ORIGINAL ARTICAL

Brain tumours and exposure to pesticides: a case–control study in southwestern France

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Occup Environ Med 2007;**64**:509–514. doi: 10.1136/oem.2006.028100

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Accepted 17 November 2006
Published Online First 30 May 2007

Background: Brain tumours are often disabling and rapidly lethal; their aetiology is largely unknown. Among potential risk factors, pesticides are suspected.
Objective: To examine the relationship between exposure to pesticides and brain tumours in adults in a population-based case–control study in southwestern France.
Methods: Between May 1999 and April 2001, 221 incident cases of brain tumours and 442 individually matched controls selected from the general population were enrolled. Histories of occupational and environmental exposures, medical and lifestyle information were collected. A cumulative index of occupational exposure to pesticides was created, based on expert review of lifelong jobs and tasks. Separate analyses were performed for gliomas and meningiomas.
Results: A non-statistically significant increase in risk was found for brain tumours when all types of occupational exposure to pesticides were considered (OR = 1.29, 95% CI 0.87 to 1.91) and slightly higher but still non-statistically significant when gliomas were considered separately (OR = 1.47, 95% CI 0.81 to 2.66). In the highest quartile of the cumulative index, a significant association was found for brain tumours (OR = 2.16, 95% CI 1.10 to 4.23) and for gliomas (OR = 3.21, 95% CI 1.13 to 9.11), but not for meningiomas. A significant increase in risk was also seen for the treatment of home plants (OR = 2.24, 95% CI 1.16 to 4.30) owing to environmental exposure to pesticides.
Conclusions: These data suggest that a high level of occupational exposure to pesticides might be associated with an excess risk of brain tumours, and especially of gliomas.

Even though recent data from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) programme suggest a stabilisation of the incidence and mortality of primary brain tumours since 1991 in the United States in all age groups,[1] an increase in incidence and mortality of these tumours has been reported in many countries in the past years, especially among the elderly.[2–7] In France, data from the cancer registries network FRANCIM show an increase in incidence and mortality rates of central nervous system tumours during the period 1980–2000.[8]

The importance of improved diagnosis in increased incidence remains debatable,[9] but changes in environmental factors offer another potential explanation for part of the increase.[10] Available toxicological and epidemiological data note exposure to pesticides as a primary concern, mainly from studies involving farmers. A meta-analysis of 33 epidemiological studies of brain cancer in farmers performed by Khuder *et al* reported a 30% increase in risk (odds ratio (OR) = 1.3; 95% CI 1.09 to 1.56).[11] Most of these studies were based on standardised incidence or mortality ratios, using death certificate or census data. Among the 10 case–control studies exploring the relationship with farming populations, and collecting accurate data on pesticide use, the greatest number of exposed cases was 74[12] and the number exposed was below 25 in half of the studies.

More recently, Lee *et al* found significant associations between agricultural pesticide use and gliomas in a large case–control study.[13] In southwestern France, in the Bordeaux area (1 284 771 inhabitants in 1999), brain tumours have been exhaustively registered since 1999 and incidence is among the highest reported in the world.[14] This geographical area is covered by 125 000 hectares of vineyards, and employed more than 10 000 farmers and 18 000 farm workers in 2000. Pesticide exposure occurs directly through mixing or spraying or indirectly in re-entry tasks (ie, tasks performed in vineyards, other than application). In vineyards, fungicides represent 80% of all pesticides used. This region, therefore, offered the opportunity to assess the potential role of pesticides in the occurrence of brain tumours.

MATERIALS AND METHODS

Study population

We ascertained all newly diagnosed cases of symptomatic primary central nervous system tumours occurring between 1 May 1999 and 30 April 2001 in adults aged 16 years and over, and living in Gironde, southwestern France, at the time of diagnosis. Primary tumours with the following International Classification of Disease-Oncology site codes were included in the analysis: C70.0–C70.9 (meninges), C71.0–C71.9 (brain) and C72.2–C72.9 (cranial nerves and other parts of the central nervous system). Tumours of the spinal meninges (C70.1) and spinal cord (C72.0–C72.1) were excluded. Pituitary tumours, tumours occurring in patients with AIDS, relapsing tumours, metastases, and tumours detected by chance (diagnosed because of another disease or event) and asymptomatic tumours were not included.

Whenever histological diagnosis was available, the slides were systematically re-examined by a pathologist not involved in the initial diagnosis. In cases with no histological diagnosis, clinical and radiological criteria were used.

For each case, two controls individually matched by age (±2 years), by sex and by residence in Gironde, were investigated. After randomisation of the town of residence, controls were selected from the electoral roll, using a procedure which took into account the proportion of subjects of the same age and sex as cases in each town of Gironde. Seven controls were initially

Table 1 A priori assessment of pesticide exposure from job title, CEREPHY study, Gironde, France, 1999–2001*

Job title	Probability	Frequency
Joiner/carpenter	3	1
Cabinet maker	2	1
Sawmill worker	2	1
Forester	1	1
Landscape gardener	3	1
Camp site manager	1	1
Vineyard worker	3	2/1†
Fruit picker	1	1
Mixed farmer/mixed farm worker	3	3/2†
Cattle farmer/cattle farm worker	2	1
Fruit and vegetable packer	1	2
Greenhouse horticulture worker	3	3
Open field horticulture worker	2/3	1

*All other jobs were considered non-exposed (p = 0, F = 0).
†To be determined more precisely a posteriori.

selected from electoral rolls. When a control could not be reached after more than 10 phone attempts, he/she was replaced by another person from the seven selected controls.

