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Occupational risk factors for brain tumors

A case-referent death-certificate analysis

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THOMAS TL, FONTHAM ETH, NORMAN SA, STEMHAGEN A, HOOVER RN. Occupational risk factors for brain tumors: A case-referent death-certificate analysis. *Scand J Work Environ Health* 12 (1986) 121—127. Numerous studies have suggested that employment in the oil refining and chemical manufacturing industries may be associated with excess brain tumor risk. A case-referent study was undertaken to evaluate brain tumor risk by occupation and industry in three geographic areas (northern New Jersey, Philadelphia, and the Gulf Coast of Louisiana) with a heavy concentration of these industries. Seven hundred and eighteen white men dying from brain tumor at age 30 years or older were ascertained from death certificates for 1978—1981. The referents were men who died of other causes, excluding epilepsy and stroke. Usual occupation and industry were obtained from the death certificates, and the maximum likelihood estimates of the relative risk were calculated for specific industries and occupations. Small nonsignificant excess risks of brain tumors were seen among persons whose usual employment was in the petroleum refining, electrical equipment manufacturing, health services, and educational services industries. Compared with other white-collar professionals, health diagnosticians, teachers, and artists/designers had a significantly elevated brain tumor risk. Among blue-collar workers, the only group with a significantly elevated brain tumor risk was precision metal workers, who are exposed to metal dusts and fumes and substances used as coolants, lubricants, and degreasers.

Key terms: artists/designers, health diagnosticians, precision metal workers, teachers.

Recent investigations of mortality among workers employed in petroleum refineries and petrochemical plants have suggested an association between excess brain tumor risk and employment in the petroleum and chemical industries. A literature review indicated that numerous occupational groups have been suggested as having an elevated risk of brain tumors (27). The most prominent associations have been noted among white-collar professional groups (suggesting diagnostic sensitivity) and workers in a variety of occupations in which there might be contact with organic solvents, lubricating oils, polycyclic aromatic hydrocarbons, formaldehyde, polyvinyl chloride, acrylonitrile, and phenolic compounds.

A case-referent study was initiated in three areas of the United States with a heavy concentration of the petroleum and chemical industries to investigate the role of petroleum and products of the refining process and the roles of a variety of other factors in the etiology of brain and central nervous system (CNS) tumors. Cases and referents who died between 1978 and 1981 were selected from death certificates of usual residents of northern New Jersey, Philadelphia (Pennsylvania), and the Gulf Coast area of Louisiana. The present analyses were based on the occupational statements on the death certificates of the cases and referents.

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Materials and methods

Three areas of the United States in which at least 5 % of the workforce was employed in the petroleum and chemical industries during the past 20 years were chosen as study areas. These were northern New Jersey, the Philadelphia standard metropolitan statistical area, and the Gulf Coast area of Louisiana.

Cases were all white men, age 30 years or older, who died of brain or other CNS tumors [International Classification of Disease (31) ninth revision codes 191, 192, 225, and 239.7] and whose death certificates indicated that they were residents of any of the selected study areas. The study period was 1 January 1979 to 31 December 1981 for New Jersey and Philadelphia, and 1 January 1978 to 30 June 1980 for Louisiana. Men who died of causes other than brain tumor, cerebrovascular disease, or epilepsy were the source of the reference group. The latter two conditions were excluded from the reference group because of the possibility that some of these deaths may have resulted from undiagnosed brain tumors. For each case, one

referent was randomly selected from white men who were the same age at death and were residents of the same study area as the case.

Death certificates for 741 cases and referents were requested from appropriate state vital records offices. Four death certificates (one case and three referents) were not located, and 21 persons whose cause of death had been incorrectly classified as a brain tumor were eliminated from the case series. One reticulum cell sarcoma of the brain was also excluded. The final series for these analyses consisted of 718 cases and 738 referents.

