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The Upper Midwest Health Study: Industry and Occupation of Glioma Cases and Controls

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Abstract

Background—Understanding glioma etiology requires determining which environmental factors are associated with glioma. Upper Midwest Health Study case–control participant work histories collected 1995–1998 were evaluated for occupational associations with glioma. “Exposures of interest” from our study protocol comprise our a priori hypotheses.

Materials and Methods—Year-long or longer jobs for 1,973 participants were assigned Standard Occupational Classifications (SOC) and Standard Industrial Classifications (SIC). The analysis file includes 8,078 SIC- and SOC-coded jobs. For each individual, SAS 9.2 programs collated employment with identical SIC-SOC coding. Distributions of longest “total employment duration” (total years worked in jobs with identical industry and occupation codes, including multiple jobs, and non-consecutive jobs) were compared between cases and controls, using an industrial hygiene algorithm to group occupations.

Results—Longest employment duration was calculated for 780 cases and 1,156 controls. More case than control longest total employment duration was in the “engineer, architect” occupational

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group [16 cases, 10 controls, odds ratio (OR) 2.50, adjusted for age group, sex, age and education, 95% confidence interval (CI) 1.12–5.60]. Employment as a food processing worker [mostly butchers and meat cutters] was of borderline significance (27 cases, 21 controls, adjusted OR: 1.78, CI: 0.99–3.18).

Conclusions—Among our exposures of interest work as engineers or as butchers and meat cutters was associated with increased glioma risk. Significant associations could be due to chance, because of multiple comparisons, but similar findings have been reported for other glioma studies. Our results suggest some possible associations but by themselves could not provide conclusive evidence.

Keywords

glioma; case–control studies; occupation; industry; occupational exposure

INTRODUCTION

The ultimate goal of analyses of disease incidence by occupation and/or industry is the identification of an agent or condition, exposure to which increases the risk of developing the disease. This goal may be difficult to achieve as workers in many occupations and industries are exposed to a large number of agents, and many agents are used in a large number of industries. Associating rare diseases with specific agents is especially difficult unless a disease cluster occurs in an industrial setting, for example, liver cancer among workers exposed to vinyl chloride.

In 1995, the National Institute for Occupational Safety and Health (NIOSH) initiated the Upper Midwest Health Study (UMHS), a population-based case–control study of glioma (brain cancer) risk in a non-metropolitan population [Davis-King et al., 1994]. The main focus of the study was farming and associated rural risk factors [Ruder et al., 2004, 2006, 2009b; Carreón et al., 2005]. The four study states—Iowa, Michigan, Minnesota, and Wisconsin—have large farm populations and higher than average brain cancer incidence. The questionnaire also included a complete occupational history so associations with non-farming employment duration could be assessed. This study evaluated associations between risk of glioma and occupation and industry of the longest duration of employment (combining jobs with the same 2-digit SIC and SOC codes) held by each of 798 cases and 1,175 population-based controls, adult (18–80) non-metropolitan residents of Iowa, Michigan, Minnesota, and Wisconsin.

Despite a number of studies of glioma, occupation and industry, the only agent conclusively associated with glioma is ionizing radiation [Wrensch et al., 2002]. Based on the literature, we designated “exposures of interest” (Table I) on which to focus. These exposures of interest were our a priori hypotheses of exposures possibly associated with increased risk of glioma. Comprehensive evaluations have been completed only for the highest priority exposures—pesticides and solvents [Hein et al., 2008, 2010; Ruder et al., 2009a; Yiin et al., 2012], for which exposure assessment for questionnaire responses was done, and for farm activities, based on a comprehensive questionnaire [Ruder et al., 2009b].

Our objective for this specific study was to characterize the spectrum of industries and occupations associated with glioma in our study population, especially those industries and occupations for which detailed questionnaire responses were not available.

MATERIALS AND METHODS

The study sample and design have been described previously [Ruder et al., 2006]. Using the glioma distribution by sex and age at diagnosis (by 10-year age groups) during a 3-year period (1989–1992) in the four study states, we selected potential controls (2:1 to projected number of cases), who resided in eligible non-metropolitan counties on January 1, 1995, from state driver's license records (ages 18–64 years) or from Health Care Financing Administration's (HCFA) Medicare data tapes (ages 65–80 years). Sampling randomly within sex–age strata, we chose a pool of potential controls as the case enrollment period began. Cases and controls reporting a prior malignancy other than a glioma (6.4% of cases, 20.6% of controls) were not excluded.

The study focused on histologically confirmed primary intracranial gliomas, rather than all brain neoplasms, to reduce heterogeneity among the case participants. A brain glioma was defined as a neoplasm having an ICD-O code 938–948 [Percy et al., 1990]. Cases diagnosed from January 1, 1995, through January 31, 1997, were identified through participating medical facilities and neurosurgeon offices. Case ascertainment, assessed by comparison with respective state tumor registry ascertainment for eligible counties, was 78% overall [Ruder et al., 2006]. Physician consent was obtained before contacting cases or their next of kin. Cases interviewed in person ($n = 438$) were interviewed an average of 196 days after diagnosis; proxy case interviews ($n = 360$) occurred an average of 420 days after diagnosis (partly due to waiting some time after a case death before approaching family members). Proxy interviews were also conducted for 34 ill or deceased controls. Among cases, 59% had a diagnosis of glioblastoma multiforme (equivalent to Stage 4 glioma); 22%, astrocytoma; 11%, oligodendroglioma; 8%, other glioma.

