Neurodegenerative Diseases: Occupational Occurrence and Potential Risk Factors, 1982 through 1991

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ABSTRACT

Objectives. To identify potential occupational risk factors, this study examined the occupational occurrence of various neurodegenerative diseases.

Methods. Death certificates from 27 states in the National Occupational Mortality Surveillance System were evaluated for 1982 to 1991. Proportionate mortality ratios were calculated by occupation for presenile dementia, Alzheimer's disease, Parkinson's disease, and motor neuron disease.

Results. Excess mortality was observed for all four categories in the following occupational categories: teachers; medical personnel; machinists and machine operators; scientists; writers/designers/entertainers; and support and clerical workers. Clusters of three neurodegenerative diseases were also found in occupations involving pesticides, solvents, and electromagnetic fields and in legal, library, social, and religious work. Early death from motor neuron disease was found for firefighters, janitors, military personnel, teachers, excavation machine operators, and veterinarians, among others.

Conclusions. Neurodegenerative disease occurs more frequently in some occupations than in others, and this distribution, which may indicate occupational risk factors, should be further investigated. (*Am J Public Health.* 1996;86:1281–1288)

Introduction

Mortality from neurodegenerative diseases (e.g., Parkinson's disease, presenile dementia, Alzheimer's disease, and motor neuron disease) is expected to increase greatly in the next 40 years. Between 1990 and 2040, the US elderly population is expected to grow from 31.6 million to 68.1 million.[1,2] Within this group, depending on the population model used, the mortality due to neurodegenerative disease is expected to increase by 119% to 231%. It is estimated that there will be 8.3 million to 13.5 million prevalent cases of neurodegenerative disease in the United States in 2040.[1,2]

Little is known about the etiology of neurodegenerative diseases. Neurologic degeneration is a natural concomitant of aging, but the role of environmental factors, such as work and work-related exposures, is still undefined. Evaluation of the occupational occurrence of neurodegenerative diseases could provide leads about etiological factors. One approach is to evaluate various neurodegenerative diseases as a group as well as individually. The rationale for this approach is that although certain neurodegenerative diseases are different at the clinical, pathological, and biochemical levels, they also share common characteristics at these levels.[3–5] Some authors suggest that the Parkinson–dementia–motor neuron disease complex may represent different aspects of a common response to nonspecific neuronal stress.[4,5]

The sensitivity of the nervous system to occupational and environmental factors (including diet, pharmaceuticals, and alcohol) is well established.[7] The possibility that the work environment can affect the nervous system in ways that contribute to neurodegeneration was considered in this study. Elucidation of the occupational distribution of neurodegenerative diseases could not only provide clues to their etiology but also give some direction to targeting prevention and therapeutic resources for the future.

Methods

The mortality for specific neurodegenerative diseases was examined for 27 states from 1982 to 1991. Data from death certificates were collected through the ongoing National Occupational Mortality Surveillance System. The underlying and contributing causes of death, the usual occupation, and various demographic variables were coded. The underlying and contributing causes of death were coded according to the *International Classification of Diseases* (ICD), 9th revision. Information was extracted for all death certificates (of people whose age at death was 15 and over) in which the following neurodegenerative diseases were ever mentioned: presenile dementia (ICD 290.1), Alzheimer's disease (ICD 331.0), Parkinson's disease (ICD 332.0), and motor neuron disease (ICD 335.2). Presenile dementia and Alzheimer's disease have different ICD codes and are shown separately even though in the *Diagnostic*

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TABLE 1—Number of Mentions on Death Certificates (n = 130 420)[a] of Neurodegenerative Disease in 27 States,[b] 1982 through 1991

Underlying or Contributing Cause of Death (ICD-9 Code)[c]	White Males	White Females	Black Males	Black Females
Presenile dementia (290.1)	5 434	9 738	297	484
Alzheimer's disease (331.0)	23 535	37 470	1 118	1 702
Parkinson's disease (332.0)	22 940	19 057	814	614
Motor neuron disease (335.2)	4 800	4 143	250	242

[a]In some cases, more than one of the targeted neurodegenerative diseases was named on a death certificate. The number of times that two neurodegenerative diseases were named on 130 420 death certificates in the database is as follows: presenile dementia and Alzheimer's disease, 71; presenile dementia and Parkinson's disease, 369; presenile dementia and motor neuron disease, 6; Alzheimer's disease and Parkinson's disease, 1643; Alzheimer's disease and motor neuron disease, 49; Parkinson's disease and motor neuron disease, 78. One case had Alzheimer's disease, Parkinson's disease, and motor neuron disease on the death certificate.

