 years and discordance for greater than 6 or more years. Discordance for a period of 5 years approximately reflects the rate at which dementia prevalence doubles between ages 65–85 [37] and provides a useful reference point for this stratification. Additional analyses included testing of interactions by zygosity and apolipoprotein E (APOE) genotype on the relationship between job characteristics and dementia. Analysis of APOE was based on MZ pairs only, stratified by those pairs with one or more APOE e4 alleles and those pairs without an e4 allele. We re-ran the models described above restricting dementia diagnosis to AD only. We also regressed dementia and AD diagnoses on education alone in both case-control and cotwin-control samples. All analyses were run using SAS statistical software, and the regression models were run using SAS Proc PHREG [38].

3. Results

Participant characteristics and descriptive information for occupational variables appear in Table 1.

3.1. Case-control analysis of dementia

Multivariate models covarying for education indicated that individuals without dementia had significantly higher complexity values on the variables reflecting: 1) work with Data, 2) Mathematical Development, and 3) SVP (Table 2). Results for the sample of AD found no significant associations with the occupational variables.

3.2. Cotwin-control analysis of dementia

Multivariate models covarying for education found that the member of the pair without dementia had significantly higher values on Reasoning Development, Mathematical Development, Language Development, and SVP (Table 2). Analysis of twin pairs discordant for dementia ($n = 96$) between 3–5 years found no effects of work characteristics with education as a covariate (p -value range = 0.58 – 0.95). Analysis of twin pairs discordant for dementia at least 6 years and covarying for education indicated that the member of the pair without dementia had significantly higher complexity on Data, Reasoning Development, Mathematical Development, Language Development, and SVP (Table 2). Although there were no significant interaction effects by zygosity, the absolute hazard coefficient relative to the null hypothesis was higher in MZ pairs than DZ pairs in 6 of the 8 complexity variables (Data, Things, Reasoning Development, Mathematical Development, Language Development, SVP), and two of the variables were significant within MZs (Things, $p = 0.048$; Reasoning Development, p

= 0.028). These models of dementia were unchanged when tested for interactions by APOE genotype.

3.3. Cotwin-control analysis of AD

Multivariate proportional hazards models assessing AD risk within twin pairs found that the member of the pair without AD had a significantly higher value on Mathematical Development. Similar to findings with dementia, no job characteristics were associated with AD in multivariate models covarying for education among twin pairs discordant for AD between 3–5 years. Among individuals discordant for AD greater than 6 years, there were significantly higher scores for the twin without AD on Mathematical Development, Language Development, and SVP. There were no significant interactions by zygosity, but the absolute hazard coefficient relative to the null hypothesis was higher in MZ pairs than DZ pairs in 7 of 8 comparisons (Data, Things, Reasoning Development, Mathematical Development, Language Development, SVP, Strength). These models of AD were unchanged when tested for interactions by APOE genotype.

3.4. Education, dementia, and job characteristics

Education was not a significant predictor of dementia or AD when used as a covariate in cotwin control models, nor was it significant in these models when tested alone as a predictor of dementia or AD. Education was a significant predictor of dementia when used as a covariate with several job characteristics in case-control models (Data, People, Things, Mathematical Development, SVP, and Strength). Education was a significant predictor of AD in case-control models when covaried with People and Things. Education was significant in case-control models when tested alone for predicting dementia ($p < .01$) and AD ($p < .05$).

4. Discussion

The current study found that higher complexity on several specific job characteristics was associated with a lower likelihood of both dementia and AD. Although there were some differences in the association between specific job characteristics and dementia when comparing case-control to cotwin-control analyses, the most consistent findings were for Mathematical Development and Specific Vocational Preparation. In cotwin-control analyses, we found that significant relationships between job characteristics and dementia were present only among twins discordant for dementia by at least 6 years. Similar results were found between job characteristics and length of discordance in analysis of AD only. Although interactions by zygosity did not change the results for either dementia or AD alone, effect sizes were generally larger in MZs than in DZs. Interactions by APOE genotype did not change the results for dementia or AD.

