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16. Abstract (Limit: 200 words)

A case/control study was carried out for 326 subjects with glioma to examine possible relationships between petrochemical exposure and brain tumors. Glioma cases were identified from medical records at a hospital and death certificates reporting a brain tumor as the underlying or immediate cause of death. Randomly selected neighborhood comparisons were matched for race, sex and age. No risk was found to be associated with occupational exposures in the petrochemical industry even after trying several composite groupings of job categories. Five of the patients and four members of the comparison group had reported petrochemical industry exposure. Histories of driving or operating gas or diesel powered vehicles were reported for 46 patients and 49 comparisons. Those employed as gas or diesel mechanics or gas station workers included 36 patients and 39 comparisons. Excesses were found among the comparisons for exposures to pesticides, paints and dyes as well as for individuals working with electrical/electronic equipment. Each of these industries has been singled out at one time or another as one in which possible exposures to carcinogens do occur.

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FINAL PERFORMANCE REPORT

Project: Occupational Exposure in Adult Glioma Patients

Award Number: R01 OH01557-04

Principal Investigator: Andrew Moss

SUMMARY

In order to examine the association between petrochemical exposure and brain tumors we carried out a case-control study of the occupational histories of 326 glioma-series patients selected (a) as patients in the neuro-oncology service of University of California medical center in San Francisco and (b) by a population-based death certificate search in 9 counties of Northern California, and of 318 matched randomly selected neighborhood controls.

We found no association with petrochemicals. 5 cases and 4 controls reported petrochemical industry exposure ($p = 0.49$). 46 cases and 49 controls reported histories of driving or operating gas or diesel powered vehicles ($p = 0.46$). 36 cases and 39 controls reported being gas or diesel mechanics or gas station workers ($p = 0.45$). We also found no association with chemical occupation exposure not elsewhere classified ($p = 0.22$). Numbers

were too scanty to examine other a priori suspect exposures such as vinyl chloride or rubber industry exposure.

We found three categories where there was a greater likelihood of exposure in controls than cases: pesticides ($p = 0.01$), paints,dyes and inks ($p = 0.01$) and electrical and electronics ($p = .065$). Since all three have been proposed as industries where there may be occupational risk of carcinogenesis, these apparently anomalous associations should be investigated further.

1. Background

Reports of excess risk for tumors of the central nervous system have appeared in a number of occupational studies[1,2,3,4,5,6,7]. Primary brain tumors of the glioma series, in particular, have been singled out in studies of four occupational groups, beginning in the 1950's with investigations of rubber workers and continuing in the 1970's and 80's with studies of vinyl chloride, chemical, and petroleum industry workers. The association between glial brain tumors and vinyl chloride appears to have the best supporting data. Vinyl chloride was accepted by Cole in his survey of occupational carcinogenesis as an industrial carcinogen[8]. The 1982 volume of the Annals of the New York Academy of Sciences was devoted to "Brain Tumors in the Chemical Industry"[9]. However, the reported associations with employment in the petroleum, rubber, and chemical industries were strongly disputed. We report on a case-control study of occupational risk associated with malignant brain tumors in adults which was carried out in response to this dispute.

2. Methodology

The feasibility of a case-control study of occupational risk for brain tumors in the San Francisco Bay area was based, in part, on the presence of petroleum refineries located in northern counties of the region. Other suspect industries in the northern

California area included the manufacturing of rocket fuel and shipbuilding. The University of California, San Francisco, Medical Center (UCSF) is the major referral center in Northern California for the treatment of brain tumors. Collaboration with the neuro-oncology service at the Brain Tumor Research Center at UCSF assured access to patients treated for malignant brain tumors at Moffitt Hospital. Tumor Registry data from the Surveillance, Epidemiology and End Results (SEER) program for the San Francisco-Oakland Standard Metropolitan Statistical Area (SMSA) indicated that approximately 50% of adult brain tumors in the five-county SMSA were seen at UCSF. In addition, a large number of patients from the Sacramento region, other smaller cities of northern California, and northern Nevada are seen on the Neuro-oncology service at Moffitt Hospital. A pilot study was carried out to assess the feasibility of recruiting and interviewing patients seen on the service. Based on the pilot study experience, we determined that it was possible to gather detailed occupational histories from brain tumor patients, but that a significant portion of patients had suffered too much neurological damage to conduct an interview or provide reliable information. Although the pilot demonstrated that a large number of brain tumor patients could be accessed from the Moffitt hospital neuro-oncology service alone, we believed a population-based sample would greatly strengthen the study. We therefore designed a protocol based on (1) interviewing as many brain tumor patients seen at Moffitt Hospital as possible during the period of the project and (2) supplementing these patients with a population-based sample by obtaining death certificates for all brain tumor related deaths during 1980-83 and contacting the next of kin for a proxy interview. The completed study is population based from death certificates reporting CNS tumors for residents of eight counties in the San Francisco-Oakland-Sacramento region of northern California: San Francisco, Marin, San Mateo, Alameda, Control Costa, Sonoma, Solano, Napa. It includes additional non-population based subjects from Northern California seen at Moffitt Hospital. Interviews were completed with 253 patients and 236 proxies. 32 of the proxy interviews were for patients seen at Moffitt hospital and the remaining 204 were with close relatives of deceased cases identified from death certificates.