[b]Alaska, Colorado, Georgia, Idaho, Indiana, Kansas, Kentucky, Maine, Missouri, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, New York (except New York City), North Carolina, Ohio, Oklahoma, Pennsylvania, Rhode Island, South Carolina, Tennessee, Utah, Vermont, Washington, West Virginia, and Wisconsin.

[c]ICD-9 is the *International Classification of Diseases,* 9th revision.

and Statistical Manual of Mental Disorders, 3rd edition, revised,[7] they are both classified as subtypes of the category "dementias arising in the senium or presenium." Information on occupation and industry was coded according to the 1980 Bureau of the Census classification. Proportionate mortality ratios (PMRs) were computed by comparing the proportion of deaths with any mention on the death certificate of each specific neurodegenerative disease to all causes of death. Age-standardized proportionate mortality ratios were calculated with a computer program developed at the National Institute for Occupational Safety and Health.[8] The ratios were computed by comparing the proportion of deaths from a specific cause within a specific occupational group with the proportion of deaths from that cause in all occupations. When the observed and expected proportions are equal the proportionate mortality ratio is 100. For each proportionate mortality ratio, 95% confidence intervals were calculated on the basis of the Poisson distribution[9] if the observed number of deaths was 1000 or less and on the basis of the Mantel-Haenszel chi-square[10] if the observed deaths were greater than 1000. For exploratory purposes, deaths were grouped into occupational categories with similar occupational characteristics or exposures. The groupings were conducted by a certified industrial hygienist and a senior epidemiologist on the basis of the judgment of commonality of tasks and exposures.

Results

Table 1 shows the distribution of the 130 420 deaths by the number of times the four neurodegenerative diseases were mentioned on the death certificates for the years 1982 through 1991 by race and gender. The 10 highest ranked occupations (by statistical significance, or lacking that, by the numerically highest proportionate mortality ratio) for each of the selected neurodegenerative diseases by race and gender are shown in Tables 2 through 5. Only occupations with at least two deaths were included.

Occupational clustering for specific neurodegenerative diseases was exhibited in specific occupational categories such as agricultural workers (presenile dementia, Parkinson's disease, and motor neuron disease), electrical workers (presenile dementia, Alzheimer's disease, and motor neuron disease), and construction workers (presenile dementia and motor neuron disease). There was a cluster for religious workers and counselors with increased proportionate mortality ratios for presenile dementia, Alzheimer's disease, and Parkinson's disease. Another common pattern was for lawyers, judges, and archivists (Alzheimer's, Parkinson's, and motor neuron disease). A large number of jobs in which workers likely to have exposure to solvents were found to have increased proportionate mortality ratios for various categories of neurodegenerative disease. Also, workers involved in various administrative support and clerical occupations were highly represented. Machinists and machine operators were also widely represented in all categories of neurodegenerative disease.

Occupations with statistically significant increased proportionate mortality ratios for deaths between ages 15 and 55 years were also assessed. These groups generally had small numbers of cases. Relatively early age at death may be a clue that an environmental factor is involved in the etiology or pathogenesis of neurodegenerative disease. More occupations with statistically significantly increased proportionate mortality ratios were found for motor neuron disease than for any of the other neurodegenerative diseases. Included in this group were firefighters (PMR 318, n = 6), teachers (PMR 214, n = 27), machinists (PMR 318, n = 3), military personnel (PMR 188, n = 27), veterinarians (PMR 1108, n = 2), excavation machine operators (PMR 538, n = 3), janitors (PMR 235, n = 9), packaging machine operators (PMR 985, n = 2), technical support (PMR 200, n = 11), and mail distribution workers (PMR 894, n = 2).