Our finding of occupational effects among twin pairs who were discordant for dementia by 6 or more years provides robust support for the role of specific job characteristics in delaying or preventing dementia. Because progressive dementias have extended latent phases and subtle early symptoms, errors may occur in diagnosis and estimation of disease onset; thus, demonstrating the protective effect of occupational characteristics in those pairs discordant for dementia symptoms for an extended period of time substantially decreases the likelihood of misclassification errors [39], and is additionally useful in identifying environmental influences like job complexity that inform ways to prevent or delay disease onset. These findings are consistent with theories that greater cognitive reserve may slow or prevent the emergence of dementia, and they specifically suggest that cognitive reserve may be augmented by certain types of job demands.

The current study differs from previous studies of job characteristics and dementia in its examination of specific variables reflecting educational development and vocational training. We found consistent effects for Mathematical Development and Specific Vocational Preparation, but also for Language Development in some models. These significant effects were associated with dementia and AD above and beyond the effects of education, and job characteristics were a more robust predictor of dementia and AD risk than education in cotwin-control models. Because formal education ends in young adulthood for most individuals, it appears that workplace tasks are important to maintaining the protective effects of complex activity into the middle and older stages of adulthood.

While the results of the current study are broadly consistent with previous findings that job characteristics with higher intellectual-type demands are associated with lower likelihood of dementia and AD, there are some differences regarding the effects of other types of job demands. One of the previous studies of job characteristics focused on factors derived from individual DOT variables in a case-control design and found that higher mental demands significantly lowered AD risk, higher physical demands significantly increased AD risk, and social demands did not influence AD risk [14]. Consistent with this study, we did not find a significant effect of social job characteristics as reflected in the People rating, but we also did not find an effect of physical activity as reflected in the Strength rating. One reason for the differences in findings may be that these authors examined factor scores, whereas we examined ratings of individual job demands. Another study using a case-control model and DOT job ratings found a protective effect of the People rating on AD, whereas the same study using a cotwin-control model found protective effects of work with Data and People [15]. Similar to this study, we found stronger effects on some occupational variables for MZ pairs, which suggests that complex occupational characteristics have influence on the outcomes of dementia and AD beyond the effects of genes alone. We did not, however, replicate the significant effects of the People rating found in the prior study, which may reflect a lower mean level of the People variable that exists in our sample relative to that study, and also relative to a sample from the U.S. labor force in 1971 [40]. It may be that the mean score for the People rating would have been higher with a representative proportion of women in the sample, which may have changed the relationship between dementia and complexity of work with People.

The current study does have some limitations to consider. Coding of occupational complexity was based on previously collected histories, which may not be as accurate as a specific interview for job analysis [4]; however, this depth of interview is typically unfeasible in population-based studies of dementia, and previous research supports the use of the DOT as a source of occupational characteristics [15,17]. As mentioned previously, the absence of women in the NAS-NRC Twins Registry may have influenced the distribution of some job characteristics and could limit the generalizability of our findings. Socioeconomic factors like wealth or work-related factors like retirement age also could not be included in this study, and these factors may influence the relationships among job complexity and dementia.

Finally, it is important to consider the current findings from the societal perspective that most individuals spend at least some of their adult life in an employment context and can potentially benefit from work that is intellectually stimulating. Although the employment spectrum is diverse in job demands, our findings suggest that efforts to integrate continuing educational activities and training into the workplace may be a way to make many jobs more cognitively engaging. We also found that educational development (Language, Mathematics, Reasoning) was a key component of cognitively beneficial job characteristics, and these characteristics in the DOT do favor experiences gained through prior formal learning. This would suggest that expanding opportunities to obtain formal education is the most direct pathway to increasing an individual's ability to engage in cognitively beneficial work later in adult life. The current results also raise potential implications for the fact that increasing numbers of individuals are

projected by choice or necessity to postpone retirement and work into older ages. Although we did not establish a dose-response association for the number of years worked relative to job demands, it is reasonable to assume that longer periods of cognitively beneficial work may have a greater protective benefit against dementia, and that this could be aided by public policies to facilitate employment among older adults. As work becomes an ever larger aspect of the lives of older adults, so too will research on how work influences both normal and abnormal cognitive aging.

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Table 1
Group means for demographics and DOT job characteristics for case-control and cotwin-control comparisons.