Occupational statements from death certificates were coded without knowledge of the case or referent status of the study subject and according to the index of occupations from the 1980 Census of the Population (2). In several of the analyses, occupational codes were grouped to include persons with presumably similar life-style characteristics and socioeconomic status. The term "white-collar professionals" included occupations classified as executive, administrative, managerial, and professional specialties (census codes 003 through 199). "Other white-collar" jobs included technical, sales, and administrative support occupations (census codes 203 through 389). Included in the "blue-collar" category were service, farming, forestry, fishing, precision production, craft and repair occupations, operators, fabricators, and laborers (census codes 403 through 889). Industry was coded according to the 1972 four-digit Standardized Industrial Classification (SIC) (17). Because there was often insufficient information to code to the four-digit level of the SIC, analyses were limited to major two-digit categories. Information on age at death, type of brain tumor diagnosis, marital status, and study area was also abstracted from the death certificates, and it formed the basis for these analyses.

Sixteen persons (6 cases, 10 referents) were reported to be unemployed or "never employed." Occupation was missing from the death certificates of 46 men, and occupations for 12 study subjects could not be classified into any of the census codes. These persons were included in the comparisons that used "all other occupations" as the reference, but were excluded from the comparisons with other white-collar professionals and other blue-collar workers. Usual industry was not recorded on 133 death certificates (31 of these also had the occupation missing), and these study subjects were included as unknowns in the analyses by industry.

Maximum likelihood estimates of the relative risk (odds ratios) for brain tumors and 95 % confidence intervals (6) were calculated for specific occupations and industries. Analyses by occupation were adjusted for the potential confounding influences of age and marital status in these data, and risk estimates by industry were adjusted for white-collar/blue-collar status of the usual occupation. The odds ratios were considered to be statistically significant when the 95 % confidence interval did not include 1.0.

Table 1. Distribution of brain cancer cases by death-certificate diagnosis.

Diagnosis	Number	Percentage
Glial tumors	366	51.0
Glioma (not otherwise specified)	77	10.7
Glioblastoma multiforme[a]	201	28.0
Astrocytoma (grades I and II)	82	11.4
Oligodendroglioma	2	0.3
Ependymoma	4	0.6
Meningioma	28	3.9
Other specified diagnoses[b]	12	1.7
Malignant brain tumor (not specified)	95	13.2
Unspecified brain tumor	212	29.5
Spinal cord tumor (not specified)	5	0.7
Total	718	100.0

[a] Includes astrocytoma specified as grade III or IV.
[b] Includes four schwannoma, two hemangioblastoma, one craniopharyngioma, two medulloblastoma, one meningiosarcoma, one retinoblastoma, and one sarcoma of the central nervous system.

Results

About half of the cases ascertained were from New Jersey (N = 361), and a third were from Philadelphia (N = 243). The smallest proportion was from Louisiana (N = 114). The age distribution resembled the pattern seen for age-specific brain cancer death rates among white males in the United States (13). Seventy-six percent of the study subjects were between the ages of 50 and 79 years at death.

Table 1 shows the distribution of cases by death-certificate diagnoses. Most cases for whom the death certificate specified the cell type of the brain tumor had glial tumors. The majority of these was glioblastoma multiforme, while a much smaller proportion was astrocytoma or unspecified gliomas. Meningioma and other cell types accounted for a very small proportion of the cell types specified. A diagnosis of only "brain tumor" appeared on 30 % of the death certificates. Less than 15 % of the certificates had a diagnosis of a "malignant brain tumor" without specification of cell type. Because a very small percentage of the case series was nonbrain CNS tumors, the term "brain tumor" has been used throughout to refer to all CNS tumors.

Maximum likelihood estimates of the relative risk for brain tumor by industry are shown in table 2. The odds ratio for manufacturing industries was 1.0. There was no excess risk of brain tumors among persons whose usual employment was reported in the chemical industry, and the odds ratio for petroleum refining was only slightly above 1.0. The only manufacturing industry with an odds ratio above 1.5 was SIC 36 (manufacture of electrical equipment). The elevated risk of brain tumors seen among persons whose usual employment was in service industries was confined to health and educational services. The excess of brain

tumors seen among workers in public administration occurred primarily among members of the armed forces.