Discussion

Limitations of the Study

The association between occupation and neurodegenerative disease can be influenced by the extent of bias to include or exclude neurodegenerative disease as a cause of death on a death certificate. In the United Kingdom, Goldacre examined the extent to which a disease present at death is not recorded on the death certificate.[11] The only neurodegenerative disease examined was Parkinson's disease, which was found to be mentioned in 61% of cases but was recorded as the underlying cause in only 30% of the cases. Lilienfeld and Perl reviewed data from the National Center for Health Statistics and found that only one fourth of decedents with Parkinson's disease have a death certificate with that disease listed as the underlying cause.[1] This was less of a problem in our study because the proportionate mortality ratio was computed on the basis of any mention of a neurodegenerative disease on the death certificate. However, if there was differential reporting by occupation or by physicians treating different occupations, some occupations might appear more frequently than others. If there was differential reporting by socioeconomic class, it would be likely that higher socioeconomic occupations would show increased proportionate mortality ratios. This is generally not the case.

For each race and gender group, there is a mixture of occupational categories with increased proportionate mortality ratios. The exception is the category of White males, which has a slightly greater number of higher socioeconomic occupations than of lower ones. When we analyzed the proportionate mortality ratios for only white-collar occupations for White males, however, the elevated proportionate mortality ratios were generally the same as in the overall analysis. Additionally, changes in the frequency of various neurodegenerative diseases during the study period could have resulted in increased misdiagnoses, which may have led to some spurious findings. For various neurodegenerative diseases, such as Alzheimer's disease and Parkinson's disease, a definitive diagnosis can be made only with neuropathological confirmation, which is not often performed on the death of an aged patient.[12–14] These factors would not be likely to lead to an overrepresentation of a neurodegenerative disease in any particular occupational category. Misclassification of occupation could lead to an underrepresentation of some occupations and overrepresentation of others if an early exposure was involved in the etiology. The designation of occupation on death certificates may be incorrect if a decedent had many occupations but only the longest held was entered on the certificate.

The proportionate mortality ratio methodology may also bias risk estimates when, for example, the overall mortality rate is higher or lower in the occupational group of interest than in the comparison population.[15–16] Also, with proportionate mortality ratios, the observed and the expected for all causes of death must be equal (since they are proportions); thus, a deficit in one disease must be compensated by an excess in another. Finally, the large number of occupations for each cause of death could by chance alone result in some proportionate mortality ratios being statistically significant.

The occupational distribution of deaths from the four neurodegenerative diseases should be assessed in light of factors that create spurious associations or mask true ones. The finding of specific clusters of occupations for a particular neurodegenerative disease was not hypothesized a priori; rather, the clusters were selected from the data. The fact that many of the occupational clusters corroborate previous findings of potential risk factors in the literature supports the validity of some of the findings. The findings, however, need to be viewed as leads, not as confirmed associations.

TABLE 2—Highest Ranked Occupations for Risk of Presenile Dementia, by Subjects' Race and Sex