Variable	Dementia n = 425	Case-control No dementia n = 6075	p	Dementia n = 110	Cotwin-control pairs		p
					No dementia n = 110		
Age	73.68 (6.13)	80.31 (3.35)	<0.01 *	73.44 (6.05)	80.91 (3.78)		<0.01 *
Education	13.18 (3.30)	13.68 (3.09)	<0.01 *	13.27 (3.33)	13.27 (3.25)		0.98
Job (years)	33.34 (10.60)	33.06 (10.48)	0.67	32.15 (11.00)	33.55 (10.89)		0.15
Data	2.11 (1.53)	1.87 (1.45)	<0.01 *	2.16 (1.63)	2.00 (1.46)		0.18
Things	4.14 (2.78)	4.26 (2.81)	0.40	4.22 (2.75)	4.12 (2.81)		0.65
People	5.11 (2.44)	4.83 (2.48)	0.03	5.17 (2.25)	5.10 (2.46)		0.70
Reason	4.19 (0.97)	4.35 (0.91)	<0.01 *	4.10 (0.95)	4.23 (0.86)		0.05
Math	3.39 (1.13)	3.58 (1.13)	<0.01 *	3.29 (1.12)	3.48 (1.03)		0.02 *
Language	3.76 (1.19)	3.94 (1.14)	<0.01 *	3.69 (1.18)	3.86 (1.13)		0.05 *
SVP	6.56 (1.63)	6.79 (1.49)	<0.01 *	6.40 (1.65)	6.71 (1.52)		0.02 *
Strength	1.22 (0.87)	1.13 (0.90)	0.06	1.20 (0.86)	1.20 (0.87)		1.00

Note. Standard deviations appear in parentheses. Age = age of onset for demented twin, age of death or censoring age for unaffected twin. Job = years in primary occupation. Reason = Reasoning Development, Math = Mathematical Development, Language = Language Development, SVP = Specific Vocational Preparation. Data, Things, and People are coded in the Dictionary of Occupational Titles such that lower scores reflect greater involvement/complexity; higher values reflect higher involvement/complexity in the remaining variables. *p*-value in case-control refers to test of mean differences *between groups*; *p*-value in cotwin-control refers to test of mean differences *within twin pairs*.

* indicates statistical significance.

Table 2

Cox proportional hazard ratios and probability of job characteristic variables predicting dementia from case-control models, overall twin-paired models, and twin pairs discordant for dementia > 6 years.

	Dementia, case-control n = 425 with dementia, 6075 without dementia		Dementia, all twin pairs N = 220 pairs		Dementia, twin pairs discordant n = 124 pairs	
	HR	p	HR	p	HR	p
Data	1.115 (1.015–1.226)	0.019*	1.158 (0.927–1.445)	0.196	1.41 (1.02–1.94)	0.037*
People	1.055 (0.946–1.177)	0.343	1.034 (0.795–1.344)	0.802	1.12 (0.814–1.535)	0.491
Things	0.996 (0.903–1.099)	0.941	1.058 (0.849–1.377)	0.620	1.10 (0.820–1.464)	0.538
Reason	0.884 (0.786–0.993)	0.053	0.741 (0.562–0.976)	0.033*	0.624 (0.432–0.901)	0.012*
Math	0.882 (0.794–0.980)	0.020*	0.742 (0.577–0.955)	0.020*	0.631 (0.452–0.880)	0.007*
Language	–0.897 (0.798–1.009)	0.083	0.755 (0.575–0.991)	0.043*	0.599 (0.415–0.863)	0.006*
SVP	0.908 (0.826–0.999)	0.045*	0.761 (0.611–0.948)	0.015*	0.625 (0.452–0.863)	0.004*
Strength	1.036 (0.935–1.147)	0.495	0.992 (0.775–1.269)	0.948	0.977 (0.705–1.355)	0.890

Note. HR = Hazard Ratio. Reason = Reasoning Development, Math = Mathematical Development, Language = Language Development, SVP = Specific Vocational Preparation. Data, Things, and People are coded in the Dictionary of Occupational Titles such that lower scores reflect greater involvement/complexity. For these 3 variables, decreased dementia hazard is indicated by HRs *greater* than 1, whereas for the remaining variables decreased hazard is indicated by HRs *less* than 1.

* indicates statistical significance.