Table 3 shows the odds ratios for brain tumors among the white-collar occupational groups. An odds ratio greater than 1.0 was seen for all white-collar workers with blue-collar workers as the reference, and professionals had a significantly elevated risk of brain tumors compared to all other study subjects. This finding was due to statistically significant odds ratios for brain tumor among health diagnosticians, teachers, and writers/artists/entertainers and a nonsignificant excess of brain tumors among engineers/architects/surveyors. Specific occupations that contributed to the excess risk in the latter two categories were artists/designers and industrial engineers.

Five of the cases and none of the referents had their usual occupation reported as industrial engineer (table 4). When other white-collar professionals were used as the reference, the odds ratio for brain tumor among health diagnosticians was 5.2 but was not statistically significant. Among the health diagnosing professionals were ten physicians, two dentists, and an optometrist. Teachers also had a significantly elevated risk of brain tumors compared to all other occupations (odds ratio 4.5, 95 % confidence interval 1.1—21.1) and had a fourfold excess risk of brain tumors in comparison to all other professionals. There

Table 2. Odds ratios for brain tumors by industry in the Louisiana, New Jersey, and Philadelphia study areas, 1978—1981.[a]

Industry[b]	Number exposed		Crude odds ratio	Adjusted odds ratio[c]	95 % confidence interval
	Cases	Referents			
Agriculture, forestry, fish (01—09)	13	19	0.7	0.8	0.4— 1.8
Mining (10—14)	8	8	1.0	1.3	0.4— 4.3
Construction (15—17)	59	70	0.8	0.9	0.6— 1.3
Manufacturing (20—39)	224	219	1.1	1.0	0.8— 1.3
Chemicals (28)	37	34	1.1	1.0	0.6— 1.7
Petroleum refining (29)	19	15	1.3	1.2	0.6— 2.6
Electrical equipment (36)	28	16	1.8	1.7	0.7— 4.2
Transportation, public utilities (40—49)	74	70	1.1	1.1	0.8— 1.6
Wholesale and retail trade (50—59)	100	120	0.8	0.7	0.5— 1.0
Finance, insurance, real estate (60—67)	28	24	1.2	1.0	0.5— 1.9
Services (70—89)	106	86	1.3	1.4	1.0— 1.9
Health services (80)	18	12	1.6	1.7	0.7— 3.4
Educational services (82)	20	11	1.9	1.8	0.8— 4.4
Public administration (91—97)	44	35	1.3	1.4	0.8— 2.2
National security (97)	10	4	2.6	4.2	1.0—20.9
Unemployed and unknown (99)	62	87	0.7	0.9	0.6— 1.3

[a] The reference group used for each odds ratio calculation was all other industries.
[b] Numbers in parentheses are Standardized Industrial Classification categories.
[c] Adjusted for age at death, marital status, and blue-collar/white-collar status.

Table 3. Odds ratios for brain tumor among white collar occupational groups in the Louisiana, New Jersey, and Philadelphia study areas, 1978—1981.[a]

Occupation[b]	Number exposed		Crude odds ratio	Adjusted odds ratio[c]	95 % confidence interval
	Cases	Referents			
All white collar (003—389) vs blue collar (403—889)	309	257	1.4	1.3	1.0— 1.7
White collar professionals (003—199)	177	113	1.8	1.7	1.3— 2.3
Executive, administrative, managerial (003—037)	89	75	1.3	1.1	0.8— 1.6
Engineers, architects, surveyors (043—063)	31	19	1.7	1.6	0.9— 3.0
Math and computer scientists (064—068)	1	1	.	.	.
Natural scientists (069—083)	3	—	.	.	.
Health diagnosing occupations (084—089)	13	2	6.8	6.8	1.4—44.9
Health treating occupations (095—106)	1	2	.	.	.
Teachers and counselors (113—163)	11	3	3.8	4.5	1.1—21.1
Social scientists and urban planners (166—173)	3	—	.	.	.
Social recreation and religious workers (174—177)	4	2	.	.	.
Lawyers and judges (178—179)	5	5	1.0	1.1	0.3— 4.7
Writers, artists, entertainers (183—199)	16	4	4.2	4.6	1.4—17.0
Technical support occupations (203—235)	10	20	0.5	0.4	0.2— 1.0
Sales occupations (243—285)	83	82	1.1	1.0	0.7— 1.4
Administrative support occupations (303—389)	39	42	1.0	1.0	0.6— 1.6

[a] The reference group for each category except all white-collar occupations was all other occupations including unknown and unemployed.
[b] Numbers in parentheses are the 1980 Census of the Population codes.
[c] Adjusted for age at death and marital status.