Occupation	No. Observed Deaths[a]	PMR	95% CI
White males			
Marine life cultivation workers	2	2196	266, 7931
Photographic process machine operators	4	454	124, 1163
Public relations specialists	7	368	148, 759
Aerospace engineers	11	344	172, 616
Graders and sorters, excluding agriculture	6	304	111, 661
Horticultural specialty farmers	6	300	110, 652
Supervisory electricians and power transmission installers	10	214	103, 394
Dentists	21	194	120, 297
Teachers	114	161	133, 194
Clergy	67	156	121, 198
White females			
Vehicle and mobile-equipment mechanics	3	403	83, 1178
Graders and sorters of agricultural products	2	281	34, 1016
Photographers	5	260	85, 608
Drafting occupations	3	232	48, 677
Dental assistants	9	219	100, 416
Related agricultural occupations	4	206	56, 527
Clinical lab technicians	8	216	93, 426
Counselors, educational and vocational	3	172	36, 504
Hairdressers and cosmetologists	82	170	135, 211
Social workers	23	158	100, 238
Black males			
Stock handlers and baggers	3	706	146, 2064
Fishers	2	550	67, 1987
Painting and paint spraying	2	496	60, 1791
Garage and service-station related	2	348	42, 1256
Personal service occupations, NEC[b]	2	289	35, 1043
Sailors and deckhands	2	270	33, 975
Pressing machine operators	2	232	28, 839
Postal occupations	6	230	84, 500
Molding and casting operators	2	188	23, 680
Carpenters	8	172	74, 339
Black females			
Construction laborers	3	1936	400, 5659
Laborers excluding construction[c]	4	1348	367, 3542
Packaging and filling operations	2	376	41, 1215
Precision production, craft, and repair	13	251	134, 424
Administrative support	14	228	124, 382
Assemblers	2	225	27, 811
Social workers	3	208	25, 751
Teachers	28	176	117, 255
Child care workers	3	166	34, 486
Health technologists	5	146	47, 341

Note. PMR = proportionate mortality ratio; CI = confidence interval.
[a]Number of deaths observed with any mention on death certificate of designated degenerative disease.
[b]NEC is not elsewhere classified.
[c]Under age 65.

Although environmental factors have been suggested as causes for the increasing crude mortality rates for Parkinson's disease and motor neuron disease over the last 15 years,[17,18] Riggs and Schochet have argued that the increase in rates can be explained by the declining mortality from ischemic heart disease and strokes, which creates the opportunity to live longer and thus be susceptible to these neurodegenerative diseases.[19] Increasingly, however, there are findings linking

TABLE 3—Highest Ranked Occupations for Risk of Alzheimer's Disease, by Subjects' Race and Sex

Occupation	No. Observed Deaths[a]	PMR	95% CI
White males			
Licensed practical nurses	6	279	103, 608
Counselors, educational and vocational	10	245	117, 450
Animal caretakers, excluding farm	8	238	103, 469
Legal assistants	9	225	103, 427
Aerospace engineers	28	184	122, 266
Metallurgical engineers	28	179	119, 259
Painters, sculptors, craft-artists, and printmakers	44	170	124, 228
Chemists	125	172	143, 204
Teachers	403	166	156, 182
Lawyers and judges	199	162	141, 187
White females			
Radiologic technicians	14	241	132, 405
Hairdressers and cosmetologists	12	209	108, 365
Bus drivers	16	179	102, 291
Health-diagnosing occupations	18	172	102, 272
Bank tellers	72	151	118, 190
Designers	92	139	112, 170
Writers, artists, entertainers, and athletes	265	135	111, 162
Management-related occupations	313	134	120, 150
Teachers	2517	134	130, 138
Secretaries, stenographers, and typists	1461	129	123, 135
Black males			
Broadcast-equipment operators	2	2924	354, α
Railroad conductors and yardmasters	3	1153	2381, 3369
Millwrights	4	663	181, 1697
Extruding- and forming-machine operators	2	620	75, 2239
Aircraft mechanics	3	534	110, 1561
Miscellaneous food-preparation occupations	7	297	119, 612
Teachers	23	270	171, 404
Precision metalworking operations	18	176	104, 278
Clergy	31	152	103, 216
Technical, sales and support	66	129	100, 165
Black females			
Dental laboratory and medical appl. technicians	3	4064	839, α
Mechanics and repairers	3	581	120, 1698
Precision metalworking occupations	5	478	115, 1115
Slicing- and cutting-machine operators	2	395	48, 1427
Information clerks	4	276	75, 706
Production inspectors, testers, and weighers	9	251	115, 477
Teachers	114	209	172, 251
Managers and administrators	27	177	117, 258
Health service occupations	43	148	107, 199
Technical, sales, and administrative support	72	136	107, 172

Note. PMR = proportionate mortality ratio; CI = confidence interval.
[a]Number of deaths observed with any mention on death certificate of designated degenerative disease.

environmental exposures to various neurodegenerative diseases.[17,20–22] The following section identifies some of the environmental factors that have been associated with neurodegenerative diseases. When these factors pertain to associations found in this study, they are highlighted. No claim is made that any of these are yet established risk factors for neurodegenerative diseases.