Case Definition and Recruitment

Cases were identified (1) from medical records of patients seen on the neuro-oncology service at Moffitt Hospital (UCSF) or (2) from death certificates for all deaths in California among residents of the specified counties for the years 1980-1983 which reported a brain tumor as the underlying or immediate cause of death. Diagnosis was confirmed by pathology for 94% of cases seen at Moffitt and was made by neuroradiology for the other 6%. For cases identified from death certificates, surgery, biopsy, or autopsy (with the presumption of pathological confirmation of tumor type) was reported on the certificate for 71%, radiology for 0.5% (1 patient), and was unknown for the remaining 29%. 37%

of recruited and interviewed cases/proxies were diagnosed with glioblastoma multiforme, 22% with anaplastic astrocytoma, 16% with astrocytoma, 8% with glioma, 2% with oligodendroglioma, .04% with ependyoma, 7% with mixed types, and 8% with tumor type unspecified ("brain tumor" on death certificate).

Cases seen at Moffitt hospital were recruited by letter to the patient and proxies for cases identified from death certificates were recruited by letter to next of kin. Initial permission to contact the patient or proxy was obtained and a visit for the interview was scheduled. Informed consent was obtained at the time of the home visit prior to the interview.

Participation rate for Moffitt patients was excellent and the rate for proxies was quite good. 253 patients were interviewed (94%) of 269 seen at Moffitt hospital who were invited to participate, 10 refused participation, 2 died before they could be interviewed, 1 was not interviewed because of language difficulty, and 3 lived too far away to be interviewed after discharge from the hospital. Among proxies who were sent letters, 236 (79%) out of 295 were interviewed. 26 were classified as refusals, 1 was deceased, 6 lived too far away to be interviewed, and 26 could not be located. Proxy respondents were a surviving spouse, parent, child, or sibling of the index case who felt he/she had a good knowledge of the case's work history. 364 interviewed cases/proxies were male and 123 were female.

Control Selection

One randomly selected neighborhood control, matched by race, sex, and age (± 5 years) was sought for each case. A block contiguous to the block of the case's residence (excluding the block directly across the street) was selected by a predetermined algorithm and an analogous address on that block was chosen as a starting point for enumerating the residents of each dwelling unit on the block. Each dwelling unit in turn was contacted by a trained interviewer, information on the residents sought, and the first eligible control found was invited to participate in the study. If an eligible control refused or could not participate for some other reason, additional dwelling units were screened. Up to 40 dwelling units were screened before the search for an eligible, consenting control was abandoned. Controls were told they were participating in a health study undertaken by the University of California; no mention was made of cancer, occupational risk, or the presence of a person with a brain tumor in the neighborhood. The algorithm for neighborhood control selection is attached (appendix B).

Matched neighborhood controls were obtained for 365 (75%) of the 487 interviewed cases. 67 cases were not matched because no eligible control could be found to meet the age, sex, and race criteria within the 40 households enumerated; 27 were not matched because the case lived too far away for control location to be feasible; 11 because the eligible control(s) refused; and 17 for miscellaneous reasons (language problem, control ill, etc.). Here we report on data from 318 cases and 326 controls from the total data set. The analysis presented here is unmatched.

Occupational History

Each case or proxy was asked for a complete occupational history, beginning with the first job held and including any job held for 6 months or longer, including military service. Job title, work performed, type of industry, and name and location of employer were recorded. In addition, self-reported exposures were recorded in response to a series of questions (see attached questionnaire) about substances worked with or inhaled as dust or fumes, exposure to ultraviolet or black light, fluorescent lighting and radiation.