Table 4. Odds ratios for brain tumor among certain white-collar professionals in the Louisiana, New Jersey, and Philadelphia study areas, 1978—1981.[a]

Occupation	Number exposed		Crude odds ratio	Adjusted odds ratio[b]	95 % confidence interval
	Cases	Referents			
Industrial engineers	5	—	.	.	.
Health diagnosing professionals	13	2	4.4	5.2	1.0—41.5
Teachers	11	3	2.4	3.9	0.7—28.2
Artists and designers	13	—	.	.	.

[a] The reference group used for each odds ratio calculation was all other white-collar professionals.
[b] Adjusted for age at death and marital status.

Table 5. Odds ratios for brain tumor among blue-collar occupational groups in the Louisiana, New Jersey, and Philadelphia study areas, 1978—1981.[a]

Occupation[b]	Number exposed		Crude odds ratio	Adjusted odds ratio[c]	95 % confidence interval
	Cases	Referents			
Service occupations (403—469)	48	64	0.8	0.8	0.5—1.2
Farming occupations (473—489)	13	18	0.7	0.8	0.3—1.7
Forestry, fishing, logging (494—499)	—	3	.	.	.
Mechanics and repairers (503—549)	34	29	1.2	1.3	0.7—2.2
Construction trades (553—599)	53	68	0.8	0.8	0.5—1.2
Extractive occupations (613—617)	3	3	1.0	1.1	0.2—6.9.
Precision production occupations (633—699)	91	74	1.3	1.3	0.9—1.8
Machine operators, assemblers, inspectors (703—799)	49	69	0.7	0.7	0.5—1.0
Transportation and material moving (803—859)	47	52	0.9	0.9	0.6—1.4
Helpers and other laborers (863—889)	45	53	0.9	0.9	0.6—1.4
Unemployed and unknown (999)	26	48	0.5	0.6	0.4—1.1

[a] The reference group for each category was all other occupations including unknown and unemployed.
[b] Numbers in parentheses are the 1980 Census of the Population codes.
[c] Adjusted for age at death and marital status.

Table 6. Odds ratios for brain tumor among precision metal workers in the Louisiana, New Jersey, and Philadelphia study areas, 1978—1981.[a]

Occupation	Number exposed		Crude odds ratio	Adjusted odds ratio[b]	95 % confidence interval
	Cases	Referents			
All precision metal workers	47	26	2.2	2.1	1.2—3.6
Machinists	26	16	1.9	1.8	0.9—3.7
Tool and die makers	7	4	2.0	1.8	0.5—7.4
Sheet metal workers	8	4	2.3	2.2	0.6—9.0

[a] The reference group used for each odds ratio calculation was all other blue-collar workers.
[b] Adjusted for age at death and marital status.

were 13 artists/designers among the cases and none among the referents. Two of the six cases who were designers had occupations as industrial designers and might have actually had drafting occupations; however, coding rules caused them to be included in the designer classification. Two of the remaining four cases were interior designers, one designed furs, and one was unspecified. Among the six professional artists, there were three commercial or graphics artists, a wildlife artist, a freelance cartoonist, and one artist/art teacher.

The only blue-collar groups for whom brain tumor odds ratios were above 1.0 were precision production workers and mechanics/repairers (table 5). Among precision production workers, only precision metal workers had statistically significant odds ratios for brain tumors when all other blue-collar occupations were used as the reference (table 6). The most common occupations within this category were machinists, tool and die makers, and sheet metal workers. The odds ratios were elevated to a similar level among persons in each of these occupational categories.