Potential Risk Factors

Generally, the etiology of neurodegenerative diseases is unknown. Some chemical, physical, and biological agents, however, have been identified as confirmed or potential risk factors for neurodegenerative diseases. Although there are conflicting findings,[23] various population-based case–control studies have shown that, among other factors, pesticide use is a risk factor for Parkinson's disease.[20,24–26]

Studies have shown that a contaminant of synthetic opiates, 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), was causal in the development of Parkinson's disease.[27–29] One might also expect substances that act like MPTP, such as certain pesticides, to be associated with Parkinson's disease. This contention was supported in our study—an excess was found in male pesticide applicators, horticultural farmers, farm workers, and graders and sorters of agricultural products. Additionally, Fleming et al. reported that a statistically significantly greater percentage of brains from case subjects who had had Parkinson's disease contained the pesticide dieldrin than did those from control subjects.[30] Parkinsonism has also been associated with the manganese-containing fungicide Maneb (manganese ethylene bisdithiocarbamate).[31]

Because many of the occupations with increased proportionate mortality ratios, such as teachers, lawyers, health personnel, counselors, and clergy members, involve interactions with large numbers of other people, one might suspect that an infectious agent could be involved in the etiology of neurodegenerative diseases. There is a body of evidence that suggests that chronic neurological diseases may have viral etiologies, but no study of tissue or body fluids has revealed the presence of active infection or immunological features of past infections in any of the major neurodegenerative diseases.[4,32]

Traumatic events, fractures, other mechanical injuries, and surgical operations have been shown to be related to amyotrophic lateral sclerosis, a category of motor neuron disease, in some but not all studies.[33–35] In our study, the proportionate mortality ratios for motor neuron disease were elevated for the occupational group that includes professional athletes. These workers may have an above-average frequency of traumatic injuries and surgical operations.[36] Hence, the popular synonym "Lou Gehrig's disease" may reflect not only a particular disease but also an occupational etiology. Semchuck et al. found that head trauma was one of the strongest predictors of Parkinson's disease.[25] Other studies[37,38] have demonstrated this, but at least one has not.[21]

In our study, we found increased proportionate mortality ratios for Alzheimer's and motor neuron diseases among occupations that could have exposure to

electromagnetic fields, such as those found in radio and television stations, power plants, airplane cockpits, or in working as an electrician or in telephone repair (under age 55). There is a small but suggestive literature on the role of ionizing and nonionizing radiation in the etiology of neurodegenerative diseases.[33,35,39–41] In a case–control study in Sweden, Gunnarsson et al. found approximately a sevenfold motor neuron disease risk for subjects employed in electrical work.[22]

Exposure to metals has often been mentioned as a candidate risk factor for neurodegenerative diseases.[42–46] As early as 1837, manganese miners were found to show signs resembling Parkinson's disease.[43] More recently, other occupational exposures to manganese have been associated with parkinsonism.[47] Mercury exposure among a multiethnic population in Singapore was related to an eightfold risk of Parkinson's.[45] The elevated proportionate mortality ratios we observed for presenile dementia in dentists and dental assistants and for Parkinson's disease in dental assistants could be related to mercury exposure. Aluminum has been considered to be a risk factor for Alzheimer's disease because of the finding of a high content of aluminum in neurofibrillary tangles associated with Alzheimer's disease. No confirmatory evidence has been found, however, and it is not clear whether aluminum deposits in cerebral neurons and/or senile plaques are secondary to an initiating event.