Method for Coding and Analyzing Occupational Data

Our approach to the occupational history data was guided by two principles: (1) to use a measure of exposure to the *a priori* suspect substances (petrochemicals, rubber and plastics production, radiation) that was as free as possible of recall bias and (2) to define categories which balance the competing demands of identifying particular exposures (narrow categories) and providing sufficient numbers for statistical analysis (broader categories in which more subjects are likely to fall). The basis for our analytic categories was a coding of each job in every work history using the nine-digit codes of the Dictionary of Occupational Title (DOT), U.S. Department of Labor, 1977.

Coders were blinded to case or control status by separating occupational histories from the questionnaires prior to coding. Each history was coded a second time by a different coder. DOT coding was performed by reading job descriptions only, without utilizing the subject's self-reported exposures to substances on the job. In addition to the DOT code, each job was assigned an industry code from the Standard Industrial Classification Manual (SIC), U.S. Office of Management and Budget, 1972.

In a second coding step, job descriptions for all assigned DOT codes were read from the occupational histories, independently of the process of assigning the codes, and were assigned to one of the predesignated exposure categories, a miscellaneous category, or the no exposure category. Up to three exposures could be coded for each DOT code with one exposure being designated as the primary exposure. As with the assigning of DOT codes, this coding step was performed independently by two different coders for each DOT job description previously assigned in coding the occupational histories. Periodically the category of "miscellaneous exposures" was scanned for possible new exposure categories and in this way several additional exposure categories were added to the a priori list. Twenty-four specific exposure categories were designated and two other categories, one for industry dependent exposures and one for miscellaneous exposures. All other jobs were classed as no exposures. Clerical, secretarial, and sales office jobs were categorized as no exposure. The list of exposure categories used in the analysis follows:

TABLE OF EXPOSURE CATEGORIES FOR DOT JOB CODING

Exposure Abbreviation	Description
AM	Ammunition, explosives, firearms, bombs, etc.
AS	Aerospace workers (not mechanics)
BI	Biological (medical workers, biological lab workers, etc.)
CE	Cement and concrete workers
CH	Chemical exposure, various or not coded in another category
CT	Construction industry, miscellaneous exposures from construction not elsewhere coded
DR	Drivers. All types including any operator of gas or diesel powered machinery or equipment
EL	Eles/fungicides--use of or manufacturing of
PH	Photographic chemicals (used in processing prints, film)

TABLE OF EXPOSURE CATEGORIES FOR DOT JOB CODING

Exposure Abbreviation	Description
PI	Plastics industry (except vinylchloride)
RR	Railroad, working on or around locomotives
RW	Rubber workers
SH s/fungicides--use of or	manufacturing of
PH	Photographic chemicals (used in processing prints, film)

TABLE OF EXPOSURE CATEGORIES FOR DOT JOB CODING

Exposure Abbreviation	Description
PI	Plastics industry (except vinylchloride)
RR	Railroad, working on or around locomotives
RW	Rubber workers
SH	Shipbuilding
VC	Vinylchloride workers
WP	Wood products (carpenters, cabinet makers, saw mill or paper mill workers, etc.)
ID	Industry Dependent. No exposure specified because job description applies to any industry, but exposures are likely; e.g., plant engineer (would depend on type of plant), miner (depends on mine), etc.
MI	Miscellaneous exposure (specific exposure(s) are indicated by job description but are not elsewhere classifiable)
NE	No exposure

Discrepancies in assigning exposure categories to DOT job descriptions were reconciled by an adjudicator who did not perform coding. Once exposure category discrepancies were reconciled, only DOT code discrepancies which resulted in different exposure categories needed to be reconciled. Since several closely related DOT job codes are often possible for a given job, this procedure greatly reduced the number of job code discrepancies which had to be reconciled. We believe these procedures resulted in an unbiased set of exposure categories broad enough to permit statistical analysis.

Two primary occupational analyses were performed using (1) the exposure categories and (2) the industry codes. A third analysis was performed using self-reported exposures for comparison with the primary analyses, which are presumed to be less biased. Because we interviewed both brain tumor patients and family member proxies to obtain the occupational histories, we performed all analyses (1) including every subject and (2) excluding the proxy interviews and their matched controls. Two sources of bias were checked for by this procedure: referral basis in the non-population based UCSF hospital cases and recall (or knowledge) bias in proxy respondents.

In a second set of analyses, primary exposure categories were analyzed separately from all exposures (since each job was coded for up to three exposure categories). Thus four tables were generated for each exposure category: (1) primary exposures in all subjects and matched controls; (2) primary exposures in interviewed patients and their matched controls only; (3) all exposures in all subjects and their controls; and (4) all exposures in interviewed patients and their matched controls only. The analyses of industry codes and self-reported exposures were also carried out separately with proxies included and excluded.