Potential participants were sent a letter of invitation, followed up with telephone calls to request participation. Informed consent was solicited from all potential participants. Among eligible potential participants, 70.4% of 1,669 controls and 91.5% of 872 cases (or their next-of-kin) agreed to participate, resulting in a study population of 1,175 controls and 798 cases [Ruder et al., 2006]. This study was approved by the NIOSH Human Subjects Review Board (HSRB 94-DSHEFS-08) and review boards of all participating institutions.

The structured questionnaire, modified from one developed by the National Cancer Institute [Chen et al., 2002], included a complete occupational history, and was administered (most in person, a few by telephone) by trained interviewers [Ruder et al., 2006]. Respondents were asked about all jobs from age 16 years through the end of 1992 held at least 1 year, including employer name (if known), industry, job title, job tasks, materials used, processes, and activities. All interviews were conducted from 1995 to 1998.

The jobs dataset contained 12,145 records (participant-jobs) for 1,967 of the 1,973 participants (6 participants were 16 years of age in 1993 with no jobs recorded), including

over 4,000 records of gaps in the work histories. Each of the 8,078 actual jobs was evaluated by an experienced industrial hygienist, very familiar (>15 years experience) with a variety of industrial processes and occupations, blinded to participant case status, and assigned a 4-digit Standard Occupational Code (SOC) [U.S. Department of Commerce, 1980] and a 4-digit Standard Industrial Code (SIC) [Office of Management and Budget, 1987]. For quality control, 10% of the initial coding for both industry and occupation was performed independently by two certified industrial hygienists (CIHs) and reconciled through discussion. The remaining 90% of coding was performed by one CIH with a 1% review by the second CIH followed by reconciliation of coding and wholesale application of any changes to other similar records in the data base.

All analyses used SAS 9.2 software. We determined, for each participant with valid occupational coding, his or her longest “total employment duration,” defined as the number of years a participant worked in a job or jobs with the same industry and occupation codes, including multiple jobs and non-consecutive jobs. We converted SIC and SOC codes to the equivalent Census codes so an algorithm to group comparable SOCs by potential exposures to make larger categories could be used [U.S. Census Bureau, 1980; Schnitzer et al., 1995]. Results are presented only for those occupational groups which included longest “total employment duration” for at least five case and five control participants.

The single longest “total employment duration” for each participant was used in our analyses. For each occupational group, the distribution of cases and controls was compared with the distribution for all other ever-employed cases and controls. We repeated the analyses restricted to jobs with “total employment duration” of >5 years, restricted to “total employment duration” that had started by 1975, and restricted to “total employment duration” that had started by 1985. Analyses used unconditional logistic regression models, adjusted for frequency-matching variables (age group, sex) and age and education. which generated odds ratios (OR) and 95% confidence intervals (95% CI).

Because 40% of our case occupational histories were provided by proxies, we wanted to know how accurate proxy respondents could be. We compared original case participant and second interviewee responses for 111 cases for whom we had two questionnaires (a second interview, with a close relative, had been conducted approximately a year after the death of the original respondent). Jobs reported in these second interviews were not included in the main analysis. We compared assigned SIC and SOC codes for these questionnaires (the coders were blinded to the relationship between the questionnaires), ignoring differences in years worked (both start and stop years and total number of years). In some cases, although the information supplied was virtually identical the jobs were not SIC and SOC coded identically, resulting in a “false negative” mismatch. If either the original respondent or the second respondent included a job not matched by the other, that counted as a job but not a match. In some cases, a “job” had more than one record in either the original or second questionnaire (e.g., a job as a soldier during WW2 that was split into three jobs in the original, by base where stationed, but was only one job (but same total number of years) in the second questionnaire. In such cases, each of the original jobs was rated as having been matched. This increased the number of matches.

RESULTS

The distribution of cases and controls and key demographics are presented in Table II.

Longest employment duration for 515 female controls (12 had no codable employment duration) averaged 18.5 ± 13 years, for 641/648 male controls, 23 ± 11.6 years; for 330/342 female cases, 16.5 ± 11 years; and for 450/456 male cases, 23 ± 12 years.

Distribution across industries differed more by gender than by case status: 59% of women's longest "total employment duration" was in trade and services sectors; men's were in manufacturing and construction.

Among the 1,973 study participants, 1,936 (748, 94% of 798 cases; 1,132, 96% of 1,175 controls) had a SIC-SOC-codable "total employment duration." OR, adjusted for frequency-matching variables (age group, sex) and age and education, by industrial sector for longest total employment duration found no sector associated with an increased risk of glioma (results not shown). There were 15 cases and 44 controls in the finance–insurance–real estate sector, with a statistically significant adjusted OR: 0.50 (CI: 0.28–0.91) reduced risk of glioma.

