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Parental Occupation and Childhood Astrocytoma: Results of a Case-Control Study[1]

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ABSTRACT

Parental occupations were investigated as possible risk factors for astrocytoma, the most frequently occurring brain tumor in children. A case-control study of 163 pairs was performed. Cases under 15 years of age at diagnosis in 1980–1986 were identified through the tumor registries of eight hospitals in Pennsylvania, New Jersey, and Delaware. Controls were selected by random-digit dialing and were matched to cases on age, race, and telephone area code. Occupations before the child's conception, during the pregnancy, and after the child's birth were studied separately.

We did not observe any strong associations. Significantly more fathers of cases were electrical or electronic repairmen, a subgroup of an occupational category previously associated with increased risk. An excess of case mothers employed as nurses was observed, which was significant for mothers of children diagnosed before 5 years of age. Elevated although not significant odds ratios were observed for some white collar and professional occupations in case parents; for paternal exposure to paint and paternal occupation in the paper and pulp mill industry, both in the period after the child's birth; and for maternal occupation as a hairdresser.

The lack of strong associations may have resulted from low statistical power for some job groupings. Our study, unlike previous studies, focused on a single type of brain tumor: childhood astrocytoma. Thus our results suggest that some parental occupations associated with childhood brain tumors in previous studies may not be risk factors for childhood astrocytoma.

INTRODUCTION

Astrocytoma, the most frequently occurring central nervous system tumor in childhood, constitutes about one-half of brain tumors and 9% of all neoplasms in children under age 15 in the United States (1). Little is known about the etiology of this tumor. A number of studies have investigated the possible role of parental occupation in the development of brain tumors in children. These studies focus almost exclusively on all childhood brain tumors combined (2–12). However, brain tumors include a variety of histological types that differ in age at onset, sex ratio, differentiation, and growth characteristics (13, 14). Different histological entities might therefore have different etiologies. For this study we investigated the association of astrocytoma and parental occupations in a case-control study. The timing of the exposures in relation to the child's conception and the relation between exposure and the child's age at diagnosis were also studied.

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METHODS

The methods are described in detail in a previous publication concerning nonoccupational factors associated with childhood astrocytoma (15) and will be summarized below.

Cases were identified through the tumor registries of eight hospitals in Pennsylvania, New Jersey, and Delaware. These hospitals included all the major centers as well as some of the smaller centers for the treatment of pediatric cancer in the time period of the study. Patients from other small centers were not included. Eligible cases were those diagnosed with astrocytoma, glioblastoma multiforme, mixed glioma with astrocytic elements, or brainstem glioma before age 15 in 1980–1986. Brainstem gliomas were included because in children, 85% of those biopsied are found to be astrocytomas (16). Additional inclusion criteria were: physician approval to contact parents; index child not adopted; biological mother English speaking and available for interview; telephone in household; and residence at diagnosis and at interview in the United States.

Controls were selected by random-digit dialing and were pair matched to cases on age, race, and telephone exchange. Age matching was accomplished by matching birthdate within 1 year for cases 0–4 years at diagnosis and within 2 years for cases 5 years and older at diagnosis. For race, matching was for black or nonblack. The random-digit dialing procedure has been described previously (17).

Mothers and fathers of cases and controls were interviewed separately by telephone. A complete occupational history was obtained for each parent. If the father was unavailable, the mother was asked to provide a proxy interview. All jobs held for at least 6 months at age 18 or older were coded by industry and job title according to the SIC[4] (18) and the SOC, respectively (19). Jobs were grouped in broad categories defined by the SIC and SOC schemes and in categories previously identified as possible risk factors for childhood brain tumors: the agricultural (2), chemical (3–5), petroleum (4, 5), newspaper and printing (4), aerospace (3, 6), paper and pulp mill (4, 5, 7), transportation (2), and construction (2, 8) industries; occupations with exposure to paint (3, 9), chemicals (3–5), petroleum (4, 5), ionizing radiation (5, 10), electromagnetic fields (5, 11), motor exhaust fumes (12), and metals (2, 8); and electrical (2), printing (4), and graphic arts workers (4). We studied two exposure levels for ionizing radiation, electromagnetic fields, and motor exhaust fumes as defined in previous studies (10, 11, 20). Although it is necessary to study each type of cancer separately, some risk factors may be shared. For example, an occupational exposure that induces new germinal mutations could increase the risk of several childhood cancers. Therefore, risk factors previously associated with other childhood cancers (21–37) were also studied.

Maternal occupations studied in addition to the SIC and SOC categories were maternal and paternal occupations previously associated with increased risk of childhood brain tumors and childhood cancer (2–12, 20–37). We also studied employment as a hairdresser, since a previous study observed an

[4] The abbreviations used are: SIC, Standard Industrial Classification; SOC, Standard Occupational Classification.

association between maternal use of hair coloring products and Wilms' tumor (38).