3. Results

(i) Analysis by Exposure Categories

None of the *a priori* exposure categories which were suspected occupational risks at the outset of the study showed a significant excess of cases over controls, regardless of whether we considered all exposures or primary exposures only, or whether we included or excluded proxy interviews. Tables 1 through 14 give the distribution of risk categories of greatest interest between cases and controls and the p-values from Fisher's exact test (1-tail). The tables are based on combined patient and proxy interviews and include all coded exposure categories, not just the primary exposure. Most categories are quite evenly distributed between patients and controls. Exceptions are job exposure to radiation/x-rays with 7 cases versus 3 controls (table 8--not enough subjects to show a statistically significant difference), and three exposures which showed a protective effect, i.e. a significant or almost significant excess among the controls. These were pesticides/fungicides (table 13) ($p = .01$), electrical/electronic equipment (table 7) ($p = .065$), and paints/dyes/inks (table 6) ($p = .01$).

Although the exposure categories formed during the coding process were for the most part broad enough to capture sufficient subjects for statistical analysis, *a priori* suspect risk categories such as radiation exposure, vinyl chloride, plastics, rubber manufacturing, aerospace and petrochemical exposures were found in relatively few subjects and the analysis of these individual risks lacks power. No subjects reported vinyl chloride exposure (table not shown); only 2 cases and 1 control reported rubber manufacturing job experience (table 2); 1 case reported work in the aerospace industry (not shown); 2 cases and 5 controls worked in plastics manufacturing (table 4); 3 cases and 2 controls had photochemical exposure (table 3); and 5 cases and 4 controls had petrochemical occupational exposure (table 1). In the broader category of chemical occupational exposure not elsewhere classified there were 14 controls and 9 cases (table 5) ($p = 0.22$).

We constructed two broader categories which involved exposure to gas, oil, grease and other petrochemical products (but not to the refining process). These were (1) drivers/operators of gas or diesel powered vehicles and equipment, and (2) mechanics and gas station workers. Both of these exposure categories were evenly distributed between cases and controls (tables 9 and 10).

Shipbuilding, with probable exposure to asbestos, was also evenly divided between cases and controls with 11 of each reporting jobs with this exposure (table 11). No differences were seen for construction work, work with wood products, cement/concrete work, janitorial work or use of cleaning solvents, railroad work, work with explosives- firearms, machining or tool and die making, or welding (tables not shown).

The two categories, miscellaneous exposures and industry dependent exposures, which might be expected to capture occupational risks missed by our choice of exposure categories, showed no differences between cases and controls (tables 15 and 16).

When farmwork was combined with pesticide exposure, significantly more controls than cases were classified with this exposure (table 17). When a variable for any occupational exposure was created (that is, one of more of any of the a priori exposure categories we used), no difference was seen between cases and controls: 52% of subjects with one or more exposures were controls and 48% were cases (table 18). Overall, about 2/3 of all subjects were classified with at least one occupational exposure, 68% of controls and 64% of cases.

Repeating the analysis above with proxy interviews excluded did not affect the results except that several differences which are statistically significant when all subjects are included do not have enough subjects with the exposure to be statistically significant when proxies are excluded.

When we looked at primary exposures only (one of the up to three exposures coded for each DOT job description was designated as primary), none of the results described above changed, although, again, some were no longer statistically significant because of smaller numbers. The three exposures showing a substantial excess of controls over cases, pesticides, paints/dyes and electrical/electronics, continued to show a protective effect when the analysis was limited to primary exposures: controls vs. cases were 16 to 4 for pesticides (p=0.006), 17 to 7 for paints/dyes (p=0.03) and 36 to 20 for electrical/electronics (p=0.02). Radiation/x-rays was 2 cases versus no controls.

(ii) Industry Analysis

Two-digit codes from the SIC Manual were used to code industry for each job; 80 codes were assigned to one or more jobs during coding. Comparing cases and controls on 80 industrial categories might be expected to produce some differences by chance alone, and some differences were found, but not in any of the *a priori* suspect industries. As with the coding of exposure categories, more of the differences showed an excess among the controls rather than the cases. Tables 19 - 22 show the four industry codes with the largest differences between cases and controls. Work in the motor freight transportation industry was a risk factor (table 19) although it should be borne in mind that the exposure category of driver showed no difference between cases and controls. Three industries showed significant excesses among the controls: agriculture (table 20), construction, other than building construction (table 21), and communications (table 22). Two different composite petrochemical industrial groupings showed no differences. Table 23 shows the larger of the two petrochemical groupings. Several other differences which were not significant, or of borderline significance with a 1-sided

Fisher's test and not significant with a 2-sided test, were wholesale trade, durable goods (risk) and textile mill products (protective), machinery (protective), general merchandise stores (protective), and justice/public order service (protective). This last industrial category is of interest because it contains fireman who have a high on the job risk for chemical exposures. 17 controls and only 7 cases were classified in this industrial category (2-sided p=0.06). Of the four industrial categories with a 2-sided p-value less than 0.05, only agriculture is consistent with the findings from the analysis of job exposure categories. A protective effect for agriculture as an industry is consistent with the protective effect seen from farmwork and pesticide exposure.