Table III presents the results by all industry-occupation categories, a priori and others, that defined the longest "total employment duration" for at least five cases and five controls. The analyses used the occupational grouping algorithm developed by Schnitzer et al. [1995] for a study of paternal exposures and birth defects. The algorithm captured 1,800 of the 1,936 longest "total employment durations." Among occupations with potential exposure to our a priori hypothesized agents, the only group statistically significantly associated with glioma was "engineers, architects" (16 cases, 10 controls, adjusted OR: 2.50, CI: 1.12–5.60). Fourteen cases and six controls had a self-described job title of engineer. The others in this group were draftsmen and designers; none was an architect. Employment as a food processing worker was of borderline significance (27 cases, 20 controls, adjusted OR: 1.78, CI: 0.99–3.18). In analyses by longest duration 5 years or more and longest duration starting by 1985 analyses, the positive associations between employment in food processing and increased risk of glioma were statistically significant: 5+ year duration, 27 cases, 20 controls, adjusted OR: 1.88, CI: 1.04–3.40; starting by 1985, 25 cases, 17 controls, adjusted OR: 2.06, CI: 1.10–3.87.

Among occupational groups assumed not to have potential exposure to our a priori hypothesized exposures of interest, only teachers whose employment started by 1975, 20 years before the first of our cases were diagnosed, were at statistically significant reduced risk: 15 cases, 48 controls, adjusted OR: 0.48, CI: 0.25–0.90).

We repeated the analyses using 2-digit SOC and SIC codes to group the responses. Results (not shown) were similar. For an exposure to have a meaningful relationship with cancer initiation, it should have begun before disease onset. We did analyses limited to longest "total employment duration" that had begun by 1985, 10 years before our first glioma diagnoses, and by 1975, 20 years before our first glioma diagnoses, and analyses limited to

“total employment duration” at least 5 years long. Results (not shown) were similar to those presented in Table III.

In our analysis, comparing original (from study participants) and repeat (from second interviewees) occupational responses, we found that the original and repeat respondents were more likely to concur on SIC and SOC codes if the study participant was female (concordance by SOC 0.45 for female, 0.38 for male; concordance by SIC 0.52 for female 0.41 for male, $P < 0.02$). Men had more jobs (mean 7.9 vs. 7.1 for women) but that difference was not statistically significant. The SIC and SOC concordance was generally highest for the oldest participants who also, as one would expect, had had more jobs (mean 8.0 for those born in the 1920s, mean 8.06 for those born in the 1930s, mean 6.8 for those born in the 1940s, mean 6 for those born in the 1950s, and mean 6.7 for those born in the 1960s).

DISCUSSION

Our results are suggestive of some possible associations but by themselves could not provide conclusive evidence for a causal glioma–occupation association. Recent studies point to physicians, firefighters, and chemical and other industrial workers as occupations at higher risk [Ohgaki, 2009], to petrochemical workers [Wrensch et al., 2002] and to the possible effect of non-ionizing radiation and magnetic fields [Villeneuve et al., 2002; Coble et al., 2009].

Analyses of occupation in recent glioma case–control studies have not consistently found similar associations. A large Canadian study found increased risk for “engineers, architects, and surveyors,” as we did, but also for teachers, who in our study population had reduced risk of glioma [Pan et al., 2005]. Exposures the Canadian “engineers, architects, and surveyors” might have had were not specified; 87.5% of our case participants in this category were engineers. The German Interphone Study looked at six occupational sectors (encompassing different occupations and industries than our sectors) and concluded that none was associated with increased risk of glioma [Samkange-Zeeb et al., 2010]. Among cases and controls in the San Francisco Bay area, grouped by an occupational classification similar to the one we used [Schnitzer et al., 1995], a statistically significant increased risk was found for legal and social service workers with 10 years latency and employment, while we found no association with glioma for these workers (Table III) [Carozza et al., 2000].

Unlike De Roos et al. [2003], who analyzed occupational associations in the National Cancer Institute glioma study, we observed no association between farming and glioma (Table III). This discrepancy could be due to differences in the study populations (ours, non-urban with population-based controls, 245 having farming as their longest job; theirs, urban with hospital controls, 15 having worked at least 5 years in farming). Like them, we found an elevated risk for butchers and meat cutters (Table III).

A population-based case–control study in Iowa (drawing cases from different years than ours did) also found an association among women between brain cancer and exposure to meat products [Zheng et al., 2001]. A hospital-based case–control study in northeast China

found statistically significant increased risk of glioma among those with occupational exposures to microwaves or to pesticides [Hu et al., 1998], while to date we have seen no association between pesticides and glioma in our study population [Ruder et al., 2004; Carreón et al., 2005; Yiin et al., 2012].

Analyses by industries and occupations group jobs to increase power at the risk of increasing exposure misclassification. The groupings in Table III used knowledge about exposures in various industries and occupations to create more meaningful clusters [Schnitzer et al., 1995], but the categories are still diverse. For example, our engineers include electrical, mechanical, and civil engineers. To explore this finding, engineer-job-specific analyses and increasing the sample size by doing collaborative analyses would be appropriate.

We used the 1987 Standard Industrial Code (SIC) for industry coding rather than the more recent North American Industry Classification System (NAICS). This choice should not have affected the findings in this study. A study of occupational coding using different coding schemes showed that recoding to a different scheme led to substantial disagreement between codes in the absence of full job descriptions, yet the associated exposures with the job code were unaffected [Kromhout and Vermeulen, 2000]. A similar result would be expected for industry coding.