Analyses were performed for employment (ever *versus* never) in job categories for each of three time periods: (*a*) prior to the child's conception; (*b*) during the pregnancy; and (*c*) between birth and the reference date (1 year prior to diagnosis for the case, and for the control, the date on which the child reached the same age as the corresponding case on his/her reference date). Analysis of the preconception period was done considering all jobs and considering only jobs held full time for at least 2 years. The results for all jobs and jobs lasting 2 or more years were compared to assess the possibility of recall bias concerning short-term jobs held many years before the interview. The results differed little, and results for jobs held for at least 2 years are presented unless otherwise stated. Analyses were performed for two subgroups defined by age at diagnosis of the case (0–4 years, 5–14 years), since some risk factors may affect these age groups differently. The two case groups contain approximately equal numbers of cases.

Demographic characteristics of cases and controls were compared by χ^2 McNemar's tests, and paired *t* tests. Odds ratios for matched pairs were calculated for potential risk factors, and the corresponding two-sided *P* values were computed using McNemar's test. For odds ratios based on 25 or fewer discordant pairs, 95% confidence intervals were calculated by the exact method (39). Otherwise, approximate confidence intervals were calculated (39). We performed conditional multiple logistic regression to adjust for differences between cases and controls in proxy interview of the father, number of jobs held, and general job category (blue collar; white collar; technical, professional, or managerial). These analyses did not affect the results substantially. Statistical significance was defined at the 5% level.

RESULTS

Cases. From the eight hospitals, 217 children diagnosed with astrocytic glioma before age 15 were identified. Of these, 12 were excluded: 1 had no telephone and 11 biological mothers were unavailable for interview. Of the 205 remaining cases, 23 could not be located and parents of 18 refused to participate. One hundred sixty-four case mothers were interviewed; for one of these, a control could not be located. The analysis includes 163 case and control mothers and 158 case and control fathers, since no information was available on three case and two control fathers.

Control Selection. Of the 163 controls, 115 (71%) were the first eligible control identified. In 39 instances (24%), the first eligible control refused and the second control identified was used. The third eligible control was used in 7 instances (4%) and the fourth in 2 (1%).

Demographic Characteristics. Case parents were more likely to have completed higher education than control parents. The differences were not statistically significant ($P = 0.39$ and 0.27 in fathers and mothers, respectively), but a tendency toward higher education of parents was observed (test for trend, $P = 0.07$ in both parents) (Table 1). Parental age at the index child's birth was similar for case and control parents.

Interview and Job Characteristics. The mother provided a proxy interview for 21 case fathers and 34 control fathers. Case and control parents did not differ significantly in mean age at first reported job, number of preconception jobs, or number of jobs during pregnancy. However, both case fathers and mothers reported more jobs after the birth of the index child than did control parents. The average number of reported jobs after the child's birth was 1.6 in cases *versus* 1.4 in controls ($P = 0.06$) for the fathers and 0.9 in cases *versus* 0.7 in controls ($P = 0.03$) for the mothers. Control parents were more likely to have blue collar jobs and less likely to have white collar jobs compared to case parents (Table 1) ($P = 0.07$).

Table 1 *Parental educational level and general job category*

	Fathers[a] (*n* = 158)				Mothers[b] (*n* = 163)			
	Case		Control		Case		Control	
	No.	%	No.	%	No.	%	No.	%
Education								
<High school	17	11	25	16	9	6	17	10
High school graduate	57	36	59	37	74	45	79	48
Some college	21	13	25	16	22	13	24	15
College graduate	37	23	32	20	39	24	27	17
Graduate/professional school	26	16	17	11	19	12	16	10
General job category								
Blue collar	63	40	81	51	8	5	18	11
White collar	41	26	27	17	102	63	93	57
Professional, technical, managerial	54	34	50	32	50	31	44	27
No job	0	0	0	0	3	2	8	5

[a] $P = 0.07$ for test of trend.
[b] $P = 0.07$ for case-control comparison.

Paternal Occupation. Results are reported in Table 2 for industries and occupations previously associated with risk for childhood brain tumors and for other interesting SIC and SOC categories.

In the analysis of paternal occupations previously associated with childhood brain tumors, no significant associations were observed. Elevated odds ratios were observed for occupations with paint exposure or in the paper or pulp mill industry, both after the child's birth; for workers in the agricultural industry before conception; and for printing workers in all three periods. In analyses of subcategories, a significantly elevated odds ratio was observed for electrical and electronic equipment repairers in the preconception period. However, work in electrical assembling, installing, and repairing combined was not associated with elevated risk. Results for graphic arts workers and the petroleum industry are not shown in Table 2 since they were based on fewer than 4 discordant pairs. We did not observe elevated odds ratios in the analysis of occupations associated with risk for other childhood cancers.