Repeating the industrial analysis with the proxy interviews removed, no significant difference was seen for agriculture nor for construction other than building. The communications industry continued to show a significant difference in the protective direction. The risk associated with the motor freight transportation persisted but the numbers were too small for statistical significance. The only difference of note was a risk associated with educational services which is not present when the proxies are included: 37 cases versus 24 controls (1-tail p=0.03, 2-tail p=0.045).

(iii) <u>Analysis by Self-Reported Occupational Exposures</u>

Subjects were asked about exposure on the job to a list of substances: rubber processing chemicals, leather processing, plastics processing, cutting, cooling, or lubricating oils, cleaning or other solvents, coal tar, soot, or pitch, other petroleum products, pesticides or herbicides, and photochemicals (table 24). Despite the seeming likelihood of recall bias among the cases and their relatives, very little evidence of self-reported elevated risk among the cases was elicited by these questions. Using photochemicals showed some difference but it was not statistically significant (OR=1.8, p=0.10). Statistically significant differences were observed in the protective direction for exposure to cleaning solvents and for other exposures (miscellaneous). Self-reported exposures were similar to the analysis of exposure categories and the analysis of industrial codes in finding even distributions between cases and controls for the _a priori_ suspect occupational exposures.

Subjects were also questioned about the use of pesticides at home and in the yard and about exposure to diagnostic and/or therapeutic x-rays or other radiation. In response to the question, "(SAY TO CASES: Before your tumor was diagnosed) did you ever receive radiation, either diagnostic x-rays or treatment, to your head or neck?", significantly more _controls_ than cases said yes (table 24). However, a separate question about the frequency of dental x-rays showed no difference between cases and controls when we looked at those who had dental x-rays once a year or more often versus those with x-rays less often or no x-rays (48% of cases versus 52% of controls had dental x-rays at least yearly). We cannot explain the anomaly of a significant excess of controls reporting head and neck x-rays. This excess persisted when we dropped proxy interviews from the analysis. Dental x-rays showed no difference and job exposure to radiation or x-rays showed an excess of cases. We cannot reconcile these results and have to conclude that there was something anomalous about the responses to x-rays to the head or neck or a bias in the question that we have overlooked.

(iv) Other risk factors

In addition to self-reported occupational exposures and other exposures to radiation and to pesticides, we examined a number of other potential risk factors which have been suggested in the literature. These other risk factors fall into several groupings by their implied etiologies: (1) viral, (2) traumatic, (3) dietary, (4) environmental, and (5) genetic. The odds ratios, p-values, and 95% confidence intervals are given for these variables in table 24.

Under (1), viral etiology, we found no risks in reported histories for a number of virally caused illnesses, including mumps, measles, German measles, polio (and receiving polio vaccine), warts, chicken pox, recurrent sinus infections, mononucleosis, or exposure to sick pets. Warts, in fact, were reported significantly more often by controls.

Category (2), trauma, did, as in several other studies, show a risk for cases. The question "did you ever have a head injury severe enough to cause symptoms such as dizziness, blurred or double vision, headaches or seizures which lasted for more than 2 or 3 days?" was answered "yes" by 54 cases versus 33 controls. As in some other studies, however, this risk was not seen in a question involving a more objective measure of medical attention: "Did a physician ever tell you that you had a concussion or a fractured skull?" Given the susceptibility of the first question to recall bias and the possibility of confounding with headaches and seizures which are part of the tumor's prodrome, the reported risk should be viewed with caution.

From the dietary questions one possible risk was seen, but only for one of three time periods asked about. Subjects were asked how often they ate certain foods 5, 10, and 15 years ago. Out of meat, charcoal broiled meat, smoked meat, green and yellow vegetables, dairy products, diet soda, and saccharine, only smoked meat consumption 5 years ago differed significantly between cases and controls (see table below). This was not the case for the other time periods.