Workers using solvents form one common group that spans all four categories of neurodegenerative diseases that we studied. It is likely that many other exposures also occurred in their workplaces, but solvents are a common feature. Various solvents have a well-defined role in affecting the nervous system by, for example, affecting response on psychometric tests that measure reaction times, learning, memory, concentration, attention, manual dexterity, and visuomotor accuracy. Whether chronic low-level exposure to industrial solvents produces organic nervous system damage is a matter of controversy, and there is little published evidence relating solvent exposure to neurodegenerative diseases. This may be due, as Shalat et al. noted in a report of a negative case–control study of solvent exposure and Alzheimer's disease, to methodological factors such as difficulty characterizing and measuring exposure to solvents.[48] A meta-analysis of the study by Shalat et al. and 10 other studies found no association between solvent exposure and Alzheimer's disease.[49] Gunnarsson et al.[22] and at least 3 other studies[33,42,44] found an association between motor neuron disease and solvents, but no association was found in another study.[50]

Various sociological and psychological factors have been considered in the literature, and we attempted to determine whether these factors were borne out in our study. Lower levels of education have been associated with increased frequency of Alzheimer's disease in studies performed in Israel, the Netherlands, Shanghai, Sweden, Finland, Italy, France, and

TABLE 4—Highest Ranked Occupations for Risk of Parkinson's Disease, by Subjects' Race and Sex

Occupation	No. Observed Deaths[a]	PMR	95% CI
White males			
Extruding- and forming-machine operators	2	1024	124, 3699
Stock handlers and baggers[b]	4	399	109, 1021
Podiatrists	11	350	175, 627
Counselors, educational and vocational	14	346	189, 580
Pattern makers and model makers, wood	9	324	148, 616
Librarians, archivists, and curators	13	278	148, 476
Biological, life, and medical scientists	14	273	149, 458
Computer equipment operators	10	243	116, 447
Teachers, postsecondary	134	211	177, 250
Airplane pilots and navigators	19	212	128, 332
White females			
Bookbinders	2	898	109, 3245
Textile winding and twisting machine operators	6	318	117, 693
Food counter and fountain–related occupations	7	292	117, 601
Supervisory mechanics and repairers	18	216	128, 342
Dental assistants	16	177	101, 288
Religious workers	45	151	110, 203
Designers	51	149	111, 196
Teachers	1277	137	131, 143
Financial officers	92	131	106, 161
Writers, artists, entertainers, and athletes	128	128	107, 152
Black males			
Lathe-turning machine set-up operators	2	4094	495, α
Hand molding, casting, and forming occupations	2	908	110, 3279
Pest control occupations	2	892	108, 3224
Health-diagnosing occupations	5	359	116, 837
Nurses	6	340	125, 740
Supervisors, food preparation and service (> age 65)	7	260	105, 537
Baggage porters and bellhops	10	252	121, 464
Furnace, kiln, and oven operators, excluding food	10	228	109, 419
Teachers	13	210	112, 358
Clergy	29	209	140, 300
Black females			
Writers	2	3337	404, α
Textile winding machine operators	2	738	84, 2665
Funeral directors	2	703	85, 2538
Material recording, scheduling, and distributing clerks	4	519	142, 1330
Protective service occupations	2	311	38, 1123
Waiters and waitresses	3	231	48, 677
Precision textile, apparel machine workers	9	224	102, 426
Sales workers	7	212	85, 437
Social workers	3	212	44, 619
Teachers	33	172	118, 241

Note. PMR = proportionate mortality ratio; CI = confidence interval.
[a]Number of deaths observed with any mention on death certificate of designated neurodegenerative disease.
[b]Under age 65.