Coding reliability and quality control are important issues for all studies with industry and occupation coding. Reliability is related to both the extent and quality of the information collected and the training and expertise of the coder. This study collected detailed information for each job via interviewer-administered questionnaires. Interviewers went through extensive training, which has been shown to be an important factor in the quality and accuracy of the information collected [Pastides and Goldberg, 1992]. For this study, the use of an expert coder and duplicate coding of the first 10% of the jobs and industries with subsequent reconciliation helped minimize the effect of coding errors on reliability.

Strengths of this study include the size, the participation rate, histological confirmation of diagnoses, and the quality of the industry and occupation coding. Limitations include the large proportion of proxy responses for cases, as well as possible memory loss by case respondents [Weitzner, 1999; Robbins et al., 2000]. Our comparison of original and proxy responses for the 111 cases for whom we collected two occupational histories found only about 50% agreement for SIC and SOC codes. This is less than the 65% (current job) and 76% (last job) repeatability of work history for jobs of 10 years or more found in a European study [Rona and Mosbech, 1989]. However, in our study, we asked about all jobs of a year or more. In addition, the original occupational history would not necessarily be a “gold standard” because of the nature of the participants’ illness.

Although recall bias is a concern for all questionnaire and interview-based retrospective studies, no preferential recall bias would be expected from the control participants since they were unaware that this was a brain cancer study. Cases may have assumed it was a brain cancer study but that should not have influenced their responses to questions about “job tasks, materials used, processes, and activities” since the only established environmental risk

factor for glioma is ionizing radiation. It was not possible to confirm tumors reported by controls against medical records; some of these may have been medical conditions other than cancer. Since the controls were generally older than the cases, and since risk of cancer increases with age, one would expect the percentage of cancer in controls to be higher. Whether or not the reported tumors were actually cancers, they do not appear to have adversely affected the employability of the controls, who generally worked more years and had more jobs than did the cases.

While selection bias must also be considered, the random selection of controls within strata and the high participation rates for both cases and controls make it less of a factor in this study [Ruder et al., 2006]. The greatest limitation in this study is the use of “industry” and “occupation”; crude stand-ins for exposures. This limitation shadows all studies based on industry and occupation, but does not invalidate their worth for hypothesis generation.

Among the a priori “exposures of interest” (Table I) that we hypothesized would be associated with increased risk of glioma only exposure to meat and possible exposure to non-ionizing radiation (by engineers) were so associated. Our a priori “exposures of interest” were based on the glioma literature through 1994. Close to 20 years later, there are still no strong, universally accepted occupational risk factors for glioma other than ionizing radiation.

CONCLUSION

Significant associations could be due to chance, because of the number of comparisons, but similar findings have been reported for other glioma studies. Our results are suggestive of some possible associations but by themselves could not provide conclusive evidence for a causal glioma occupation association. Our objective for this specific study was to characterize the industries and occupations significantly associated with glioma in our study population. UMHS analyses using comprehensive exposure assessment across all jobs will be reported separately. Collaborative studies with other research groups, including questionnaire responses and biological specimens, may then have sufficient power to identify gene–environment associations strongly associated with glioma. Such studies should pool data on occupational and environmental exposures and genetic polymorphisms, especially in the genes coding enzymes that process toxicants.