TABLE: CONSUMPTION OF SMOKED MEAT

Amount of smoked meat consumption 5 years ago	No. of Cases	No. of Controls	Percent Cases	Odds Ratio
Never	6	14	30	1.0
Rarely	58	81	42	1.7
Sometimes	78	64	55	2.8
Often	32	23	58	3.3
Almost Every Day	11	7	61	3.7

Chi-square for trend = 9.30 w/ 1 d.f. $p = 0.004$

There was also no difference between cases and controls in reported use of vitamins. No difference was found in smoking history.

Environmental risks were looked at by comparing rural and urban residence (current and before age 18) and by asking about residence near a factory or some type of heavy industry or near a disposal area for chemicals, radioactive materials, or other hazardous materials. No statistically significant differences were found although more cases than controls reported living near a hazardous materials dump site (OR=1.7, p=0.07). 51% of those brought up on a farm were controls and 49% cases and exactly the same percentages applied to those reporting living near a factory or heavy industry.

The last group of risk factors concerned family history of disease. Because we did not verify reported familial cancers, this data also has to be regarded as among the items most likely to be overreported by brain tumor patients or their family members. Cases reported significantly more disease "that seems to run in your mother's or father's family," significantly more cancer among parents, grandparents, siblings, or children, significantly more conditions among those same relatives causing problems with coordination, walking, memory, or tremors, and more brain tumors among blood relatives (this last difference was not statistically significant).

Cases reported more use of barbituates (prior to diagnosis) and a more frequent history of epilepsy. Epilepsy is likely to be prodromal for a brain tumor and barbituates are likely to be prescribed to treat prodromal symptoms. These associations, reported by other researchers, were therefore expected, and although we cannot rule out a etiologic role for epilepsy or barbituates, the presumption has to be that they are markers rather than causes.

Demographically, cases and controls were very similar, having the same distribution of education, marital status, and religion of upbringing (an indication that the neighborhood control matching procedure was successful in controlling for socio-economic status). Cases and controls were matched on sex, race, and age. There was a small difference in current religion, 19 cases reported Jewish as current religion versus 9 controls, although no difference was seen among those who reported Jewish as their religion of upbringing.

4. Discussion

We found no risk associated with the occupational exposures or industries suggested in the literature with the possible exception of occupational exposure to radiation, where we lacked numbers large enough to show a statistically significant difference. The occupational radiation risk was obscured somewhat by the report of more radiation to the head and neck from medical care in controls than in cases.

We found no evidence for the a priori suspect petrochemical risk category which began this study, even after trying several composite groupings of both job exposure categories and industries.

The differences we did detect were excesses in the controls. These were in pesticide exposures, paint and dye exposures, and electrical/electronic equipment. None of the excesses in controls seem biologically plausible as protective factors. Several other explanations are possible. All of the above have been postulated as carcinogens in recent studies and there may be a recall bias of some kind. However, this seems unlikely given the clear evidence of lack of bias in many aspects of the current study. Second, given the large numbers of categories that we examined, some chance differences might be expected. However, perhaps it is most likely that there is some kind of selection bias at work, with a selection into the above groups of persons who are at low risk for brain tumors, and that this selection is not controlled for by the random neighborhood control matching used in this study. This could be the case with pesticide exposure, for example, if those exposed to pesticides were migrant workers from ethnic groups at low risk of brain tumor. Mormon and Seventh Day Adventists are also at low risk of tumors of all kinds in California, although we have no evidence that they are selected into the above occupations. The protective effects seen are likely to be real, they are intriguing, and they point to areas of epidemiological interest in the study of brain tumors. We intend to pursue them.

Overall, cases and controls were equally likely to fall into the "no exposure" category. The results from our "unbiased" coding of exposure categories were also corroborated by the subjects' self report of occupational exposures where no risk factors for brain tumor were seen. This last result was somewhat surprising since we had anticipated some recall bias in these questions and thought it would be likely for the cases and their proxies to overreport exposures. We were also surprised by the very high consistency of our findings when we analyzed the data with all interviews included and with the proxy interviews excluded. We believe the study has shown that it is possible to obtain reasonably good occupational data from carefully chosen proxy respondents.

Our findings on other risk factors corroborate other reports of associations with family history of cancer and with head trauma[10,11,12], but also share the weakness of many other studies in not having objective confirmation of these findings. The associations we and others observed with epilepsy and use of barbituates are more likely to be prodromal than causal. The one dietary risk we observed for consumption of smoked meats 5 years ago is not very plausible since the association is not as strong for smoked meats 10 and 15 years ago. We found no evidence for the previously reported risk for rural versus urban residence.