No significant differences were observed when paternal employment was analyzed by groupings according to SIC and SOC. Elevated odds ratios were observed for teachers, sales occupations, clerical occupations, occupations in the mining industry (primarily coal), and in retail trade. No significant results were observed when analyses were performed for smaller subgroups in the categories with case excesses.

Maternal Occupation. Results of occupations with elevated odds ratios are reported in Table 3.

We studied maternal occupations previously associated with risk for childhood cancer. Elevated although not significant odds ratios were observed for hairdressers. Paternal occupations previously associated with increased risk were also studied in the mothers, but no significant associations were observed.

In the analyses of maternal occupations in categories according to the SIC and SOC schemes, we observed modestly but not significantly elevated odds ratios for retail trade, finance and public administration, teaching, and nursing. For nurses,

Table 2 *Selected results for paternal occupation*

Industry or occupation	Preconception			Pregnancy			Postnatal		
	OR[a]	Ratio[b]	95% CI[c]	OR	Ratio	95% CI	OR	Ratio	95% CI
Industry									
Agricultural	1.8	11:6	0.6–6.0	1.0	5:5	0.2–4.3	1.3	5:4	0.7–6.3
Chemical	1.0	5:5	0.2–4.3	1.3	5:4	0.7–6.3	1.7	5:3	0.3–10.7
Newspaper and printing	1.5	6:4	0.4–7.2	1.3	5:4	0.7–6.3	1.2	7:6	0.3–4.2
Aerospace	0.2	1:5	0.0–1.8	0.0	0:2	0.0–5.3	0.0	0:2	0.0–5.3
Paper and pulp mill	2.0	2:1	0.1–118.0	NC[d]	2:0	0.2–NC	5.0	5:1	0.6–237.1
Transportation	0.5	7:14	0.2–1.3	0.1	2:14	0.0–0.6[e]	0.6	11:19	0.2–1.4
Construction	0.8	18:22	0.4–1.7	0.8	13:17	0.3–1.8	1.1	20:19	0.5–2.2
Retail trade	1.5	28:19	0.8–2.9	2.9	23:8	1.1–7.8	2.3	25:11	1.0–5.3
Mining industry	NC	2:0	0.2–NC	NC	2:0	0.2–NC	NC	5:0	0.9–NC
Occupation									
Paint exposure	NC	1:0	0.0–NC	NC	1:0	0.0–NC	NC	4:0	0.7–NC
Chemical and petroleum workers with high exposure	1.3	5:4	0.7–6.3	1.0	4:4	0.2–5.4	0.6	3:5	0.1–3.1
Ionizing radiation									
More exposure	NC	2:0	0.2–NC	NC	1:0	0.0–NC	NC	1:0	00–NC
Less exposure	0.9	12:13	0.4–2.2	1.1	9:8	0.4–3.4	1.0	9:9	0.4–2.8
Electromagnetic fields									
Definite exposure	1.1	10:9	0.4–3.1	0.9	8:9	0.3–2.6	0.8	7:9	0.2–2.3
Probable exposure	1.7	17:10	0.7–4.4	1.6	13:8	0.6–4.5	1.3	12:9	0.5–3.6
Motor exhaust fumes									
More exposure	0.9	15:17	0.4–2.0	0.7	5:7	0.2–2.6	1.0	1:1	0.0–78.4
Less exposure	0.6	12:20	0.3–1.4	0.5	8:15	0.2–1.3	0.7	11:16	0.3–1.7
Metal-related occupation	1.1	21:20	0.5–2.1	0.9	15:17	0.4–2.0	0.8	15:18	0.4–1.8
Electrical assembling, installing, and repairing	1.0	9:9	0.4–2.8	1.0	6:6	0.3–3.7	1.0	6:6	0.3–3.7
Electrical repairing only	8.0	8:1	1.1–356.1[e]	5.0	5:1	0.6–237.1	2.5	5:2	0.4–26.2
Printing workers	4.0	4:1	0.4–195.1	3.0	3:1	0.2–157.7	2.5	5:2	0.4–26.2
Teachers	1.6	11:7	0.6–4.8	1.7	10:6	0.5–5.6	1.5	9:6	0.5–5.1
Sales	2.4	17:7	1.0–6.9	2.8	14:5	1.0–9.9	2.7	16:6	1.0–8.3
Clerical	1.2	21:18	0.6–2.4	3.2	13:4	1.0–13.7	2.2	11:5	0.7–8.1

[a] Odds ratio.
[b] Ratio of case-exposed/control-unexposed to case-unexposed/control-exposed pairs.
[c] 95% confidence intervals.
[d] NC, not calculable.
[e] $P < 0.05$.