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REFERENCES

- Ahlbom A, Navier IL, Norell S, Olin R, Spannare B. Nonoccupational risk indicators for astrocytomas in adults. *Am J Epidemiol*. 1986; 124(2):334–337. [PubMed: 3728449]
- Anttila A, Heikkilä P, Nykyri E, Kauppinen T, Pukkala E, Hernberg S, Hemminki K. Risk of nervous system cancer among workers exposed to lead. *J Occup Environ Med*. 1996; 38(2):131–136. [PubMed: 8673517]
- Blair A. Cancer risks associated with agriculture: Epidemiologic evidence. *Basic Life Sci*. 1982; 21:93–111. [PubMed: 7150208]
- Blair A, Hayes HM Jr. Mortality patterns among US veterinarians, 1947–1977: An expanded study. *Int J Epidemiol*. 1982; 11(4):391–397. [PubMed: 7152791]
- Blair A, Malke H, Cantor KP, Burmeister L, Wiklund K. Cancer among farmers. A review. *Scand J Work Environ Health*. 1985; 11(6):397–407. [PubMed: 3912986]
- Blew, JO, Jr. Preservative treatment of wood for farm use. Madison, WI: U.S Department of Agriculture, Forest Service, Forest Products Laboratory; 1965. p. 1-12. Report nr FPL-085.
- Burch JD, Craib KJ, Choi BC, Miller AB, Risch HA, Howe GR. An exploratory case-control study of brain tumors in adults. *J Natl Cancer Inst*. 1987; 78(4):601–609. [PubMed: 3104645]
- Cantor KP, Sontag JM, Heid MF. Patterns of mortality among plumbers and pipefitters. *Am J Ind Med*. 1986; 10(1):73–89. [PubMed: 3740068]
- Carozza SE, Wrensch M, Miike R, Newman B, Olshan AF, Savitz DA, Yost M, Lee M. Occupation and adult gliomas. *Am J Epidemiol*. 2000; 152(9):838–846. [PubMed: 11085395]
- Carreón T, Butler MA, Ruder AM, Waters MA, Davis-King KE, Calvert GM, Schulte PA, Connally LB, Sanderson W, Ward EM, Heineman EF, Mandel JS, Morton RF, Reding DJ, Roseman KD, Talaska G. Gliomas and farm pesticide exposure in women: The Upper Midwest Health Study. *Environ Health Perspect*. 2005; 113(5):546–551. [PubMed: 15866761]
- Chen H, Ward MH, Tucker KL, Graubard BI, McComb RD, Potischman NA, Weisenburger DD, Heineman EF. Diet and risk of adult glioma in eastern Nebraska, United States. *Cancer Causes Control*. 2002; 13(7):647–655. [PubMed: 12296512]
- Coble JB, Dosemeci M, Stewart PA, Blair A, Bowman J, Fine HA, Shapiro WR, Selker RG, Loeffler JS, Black PM, et al. Occupational exposure to magnetic fields and the risk of brain tumors. *Neuro Oncol*. 2009; 11(3):242–249. [PubMed: 19234232]
- Cooper WC. Epidemiologic study of vinyl chloride workers: Mortality through December 31, 1972. *Environ Health Perspect*. 1981; 41:101–106. [PubMed: 7199425]
- Davis-King, KE.; Calvert, GM.; Heineman, E.; Ihry, T.; Ruder, AM.; Sanderson, WT.; Schulte, PA.; Talaska, G.; Wall, D.; Ward, EM. Protocol: A case-control study of primary intracranial brain gliomas among rural residents: The Upper Midwest Health Study. Cincinnati, OH: DHHS; 1994. p. 1-304.
- De Roos AJ, Stewart PA, Linet MS, Heineman EF, Dosemeci M, Wilcosky T, Shapiro WR, Selker RG, Fine HA, Black PM, Inskip PD. Occupation and the risk of adult glioma in the United States. *Cancer Causes Control*. 2003; 14(2):139–150. [PubMed: 12749719]
- Fincham S, Hanson J, Berkel J. Patterns and risks of cancer in farmers in Alberta. *Cancer*. 1992; 69(5):1276–1285. [PubMed: 1739927]
- Floderus B, Persson T, Stenlund C, Wennberg A, Ost A, Knave B. Occupational exposure to electromagnetic fields in relation to leukemia and brain tumors: A case-control study in Sweden. *Cancer Causes Control*. 1993; 4(5):465–476. [PubMed: 8218879]
- Floderus B, Tornqvist S, Stenlund C. Incidence of selected cancers in Swedish railway workers, 1961–79. *Cancer Causes Control*. 1994; 5(2):189–194. [PubMed: 8167266]
- Hein MJ, Waters MA, van Wijngaarden E, Deddens JA, Stewart PA. Issues when modeling benzene, toluene, and xylene exposures using a literature database. *J Occup Environ Hyg*. 2008; 5(1):36–47. [PubMed: 18041643]
- Hein MJ, Waters MA, Ruder AM, Stenzel MR, Blair A, Stewart PA. Statistical modeling of occupational chlorinated solvent exposures for case-control studies using a literature-based database. *Ann Occup Hyg*. 2010; 54(4):459–472. [PubMed: 20418277]