Overall, our study shows few differences between cases and controls. It is possible that there are occupational risks we missed, but the weight of our study is heavily against occupational risk in general and petrochemical exposure in particular as a significant risk factor in the etiology of brain tumors.

Table 1: Petrochemical occupational exposure

	Controls	Cases	Total
No job exposure	322	313	635
(row %)	(51)	(49)	
Some job exposure	4	5	9
(row %)	(44)	(56)	
Total	326	318	644

p = 0.49 (Fisher's exact test, 1-tail)

Table 2: Rubber manufacturing occupational exposure

	Controls	Cases	Total
No job exposure	325	316	641
(row %)	(51)	(49)	
Some job exposure	1	2	3
(row %)	(33)	(67)	
Total	326	318	644

p = 0.49 (Fisher's exact test, 1-tail)

Table 3: Photochemical occupational exposure

	Controls	Cases	Total
No job exposure	324	315	639
(row %)	(51)	(49)	
Some job exposure	2	3	5
(row %)	(40)	(60)	
Total	326	318	644

p = 0.48 (Fisher's exact test, 1-tail)

Table 4: Plastics manufacturing occupational exposure

	Controls	Cases	Total
No job exposure	321	316	637
(row %)	(50)	(50)	
Some job exposure	5	2	7
(row %)	(71)	(29)	
Total	326	318	644

p = 0.24 (Fisher's exact test, 1-tail)

Table 5: Chemical occupational exposure not elsewhere classified (excludes petrochemicals, rubber manufacturing, vinyl chloride, pesticides and fungicides, paints and dyes)

	Controls	Cases	Total
No job exposure	312	309	621
(row %)	(50)	(50)	
Some job exposure	14	9	23
(row %)	(61)	(39)	
Total	326	318	644

p = 0.22 (Fisher's exact test, 1-tail)

Table 6: Paints, dyes, inks occupational exposure

	Controls	Cases	Total
No job exposure	293	302	595
(row %)	(49)	(51)	
Some job exposure	33	16	49
(row %)	(67)	(33)	
Total	326	318	644

p = 0.01 (Fisher's exact test, 1-tail)

p = 0.02 (2-tail)

Table 7: Electrical and electronics occupational exposure

	Controls	Cases	Total
No job exposure	289	294	583
(row %)	(50)	(50)	
Some job exposure	37	24	61
(row %)	(61)	(39)	
Total	326	318	644

p = 0.065 (Fisher's exact test, 1-tail)

Table 8: Radiation/nuclear occupational exposure

	Controls	Cases	Total
No job exposure (row %)	323 (51)	311 (49)	634
Some job exposure (row %)	3 (30)	7 (70)	10
Total	326	318	644

p = 0.16 (Fisher's exact test, 1-tail)

Table 9: Drivers/operators of gas or diesel powered vehicles/equipment

	Controls	Cases	Total
No job exposure	277	272	549
(row %)	(50)	(50)	
Some job exposure	49	46	95
(row %)	(52)	(48)	
Total	326	318	644

p = 0.46 (Fisher's exact test, 1-tail)

Table 10: Gas or diesel mechanics/gas station workers

	Controls	Cases	Total
No job exposure	287	282	569
(row %)	(52)	(48)	
Some job exposure	39	36	75
(row %)	(52)	(48)	
Total	326	318	644

p = 0.45 (Fisher's exact test, 1-tail)

Table 11: Shipbuilding occupational exposure

	Controls	Cases	Total
No job exposure	315	307	622
(row %)	(51)	(49)	
Some job exposure	11	11	22
(row %)	(50)	(50)	
Total	326	318	644

p = 0.56 (Fisher's exact test, 1-tail)

Table 12: Biological occupational exposure (medical work, biological laboratory, livestock)

	Controls	Cases	Total
No job exposure	300	293	593
(row %)	(51)	(49)	
Some job exposure	26	25	51
(row %)	(51)	(49)	
Total	326	318	644

$p = 0.54$ (Fisher's exact test, 1-tail)

Table 13: Pesticide/fungicide occupational exposure

	Controls	Cases	Total
No job exposure	306	311	617
(row %)	(50)	(50)	
Some job exposure	20	7	27
(row %)	(74)	(26)	
Total	326	318	644

p = 0.01 (Fisher's exact test, 1-tail)

p = 0.02 (2-tail)

Table 14: Farmwork and ranchwork occupational exposure (not elsewhere classified under pesticide or biological exposure)

	Controls	Cases	Total
No job exposure	293	295	588
(row %)	(50)	(50)	
Some job exposure	33	23	56
(row %)	(59)	(41)	
Total	326	318	644

p = 0.12 (Fisher's exact test, 1-tail)