Because brain tumor risk was elevated among certain white-collar groups and some skilled blue-collar workers, an attempt was made to address the diagnostic sensitivity issue. Table 7 shows the distribution of cases in occupational categories by death-certificate brain tumor diagnosis. Almost one-half of the blue-collar workers and unknown occupations had unspecified brain tumor diagnoses on their death certificates, while 32 % of white-collar professionals had unspecified diagnoses. Glial tumors accounted for over 60 % of the death-certificate diagnoses among white-collar professionals and less than 50 % among other workers. With blue-collar workers as the reference, white-collar

Table 7. Distribution of cases by occupational category and death-certificate diagnosis. (CNS = central nervous system)

Occupation	Death-certificate diagnosis								Total number
	Glial tumor		Other cell type		Malignant brain tumor		Unspecified brain or CNS tumor		
	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage	
All white-collar professional	109	61.6	11	6.2	21	11.9	36	20.3	177
Other white-collar workers	65	49.2	8	6.1	19	14.4	40	30.3	132
All blue-collar workers	181	47.3	19	5.0	50	13.1	133	34.7	383
Unknown	11	42.3	2	7.7	5	19.2	8	30.8	26

Table 8. Odds ratios for brain tumor by death-certificate diagnosis in the Louisiana, New Jersey, and Philadelphia study areas, 1978—1981.

Occupation	Cell type known		Cell type unknown	
	Exposed cases	Adjusted odds ratio	Exposed cases	Adjusted odds ratio
White-collar workers vs blue-collar workers	193	1.5	116	1.1
White-collar professionals vs other white-collar workers	120	2.0	57	1.3
Health diagnosticians vs other professionals	10	5.1	3	2.7
Teachers vs other professionals	6	3.1	5	8.9
Artists/designers vs other professionals	9	.	4	.
Precision metal workers vs other blue-collar workers	24	2.0	23	2.1
Machinists vs other blue-collar workers	16	2.3	10	1.3
Tool & die makers vs other blue-collar workers	4	1.8	3	1.7
Sheet metal workers vs other blue-collar workers	3	1.6	5	3.3

workers had a significantly elevated risk for brain tumors with known cell types but not for unknown cell types (table 8). A similar result was seen for professionals when all other white-collar workers were used as the reference. Subsequent results, presented in table 8, were therefore calculated with all other white-collar professionals as the reference for each of the professional groups and all other blue-collar workers as the reference for the precision metal workers. In general, odds ratios were elevated for known and for unknown cell types of brain tumors among workers in each of the groups shown.

Discussion

Caution must be exercised in interpreting the results of the present study. Even though death certificates are supposed to have information on the deceased's usual occupation during his lifetime, it is very likely that the information recorded is often the last occupation; thus it may not be the deceased's longest job. Because death certificates record only one occupation and industry, one cannot evaluate risks for all jobs in which study subjects might have been "ever employed." The occupational statement on the death certificate may be a good description of longest occupation for some groups, however, because it is unlikely that trained professionals or other skilled workers change careers often.

A second limitation is the use of death certificates to identify brain tumor cases. Because the brain is a common site for metastases from other cancer sites, some of the diagnoses listed as "brain cancer" or "brain tumor" may not actually be primary brain tumors. This is probably not a major limitation, however, because a review of death certificates in Third National Cancer Survey areas indicated that about 10 % of the death certificates that listed a malignancy of the brain as underlying cause were not confirmed by hospital records (19). Thus only about 72 of our 718 cases might represent misdiagnoses.

Finally, because we have made multiple comparisons, some statistically significant results would be expected due to chance alone. Despite these limitations, analyses of death-certificate occupational information may provide useful clues for planning detailed analyses of complete occupational history data obtained from interviews, particularly for skilled workers or professionals.