- Hu J, Johnson KC, Mao Y, Guo L, Zhao X, Jia X, Bi D, Huang G, Liu R. Risk factors for glioma in adults: A case-control study in northeast China. *Cancer Detect Prev.* 1998; 22(2):100–108. [PubMed: 9544430]
- Kromhout H, Vermeulen R. Long-term trends in occupational exposure: Are they real? What causes them? What shall we do with them? *Ann Occup Hyg.* 2000; 44(5):325–327. [PubMed: 10930496]
- Lawhorne L. The health of farmers. *J Iowa Med Soc.* 1976; 66(10):409–418. [PubMed: 987116]
- Loomis DP, Savitz DA. Mortality from brain cancer and leukaemia among electrical workers. *Br J Ind Med.* 1990; 47(9):633–638. [PubMed: 2207035]
- Loomis DP, Wolf SH. Mortality of workers at a nuclear materials production plant at Oak Ridge, Tennessee, 1947–1990. *Am J Ind Med.* 1996; 29(2):131–141. [PubMed: 8821356]
- Lynch DW, Lewis TR, Moorman WJ, Burg JR, Groth DH, Khan A, Ackerman LJ, Cockrell BY. Carcinogenic and toxicologic effects of inhaled ethylene oxide and propylene oxide in F344 rats. *Toxicol Appl Pharmacol.* 1984; 76:69–84. [PubMed: 6484993]
- Mallin K, Rubin M, Joo E. Occupational cancer mortality in Illinois white and black males, 1979–1984, for seven cancer sites. *Am J Ind Med.* 1989; 15(6):699–717. [PubMed: 2665480]
- Mancuso TF. Epidemiological study of tumors of the central nervous system in Ohio. *Ann N Y Acad Sci.* 1982; 381:17–39. [PubMed: 6953787]
- Musicco M, Filippini G, Bordo BM, Melotto A, Morello G, Berrino F. Gliomas and occupational exposure to carcinogens: Case-control study. *Am J Epidemiol.* 1982; 116(5):782–790. [PubMed: 7148804]
- Musicco M, Sant M, Molinari S, Filippini G, Gatta G, Berrino F. A case-control study of brain gliomas and occupational exposure to chemical carcinogens: The risk to farmers. *Am J Epidemiol.* 1988; 128(4):778–785. [PubMed: 3421243]
- Office of Management and Budget. *Standard Industrial Classification Manual.* Washington, D.C: Office of Management and Budget; 1987.
- Ohgaki H. Epidemiology of brain tumors. *Methods Mol Biol.* 2009; 472:323–342. [PubMed: 19107440]
- Pan SY, Ugnat AM, Mao Y, Group CCRER. Occupational risk factors for brain cancer in Canada. *J Occup Environ Med.* 2005; 47(7):704–717. [PubMed: 16010197]
- Pastides H, Goldberg RJ. Case-control studies in pediatric epidemiology: Parent surrogates and potential pitfalls of inaccurate and selective recall. *Soz Präventivmed.* 1992; 37(1):22–26. [PubMed: 1414002]
- Percy, C.; Van Holten, V.; Muir, C. Geneva, Switzerland: World Health Organization; 1990. *International Classification of Diseases for Oncology.*
- Preston-Martin S, Mack W, Henderson BE. Risk factors for gliomas and meningiomas in males in Los Angeles County. *Cancer Res.* 1989; 49(21):6137–6143. [PubMed: 2790826]
- Robbins JM, Wolfson CM, Bergman H, Clarfield AM, Kleiman S, Bilker W, Baumgarten M. Agreement between older subjects and proxy informants on history of surgery and childbirth. *J Am Geriatr Soc.* 2000; 48(8):975–979. [PubMed: 10968305]
- Rona RJ, Mosbech J. Validity and repeatability of self-reported occupational and industrial history from patients in EEC countries. *Int J Epidemiol.* 1989; 18(3):674–679. [PubMed: 2807673]
- Ruder AM, Waters MA, Butler MA, Carreon T, Calvert GM, Davis-King KE, Schulte PA, Sanderson WT, Ward EM, Connally LB, Heineman EF, Mandel JS, Morton RF, Reding DJ, Rosenman KD, Talaska G. Gliomas and farm pesticide exposure in men: The Upper Midwest Health Study. *Arch Environ Health.* 2004; 59(12):650–657. [PubMed: 16789473]
- Ruder AM, Waters MA, Carreon T, Butler MA, Davis-King KE, Calvert GM, Schulte PA, Ward EM, Connally LB, Lu J, Wall D, Zivkovich Z, Heineman EF, Mandel JS, Morton RF, Reding DJ, Rosenman KD. The Upper Midwest Health Study: A case-control study of primary intracranial gliomas in farm and rural residents. *J Agric Saf Health.* 2006; 12(4):255–274. [PubMed: 17131948]
- Ruder AM, Butler MA, Sanderson W, Carreón T, Waters MA, Zivkovich Z. The NIOSH Retrospective Pesticide Reference Database. *J Agric Saf Health.* 2009a; 15(2):143–156. [PubMed: 19496343]

- Ruder AM, Carreon T, Butler MA, Calvert GM, Davis-King KE, Waters MA, Schulte PA, Mandel JS, Morton RF, Reding DJ, Rosenman KD. Exposure to farm crops, livestock, and farm tasks and risk of glioma: The Upper Midwest Health Study. *Am J Epidemiol.* 2009b; 169(12):1479–1491. [PubMed: 19403843]
- Samkange-Zeeb F, Schlehofer B, Schuz J, Schlaefer K, Berg-Beckhoff G, Wahrendorf J, Blettner M. Occupation and risk of glioma, meningioma and acoustic neuroma: Results from a German case-control study (interphone study group, Germany). *Cancer Epidemiol.* 2010; 34(1):55–61. [PubMed: 20061201]
- Sanderson WT, Talaska G, Zaebs D, Davis-King K, Calvert G. Pesticide prioritization for a brain cancer case-control study. *Environ Res.* 1997; 74(2):133–144. [PubMed: 9339226]
- Schnitzer PG, Teschke K, Olshan AF. A classification scheme for aggregating U.S. census occupation and industry codes. *Am J Ind Med.* 1995; 28(2):185–191. [PubMed: 8585516]
- Sinks T, Steele G, Smith AB, Watkins K, Shults RA. Mortality among workers exposed to polychlorinated biphenyls. *Am J Epidemiol.* 1992; 136(4):389–398. [PubMed: 1415158]
- Swaen GM, van Vliet C, Slangen JJ, Sturmans F. Cancer mortality among licensed herbicide applicators. *Scand J Work Environ Health.* 1992; 18(3):201–204. [PubMed: 1615295]
- Thériault G, Provencher S. Mortality study of oil refinery workers: Five-year follow-up. *J Occup Med.* 1987; 29(4):357–360. [PubMed: 3585568]
- Thomas TL, Waxweiler RJ. Brain tumors and occupational risk factors. *Scand J Work Environ Health.* 1986; 12:1–15.
- Thomas TL, Fontham ET, Norman SA, Stemhagen A, Hoover RN. Occupational risk factors for brain tumors. A case-referent death-certificate analysis. *Scand J Work Environ Health.* 1986; 12(2):121–127. [PubMed: 3726493]
- Thomas TL, Stolley PD, Stemhagen A, Fontham ET, Bleecker ML, Stewart PA, Hoover RN. Brain tumor mortality risk among men with electrical and electronics jobs: A case-control study. *J Natl Cancer Inst.* 1987; 79(2):233–238. [PubMed: 3474455]
- U.S. Census Bureau. 1980 Census of Population: Classified Index of Industries and Occupations. Washington, DC: U.S. Department of Commerce; 1980.
- U. S. Department of Commerce. Standard Occupational Classification Manual. Washington D.C: Office of Federal Statistical Policy and Standards; 1980.
- Villeneuve PJ, Agnew DA, Johnson KC, Mao Y. Brain cancer and occupational exposure to magnetic fields among men: Results from a Canadian population-based case-control study. *Int J Epidemiol.* 2002; 31(1):210–217. [PubMed: 11914323]
- Waxweiler RJ, Stringer W, Wagoner JK, Jones J, Falk H, Carter C. Neoplastic risk among workers exposed to vinyl chloride. *Ann N Y Acad Sci.* 1976; 271:40–48. [PubMed: 1069531]
- Waxweiler RJ, Alexander V, Leffingwell SS, Haring M, Lloyd JW. Mortality from brain tumor and other causes in a cohort of petrochemical workers. *J Natl Cancer Inst.* 1983; 70(1):75–81. [PubMed: 6571925]
- Weitzner MA. Psychosocial and neuropsychiatric aspects of patients with primary brain tumors. *Cancer Invest.* 1999; 17(4):285–291. [PubMed: 10225009]
- Wrensch M, Minn Y, Chew T, Bondy M, Berger MS. Epidemiology of primary brain tumors: Current concepts and review of the literature. *Neuro Oncol.* 2002; 4(4):278–299. [PubMed: 12356358]
- Yiin J, Ruder AM, Waters MA, Stewart PA, Carreon T, Butler MA, Calvert GM, Davis-King KE, Schulte PA, Mandel JS, Morton RF, Reding DJ, Rosenman KD. The Upper Midwest Health Study: Risk of glioma among farm pesticide applicators. *Environ Health.* 2012; 11:39. [PubMed: 22691464]
- Zheng T, Cantor KP, Zhang Y, Keim S, Lynch CF. Occupational risk factors for brain cancer: A population-based case-control study in Iowa. *J Occup Environ Med.* 2001; 43(4):317–324. [PubMed: 11322092]