Table 3 *Selected results for maternal occupation*

Industry or occupation	Preconception			Pregnancy			Postnatal		
	OR[a]	Ratio[b]	95% CI[c]	OR	Ratio	95% CI	OR	Ratio	95% CI
Industry									
Retail trade industry	1.2	25:21	0.6–2.3	1.0	15:15	0.4–2.3	1.9	21:11	0.8–4.6
Finance industry	0.7	12:17	0.3–1.7	2.2	9:4	0.6–10.0	2.0	10:5	0.6–7.5
Public administration industry	1.3	10:8	0.4–3.6	1.5	9:6	0.5–5.1	2.2	9:4	0.6–10.0
Occupation									
Teacher	1.1	14:13	0.4–2.6	1.8	11:6	0.6–6.0	1.8	9:5	0.5–6.8
Nurse									
All cases	2.2	11:5	0.7–8.1	1.8	9:5	0.5–6.8	1.8	9:5	0.5–6.8
Cases 0–4 years	8.0[d]	8:1	1.1–356.1	7.0	7:1	0.9–311.5	5.0	5:1	0.6–237.1
Hairdresser	2.5	5:2	0.4–26.2	1.5	3:2	0.2–18.0	3.0	3:1	0.2–157.7

[a] Odds ratio.
[b] Ratio of case-exposed/control-unexposed to case-unexposed/control-exposed pairs.
[c] 95% confidence intervals.
[d] $P < 0.05$.

higher odds ratios were observed when the analysis was restricted to cases diagnosed before 5 years of age. The odds ratio for the preconception period was statistically significant (odds ratio, 8.0).

DISCUSSION

We have described our findings on parental occupation from the first case-control study of a single histological type of

childhood brain tumor. Despite the homogeneous case group, we observed very few significant findings. However, some factors associated with increased risk are of interest in light of previous observations. Case parents were more likely to have completed higher education and to hold white collar and professional jobs with no obvious carcinogenic exposure. The association with higher education and professional occupation may reflect an increased incidence of childhood brain tumors in the higher social classes, as has been reported for other childhood cancers (8, 23) and adult brain tumors (40). Social class may be associated with childhood cancer through occupational or other exposures. Alternatively, as has been postulated, children in the lower social classes may be more likely to die from some other cause during the preclinical phase of their cancer or to have their cancer misdiagnosed compared to other children (23). While in adults the association between brain tumors and professional jobs may be explained by a difference in access to diagnostic services (41), pediatric oncologists believe this probably is not the case in children.

The possible risk to children of electrical workers or those exposed to electromagnetic fields has been the subject of some epidemiological reports (2, 5, 11, 29, 34, 36, 37). In our study, a significant association was observed with electrical or electronic repairman during the preconception period. However, this finding has to be interpreted very cautiously, since it was based on only 9 discordant pairs and since we were unable to replicate the previously observed elevated risk in the combined group of electrical assembling, installing, and repairing (2). Furthermore, odds ratios for electromagnetic field exposure were only slightly elevated.

Elevated although not significant odds ratios were obtained for a few other exposures previously reported to be associated with childhood brain tumors: exposure to paint; occupation in the paper and pulp mill industry (both predominantly in the period after the birth of the child); agriculture; and the printing industry. As observed in an earlier report on all childhood cancers combined, more case than control fathers worked in the mining industry (12).

Maternal occupation as a nurse was more common among cases than controls. An elevated frequency of nervous system cancers was seen among registered nurses in a previous study (42) (odds ratio, 1.61). An exposure common to nurses could be related to X-rays or other hospital-related factors. However, other professionals working in hospitals did not seem to be at increased risk.

For many occupational groupings, the power to detect odds ratios of even 5.0 was low. However, for agricultural workers and electrical assemblers, installers, and repairers, the power was adequate for odds ratios of 5.0 or higher. The study had sufficient power to detect an odds ratio of 3.0 for metal-related occupations; occupations with exposure to electromagnetic fields, ionizing radiation, and motor exhaust fumes; and occupations in the transportation and construction industries. These minimum detectable odds ratios are in general higher than those previously reported for these occupational groupings. However, all of our cases were astrocytomas, while about one-half of the cases in previous studies were astrocytomas. Thus associations for risk factors specific for astrocytomas should have been stronger in our study than in studies with more heterogeneous case groups. Several possible explanations for our negative results exist. Perhaps the previously suggested risk factors are not specific for astrocytoma but apply equally to all types of childhood brain tumors. In that case, our study would not have had adequate power to detect the reported relative risks. Another possibility is that the reported risk factors are associated only with tumor types other than astrocytoma. Finally, since most previously reported associations arose from exploratory analyses, some of them are likely to have occurred by chance. The results from this study suggest that some parental occupations associated with childhood brain tumors in previous studies may not be risk factors for childhood astrocytoma.

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