Greenwald et al (7) suggested that diagnostic sensitivity may account for the elevated brain tumor risks observed in numerous occupational groups. In other words, brain tumors might be more likely to be diagnosed among groups that have good access to medical care than among those who might not receive regular medical surveillance. In our study, excess brain tumor risk was observed among white-collar occupations and members of the military; however, diagnostic sensi-

tivity does not entirely explain these findings. Teachers, health diagnosticians, and artists/designers had elevated risk of brain tumors even when all other white-collar professionals were used as the reference, and there is no reason to believe that they should have better access to medical care than other white-collar professional groups. The distribution of diagnoses in table 7 shows that there are some variations in the specificity of the death certificate diagnoses by occupational category. Although it is not known whether professionals are more likely to have a brain tumor diagnosed than other workers, the presence of a higher proportion of cell type diagnoses on the death certificates might result from greater access to medical diagnostic techniques. Thus, if diagnostic sensitivity were responsible for excess brain tumor risk in a particular group, one might expect elevated odds ratios for known tumor cell types but not for unknown tumor cell types. In table 8, risks for brain tumors of known and of unknown cell types were elevated among all of the groups listed. Even though some groups had a cell type recorded more often than others, their risk of "cell type known" tumors was similar to their risk of "cell type unknown." Elevated risk was not due to an excess risk for known tumor cell types alone.

No excess risk of brain tumors was seen among persons whose usual employment was in the chemical manufacturing industry. Studies of individual plants and chemical operators in Texas indicated that there may be elevated risk of brain tumors associated with employment in the chemical manufacturing industry (16, 21, 29), and a study of pharmaceutical workers showed a significantly elevated frequency of brain tumors among production workers (26). Previous epidemiologic analyses indicated a possible excess risk of brain tumors among workers in petroleum refineries (22, 25, 28), but the present analysis indicated only a small nonsignificant excess risk of brain tumors associated with usual employment in petroleum refining.

Elevated odds ratios for brain tumors seen among persons in the health and educational services are accounted for by the excess risk seen among health diagnosticians and teachers. Epidemiologic studies have suggested elevated brain tumor risk among registered female nurses (11) and veterinarians (1), but not among other health professionals. Exposures in the medical setting include numerous biological agents, and chemicals like disinfectants, antiseptics, and pharmaceutical preparations (12). Similar occupational exposures occur among chemists (18), pathologists (10), and anatomists (23) reported to have an elevated brain tumor risk.

A proportionate mortality ratio analysis of deaths among professional artists showed a significantly elevated frequency of brain tumors (15); however, this elevated frequency was not associated with any particular art specialty. A slight excess frequency of brain cancer deaths was also seen among artists and art teachers in a California survey (20). Artists are exposed to numerous chemicals, including inks, solvents, paints, and pigments (14). In our study, most of the artists/designers were commercial artists or draftsmen whose primary occupational exposures presumably are to inks and solvents.

Three surveys of mortality by occupation have shown elevated frequencies of brain cancer among teachers (5, 8, 20). In these surveys and in our study it was not possible to determine whether this excess might be confined to one teaching specialty (eg, laboratory science teachers) or whether the excess risk occurs among all teachers.

Our study showed a significantly elevated risk of brain tumors among precision metal workers, including machinists, tool and die makers, and sheet metal workers. These findings are consistent with occupational mortality surveys that suggest excess mortality from brain tumors among machinists (5, 8). More deaths from brain tumors than expected were reported among workers in three nuclear fuels and weapons fabrication facilities (3, 9, 30) which had large machining operations. Blue-collar (hourly) workers in an aviation electronics plant had a significantly elevated frequency of brain cancer (24), and all five of the hourly workers with brain cancer were machinists. A slight excess brain cancer risk was also reported among automobile machinists hired after 1948 (4). Machinists are exposed to metal dusts and fumes, lubricating oils, and solvents (12). Epidemiologic studies of numerous occupational groups with exposure to lubricating oils and solvents have also reported excess mortality from brain tumors (27).

Findings of this preliminary analysis indicate that elevated brain tumor risk may be associated with certain occupational exposures. Interviews are being conducted to obtain lifetime occupational histories from the next-of-kin of cases and referents. A hospital record and pathology review will allow case-referent analyses by the cell type of the brain tumor.

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