TABLE I

Exposures of Interest Associated With Glioma Risk*

Exposure	Relevant occupations	References
Pesticides	Farmers, pesticide applicators	Ahlbom et al. [1986], Blair, [1982], Blair et al. [1985], Fincham et al. [1992], Musicco et al. [1982], Musicco et al. [1988], Swaen et al. [1992]
Solvents	Dry cleaners, metalworkers	Blair et al. [1985], Thériault and Provencher [1987], Thomas et al. [1986], Waxweiler et al. [1983]
Organic and inorganic dusts	Farmers	Blair et al. [1985], Fincham et al. [1992], Lawhorne [1976]
Polychlorinated aromatic hydrocarbons	Petrochemical workers	Thériault and Provencher [1987], Waxweiler et al. [1983]
Cutting oils and metalworking fluids	Metalworkers	Thomas et al. [1986], Thomas and Waxweiler [1986]
Paints	Painters, artists	Thomas et al. [1986], Thomas and Waxweiler [1986]
Gasoline and diesel exhaust	Truckers, miners, farmers	Fincham et al. [1992]
Gasoline	Gasoline station attendants, farmers	Blair et al. [1985]
Raw meat (animals)	Farmers, meat-processing workers, veterinarians	Blair and Hayes [1982], Lawhorne [1976]
Lead	Gasoline station attendants, battery reclamation workers, plumbers, glass workers	Anttila et al. [1996], Cantor et al. [1986], Mallin et al. [1989]
Wood preservatives	Farmers, railroad tie, and telephone pole maintenance workers	Blew [1965], Sanderson et al. [1997]
Ionizing radiation	Radiologists, nuclear manufacturing workers, X-ray technicians	Loomis and Wolf [1996], Preston-Martin et al. [1989]
Non-ionizing radiation	Welders, engineers	Floderus et al. [1993], Floderus et al. [1994], Loomis and Savitz [1990], Thomas et al. [1987]
Biological aerosols (bacteria, viruses, fungi endotoxins)	Farmers, meat-processing workers, veterinarians, health-care workers	Blair et al. [1985], Lawhorne [1976]
Polychlorinated biphenyls	Capacitor and transformer manufacturing workers, electrical workers, construction workers	Loomis and Savitz [1990], Sinks et al. [1992]
Fertilizers	Farmers	Fincham et al. [1992], Musicco et al. [1982], Musicco et al. [1988]
N-nitroso compounds	Rubber manufacturing workers	Ahlbom et al. [1986], Mancuso [1982]
Nitrates	Farmers	Burch et al. [1987], Lawhorne [1976]
Hair dyes	Hairdressers	Burch et al. [1987]
Vinyl chloride	PVC manufacturing workers	Cooper [1981], Waxweiler et al. [1976]
Ethylene oxide	Sterilizers	Lynch et al. [1984]

*The study protocol [Davis-King et al., 1994] provides extended rationales for these exposures of interest.