TABLE 5—Highest Ranked Occupations for Risk of Motor Neuron Disease, by Subjects' Race and Sex

Occupation	No. Observed Deaths[a]	PMR	95% CI
White males			
Duplicating, mail, and other office machine operators	3	968	200, 2828
Geologists and geodesists	11	557	278, 996
Health-diagnosing practitioners, NEC[b]	7	422	170, 870
Veterinarians	5	337	109, 787
Chemical engineers	17	301	175, 481
Athletes	6	295	108, 641
Communication equipment operators	7	284	114, 586
Power plant operators	8	274	118, 540
Miscellaneous electrical equipment repairers	7	270	108, 555
Architects	7	262	105, 540
White females			
Production testers[c]	2	850	103, 3072
Graders and sorters, excluding agriculture[c]	3	507	105, 1483
Painters, sculptors, craft artists	11	252	126, 452
Designers	19	233	140, 364
Clinical laboratory technicians	10	223	107, 410
Writers, artists, entertainers, and athletes	41	169	121, 224
Teachers	227	160	140, 1183
Information clerks	27	165	108, 231
Nurses	27	140	104, 185
Financial records processing	95	127	102, 155
Black males			
Sales representatives, commodities	2	2051	248, 7410
Physicians	2	1119	135, 4041
Miscellaneous material-moving equipment operators	3	811	167, 2371
Managers, farms	2	707	86, 2553
Bakers	2	419	51, 1512
Waiters and waitresses	3	405	84, 1183
Excavating, grading, road machine operators	4	314	861, 805
Miscellaneous textile machine operators	3	231	48, 674
Technicians and related support occupations	3	206	43, 602
Cleaning and building services occupations	30	157	106, 224
Black females			
Supervisory cleaning and building services[c]	2	1252	151, 4522
Supervisory food preparation[c]	2	1074	130, 3878
Librarians, archivists, and curators	2	966	117, 3488
Elevator operators	2	779	94, 2815
Hairdressers and cosmetologists	8	306	132, 603
Packaging and filling machine operators	2	304	37, 1099
Child care, excluding private household	3	299	62, 877
Production inspectors, checkers, and examiners	2	246	30, 888
Teachers	14	209	114, 350
Farm workers	4	209	57, 536

Note. PMR = proportionate mortality ratio; CI = confidence interval.
[a]Number of deaths observed with any mention on death certificate of designated neurodegenerative diseases.
[b]NEC is not elsewhere classified.
[c]Under age 65.

East Boston, but not in a study in Minnesota.[51,52] Friedland has reviewed the question of education effects and concluded that education could be viewed (1) as a composite or surrogate variable related to many features of early life experience, such as access to medical care, occupational and recreational activities, nutrition, income, responsibility for health behavior, alcohol intake, and smoking, and (2) as reflecting an innate central nervous system capacity—"neuronal reserve."[53]

White et al. evaluated the incidence of cognitive impairment in more than 7000 elderly subjects and concluded that neither the number of years spent sitting in a classroom nor occupation influences cognitive decline, but that both serve as surrogates for other factors, events, exposures, and/or experiences that directly affect the development of cognitive impairments.[54] Dartiques et al. found that when education was controlled for, laborers were two to three times more likely to develop dementia than professionals.[55]

Our review of the occupational occurrence of Alzheimer's disease did not show that the risks were inversely correlated with education since, for example, among White males, the 10 highest proportionate mortality ratio categories included chemists, teachers, lawyers, judges, and engineers. Fewer professional categories are present in the 10 highest risk categories for White or Black females or Black males. The proportionate mortality ratios for professionals may be biased upward because of the lower overall mortality rates normally seen in occupational groups with high socioeconomic status.

Two other psychosocial factors that are correlated with occupation, cigarette smoking and personality, have also been associated with neurodegenerative diseases. Cigarette smoking has a negative association with Parkinson's disease and Alzheimer's disease.[56,57] One hypothesis regarding Parkinson's disease is that nicotine, like MPTP, is a pyridine derivative, and competitive inhibition of MPTP-like toxins can be postulated.[14] Despite the possibility of biased ascertainment, Parkinson's disease has also been associated with a personality type characterized as relatively quiet, uncreative, and rule abiding.[58] Someone with this personality may be less likely to smoke. No other mechanism has been strongly suggested for how personality type could be related to Parkinson's disease.