Table 15: Miscellaneous occupational exposure (not elsewhere classifiable)

	Controls	Cases	Total
No job exposure	264	268	532
(row %)	(50)	(50)	
Some job exposure	62	50	112
(row %)	(55)	(45)	
Total	326	318	644

p = 0.16 (Fisher's exact test, 1-tail)

Table 16: Industry dependent exposure (examples: plant engineer, miner--depends on type of plant, mine)

	Controls	Cases	Total
No job exposure	288	280	568
(row %)	(51)	(49)	
Some job exposure	38	38	76
(row %)	(50)	(50)	
Total	326	318	644

p = 0.50 (Fisher's exact test, 1-tail)

Table 17: Combined farmwork/ranchwork occupational exposure and/or pesticide/fungicide occupational exposure

	Controls	Cases	Total
No job exposure	280	292	572
(row %)	(49)	(51)	
Some job exposure	46	26	72
(row %)	(64)	(36)	
Total	326	318	644

p = 0.01 (Fisher's exact test, 1-tail)

p = 0.02 (2-tail)

Table 18: Any category of occupational exposure

	Controls	Cases	Total
No job exposure	104	113	217
(row %)	(48)	(52)	
Some job exposure	222	205	427
(row %)	(52)	(48)	
Total	326	318	644

p = 0.19 (Fisher's exact test, 1-tail)

Table 19: Industry: Motor freight transportation

	Controls	Cases	Total
No job exposure	318	300	618
(row %)	(51)	(49)	
Some job exposure	8	18	26
(row %)	(31)	(69)	
Total	326	318	644

p = 0.03 (Fisher's exact test, 1-tail)

p = 0.045 (2-tail)

Table 20: Industry: agricultural services

	Controls	Cases	Total
No job exposure	311	314	625
(row %)	(50)	(50)	
Some job exposure	15	4	19
(row %)	(79)	(21)	
Total	326	318	644

p = 0.01 (Fisher's exact test, 1-tail)

p = 0.02 (2-tail)

Table 21: Industry: construction, other than building construction

	Controls	Cases	Total
No job exposure	310	313	623
(row %)	(50)	(50)	
Some job exposure	16	5	21
(row %)	(76)	(24)	
Total	326	318	644

$p = 0.01$ (Fisher's exact test, 1-tail)

$p = 0.02$ (2-tail)

Table 22: Industry: communications

	Controls	Cases	Total
No job exposure	308	312	620
(row %)	(50)	(50)	
Some job exposure	18	6	24
(row %)	(75)	(25)	
Total	326	318	644

p = 0.01 (Fisher's exact test, 1-tail)

p = 0.02 (2-tail)

Table 23: Industry: composite of industrial codes pertaining to petrochemical industry (SIC 2-digit codes: 11 12 13 39 49 55 75)

	Controls	Cases	Total
No job exposure	272	263	535
(row %)	(51)	(49)	
Some job exposure	54	55	109
(row %)	(50)	(50)	
Total	326	318	644

p = 0.44 (Fisher's exact test, 1-tail)

Table 24: Odds Ratios for differences between adult glioma patients and matched controls on possible risk factors

Variable	Odds Ratio	p-value	95% CI
Work and environmental exposures			
Petrochemicals	0.9	0.69	0.6-1.4
Pesticides--on job	0.9	0.75	0.4-1.6
Pesticides--house/yard	1.0	0.65	0.7-1.3
Photochemicals	1.8	0.10	0.8-4.6
Leather processing chemicals	1.7	0.45	0.2-20.4
Rubber processing chemicals	0.8	0.72	0.2-2.8
Plastics processing chemicals	0.7	0.86	0.3-1.6
Cutting/cooling/lubricating oils	0.8	0.92	0.5-1.0
Cleaning or other solvents	0.7	0.03	0.5-1.0
Other (miscellaneous exposures)	0.5	0.002	0.3-0.8
Living on farm before age 18	1.0	0.50	0.6-1.6
Living near factory/heavy industry	1.0	0.47	0.7-1.4
Living near chemical or other hazardous waste disposal site	1.7	0.07	0.9-3.5
Viral exposures			
Measles (rubeola)	1.0	0.55	0.7-1.5
German measles (rubella)	1.1	0.40	0.7-1.6
Mumps	0.8	0.86	0.6-1.2
Chicken pox (varicella)	0.9	0.75	0.6-1.4
Mononucleosis	0.6	0.92	0.3-1.5
Polio vaccination	1.2	0.33	0.6-2.3
Warts	0.5	<0.001	0.4-0.7

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