TABLE II
 Characteristics of Cases and Controls and Risk of Glioma, According to Respondent Status

	Including proxy-only interviews ^d		Excluding proxy-only interviews ^d	
	Cases (798)	Controls (1,175)	OR (95%CI) ^b	OR (95%CI) ^b
Ever non-farm job 1 year (vs. never)	762	1,105	1.36 (0.89–2.08)	1.076
Ever pesticides on non-farm job (vs. never)	707/62	119/1,105	0.77 (0.56–1.06)	1.18/1.076
Longest job				
Professional	234	345	Referent	337
Trades	296	412	0.97 (0.74–1.27)	398
Service	230	346	0.94 (0.72–1.23)	339
TV hours/day after age 18 years ^{c, d}	2.7 ± 1.7	2.6 ± 1.4	1.05 (0.98–1.11)	2.6 ± 1.4
Hay fever/allergy prescription (vs. none)	88	143	0.82 (0.62–1.10)	139
Ever panoramic dental X-ray (vs. never)	230	394	0.75 (0.61–0.92)	388
White non-Latino (vs. all other)	783	1,152	1.36 (0.70–2.66)	1,119
Education				
College graduate	132	201	Referent	199
High school graduate	522	767	1.11 (0.87–1.43)	751
<12 years	144	207	1.31 (0.95–1.82)	191
Smoking				
Never	363	526	Referent	514
Former	236	422	0.89 (0.71–1.11)	407
Current (through 1 Jan. 1993)	199	227	1.21 (0.94–1.55)	220
Ever drank alcohol (vs. never)	582	900	0.73 (0.59–0.92)	881
Women				
Ever pregnant (vs. never)	300/341	458/527	1.20 (0.75–1.93)	169/196
Number of pregnancies ^d	3.5 ± 2.0	3.9 ± 2.3	0.96 (0.89–1.03)	3.9 ± 2.3
Menstruating through 1992 (vs. postmenopausal)	130	159	0.64 (0.37–1.10)	159

Based on Table 4 from Ruder et al. [2006].

^a Includes subject + proxy interviews for 137 cases and 49 controls.

^b Adjusted for age, 10-year age strata, education, state, and gender (except for women-only variables).

^cContinuous variable (mean, SD); OR is for 1 unit (year, hour, pregnancy).

^pQuestion asked only of participants 18 or older by 1992.

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TABLE III

Longest Case and Control “Total Employment Duration” in Occupational Groups and Adjusted Odds Ratio of Glioma*

Occupational groups ^a	Longest total employment duration		
	Cases	Controls	Adjusted OR ^b (95% CI)
All workers	780	1,159	
A priori occupations of interest			
Engineers, architects	16	10	2.50 (1.12–5.60) ^c
Food processing workers ^d	27	21	1.78 (0.99–3.18)
Farm managers, workers	93	155	0.91 (0.69–1.21)
Welders, cutters	5	8	0.89 (0.29–2.76)
Electricians, electrical workers	11	24	0.69 (0.33–1.42)
Carpenters, wood workers	8	16	0.67 (0.28–1.59)
Painters	7	8	1.27 (0.45–3.54)
Material moving equipment operators	17	19	1.20 (0.61–2.36)
Motor vehicle operators	26	38	0.97 (0.58–1.63)
Vehicle mechanics	20	25	1.06 (0.58–1.93)
Occupational groups not of a priori interest			
Managers, administrators	38	52	1.11 (0.72–1.72)
Mathematical, physical, computer scientists	6	12	0.72 (0.26–1.94)
Nurses, health technicians	28	44	0.93 (0.57–1.52)
Teachers, librarians	30	64	0.69 (0.43–1.11)
Legal and social service workers	11	20	0.85 (0.40–1.80)
Salesmen	79	96	1.28 (0.94–1.76)
Clerks	76	100	1.25 (0.90–1.75)
Shippers	26	25	1.45 (0.83–2.56)
Messengers	7	17	0.67 (0.27–1.64)
Electronic equipment operators	8	19	0.62 (0.27–1.44)
Policemen, guards	8	11	1.03 (0.41–2.58)
Janitors	12	24	0.68 (0.34–1.39)
Personal service workers	13	30	0.64 (0.33–1.25)
Textile workers	6	6	1.51 (0.48–4.77)
Food service workers	33	62	0.75 (0.48–1.18)
Paper workers	5	6	1.09 (0.33–3.60)
Sheetmetal workers, etc.	16	31	0.73 (0.39–1.36)
Construction workers	15	19	1.11 (0.55–2.22)
Other (non-vehicle) mechanics	12	24	0.72 (0.35–1.45)
Vehicle manufacturing workers	12	9	1.98 (0.90–4.73)

* Occupational groups with potential exposure to a priori “exposures of interest” and occupational groups not of a priori interest are listed consecutively. Only those groups with at least five case and five control participants are presented.

^a Analyses used an occupational grouping algorithm developed for a study of paternal exposures and birth defects [Schnitzer et al., 1995].

^b Logistic regression analyses adjusted for frequency-matching variables (age group, sex) and age and education. Adj. OR = adjusted odds ratio; 95% CI = 95% confidence interval.

^c $P < 0.05$.

^d In our study population, butchers and meat cutters comprised most of those working in food processing, with an occupation in precision production either in food manufacturing (4/8) or in food stores (9/11). For both industry–occupation combinations, there were too few participants to do separate calculations. Combining the two categories, for 12 cases and 6 controls this was the longest employment duration, with an elevated risk of glioma (adjusted OR: 2.73, CI: 1.01–7.39).

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