The findings of increased proportionate mortality ratios for workers aged between 15 and 55 may identify which occupations are likely to contribute to the risk of neurodegenerative disease separate from age.[59] Early age at onset can also be the result of familial genetic risk factors; however, these factors may not explain risks, such as for Alzheimer's disease in telephone installers and repairers or for motor neuron disease in firefighters, military personnel, janitors, or others with large exposures to potential toxins.

When evaluating the four neurodegenerative disease categories by occupations with similar characteristics, we found a consistency of risks by occupation in some categories. Thus, particularly teachers but also medical personnel, machinists and machine operators, scientists, writers/designers/entertainers, administrative support and clerical workers, and workers using solvents were represented in all four disease categories. This suggests the possibility of a common risk factor for these neurodegenerative diseases in each of these occupations. Elucidation of these potential risk factors is speculative at this point, and other common lifestyle factors or accessibility to diagnostic services could also account for occupational clusters. Identifying these occupations, however, provides a lead on where to begin looking. We may not need to search for a single agent, but rather for the combination of factors that cause neuron stress leading to neuronal death. This combination could include both extrinsic neurotoxins, such as pesticides, and intrinsic neurotoxins, such as free radicals and excitatory amino acids (excitotoxins),[60,61] but this is still unproven. Other factors, such as autoimmunity, late expression of a lethal gene, or a defect in vital function, could be involved as well.[4] At this time, there is too little information on etiology and pathogenesis of these diseases.

Research Needs

Calne et al. have hypothesized that Alzheimer's disease, Parkinson's disease, and motor neuron disease result from environmental damage to specific regions of the central nervous system and that the damage remains subclinical for several decades but makes those affected susceptible to the consequences of age-related neuronal attrition.[62] If this speculation is true, in future studies it may be more important to identify occupational exposures and experiences that occur early in one's working life rather than those occurring later or for much of one's working life. It is not likely that there is a single toxicant or agent involved in the etiology of neurodegenerative diseases. Rather, various factors that can lead to neuronal damage might be responsible. Research efforts should focus on a range of possible exposures.

A number of research leads that merit pursuit have been identified. Certain occupations, such as teaching, farming and pesticides handling, electrical work, solvent handling, medical and health occupations, and machinists, should be considered for further study that focuses on characterizing detailed exposure.

Studies to identify occupational and environmental factors will perforce need to exclude or accommodate genetic factors. For example, a genetic polymorphism of the hepatic detoxifying enzyme CYP2D6 has been associated with Parkinson's disease[63] although its role is still unclear.[64] This genetic polymorphism could be used to identify people in various occupations with chemical exposures who might be included in studies of those exposures. It is likely that researchers will identify various genetic markers that account for some proportion of neurodegenerative disease.[65,66] Studies that use this information and that control for genetic factors will be more likely to identify environmental factors than studies that do not. Integrated studies of animals and humans should also be conducted. The finding of the MPTP-parkinsonism link in humans and animals has served to support the contention that the link exists. Structural analogues to MPTP, especially among pesticides, should be sought and tested in animals and assessed in human epidemiological studies.

The fact that many occupations with elevated proportionate mortality ratios involve extensive interaction with the public provides two leads that merit further study. One is on the role of infectious agents. Exposure to viral and bacterial agents is quite likely in those occupations. Studies of the historic exposure to biological agents in these occupations could clarify some of the uncertainty in the literature. The other aspect of public work, such as among teachers, lawyers, judges, and social workers, is psychosocial stress. This has not been widely assessed with regard to neurodegenerative diseases. Stress might be considered a factor that affects the processes of neuronal loss, compensation, and aging, rather than serving as an initiating event.

Conclusion

This study identified occupations and potential risk factors associated with various neurodegenerative diseases. These findings should be viewed as the stimulus for further study rather than as a definitive indication that people in the identified occupations are at increased risk for neurodegenerative disease owing to their occupations. The projected increase in the prevalence of neurodegenerative changes will require increases in the number of professional and paraprofessional health care workers with training in the care of persons with major neurodegenerative diseases. Identifications of occupations with increased risks for these diseases may be helpful in targeting such resources. □

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