Data collection

The standardised questionnaire was completed during a face to face interview and included detailed information on individual characteristics (age, sex, educational level and marital status), lifestyle (smoking and alcohol consumption), medical history (other cancerous disease, head trauma), environmental risk factors (pesticides, electromagnetic fields, handheld cellular telephone use, chemical agents), ionising radiation and aspartame consumption. Furthermore, occupational and residential histories were collected for all subjects. For each job, the kind of industry, the duration and the activity were collected. ''Educational level'' was considered in four classes: no or primary school, middle school, high school and university. Occupational chemical exposures and non-ionising radiation (use of mobile phone, proximity of power line) were used as dichotomous variables in our analysis. The ''alcohol consumption'' variable concerned wine, beer and aperitif and was categorised in three classes: no consumption, moderate intake (less than 30 g/day for men and 20 g/day for women) and excessive intake.

Assessment of pesticide exposure

The first step of the exposure assessment consisted in the review by two industrial hygienists of all job titles collected in work histories. They provided an a priori assessment of pesticide exposure based on their knowledge of occupations (table 1). The probability (p) was coded 0 for non-exposed, 1 for possibly exposed (<50% of the subjects being exposed), 2 for probably exposed (50–90% of the subjects being exposed), 3 for very probably exposed (>90% of the subjects exposed). The frequency (F) was based on the proportion of time that pesticide exposure occurs in a given job and was coded 1 when <5% of the work time, 2 when 5–30%, 3 when >30–70%, 4 when >70% of the work time. Table 1 presents the values of F and p for exposed jobs.

The second step consisted of compiling information from a supplemental questionnaire, applied to subjects who used pesticides (insecticides, fungicides and herbicides) in agriculture. This questionnaire included the type of crops with start and end dates, type of tasks (mixing, application, cleaning or repairing equipment), type of equipment (tractors, sprayers), use of protective devices and number of treatment days a year.

Considering this individual detailed information, the a posteriori likelihood and frequency of use were determined by the two hygienists, who were unaware of the disease status, for each subject. Duration (D) of each exposed job was calculated in years. Finally, a cumulative index of occupational exposure to pesticides during life was calculated as follows: $I = \Sigma^{i=n} P_i \times F_i \times D_i$, where subscript ''i'' indicates an exposed job.

Occupational exposure was primarily examined as a dichotomous variable (ie, exposed versus never exposed) and secondarily by quartiles of the index.

Measures for environmental exposure to pesticides were determined for both house and surroundings. Subjects were questioned about indoor treatment for insects, about pesticide use in gardening and about treatments for termites. Treatment of house plants was characterised by a positive answer to the question: ''Do you usually treat your house plants''. For outdoor exposure, two definitions were used: ''living in a rural area''(-defined according to the Institut National de la Statistique et des Etudes Economiques[15]), expressed as the number of years ''ever lived in a rural area'', and ''living in a vineyard area''. The latter variable was based on the proportion of acreage planted with vines in the district at the time of interview. When the proportion exceeded 25% (75th centile for the distribution), the district was considered to be ''planted with vines''.

Table 2 Distribution of cases according to histological type by sex, CEREPHY study, Gironde, France, 1999–2001

Histological type	Men (n = 95)	Women (n = 126)	All subjects (n = 221)
Gliomas	60 (63.2)	45 (35.7)	105 (47.5)
Glioblastomas	43 (71.7)	29 (64.4)	72 (68.6)
Astrocytomas			
Grade III	5 (8.3)	3 (6.7)	8 (7.6)
Grade II	5 (8.3)	5 (11.1)	10 (9.5)
Grade I	4 (6.7)	2 (4.5)	6 (5.7)
Other	3 (5.0)	6 (13.3)	9 (8.6)
Meningiomas	7 (7.4)	60 (47.6)	67 (30.3)
Neurinomas	18 (18.9)	15 (11.9)	33 (14.9)
Lymphomas	4 (4.2)	3 (2.4)	7 (3.2)
Other types*	6 (6.3)	3 (2.4)	9 (4.1)

Results are shown as No (%)
*Included haemangioblastomas (n = 7), choroid plexus papilloma (n = 1) and medulloblastoma (n = 1).

Analysis

For a power of 80% and an α risk of 5%, in a sample including 221 cases and 442 controls, considering that 34.6% of controls were exposed, the detectable risk was 1.6 for all brain tumours, 2.2 for gliomas and 2.6 for meningiomas.

Characteristics and pesticide exposures of the cases and controls were described and compared using the usual tests (χ^2, *t* test). Conditional logistic regression analysis for matched studies was performed with the SAS statistical program (SAS PHREG procedure). Thereby, ORs and 95% CIs were obtained. We performed univariate analyses to search for an association between potential risk factors and the pathology. For indoor insecticides, pesticides used in gardening, and residence in an area planted with vines, univariate analysis did not show any association with brain tumours. For occupational exposure to pesticides, treatment of house plants, place of residence in a rural area, multivariate analyses were performed. We retained in the full models the variables for which the adjusted relative risk differed from the crude relative risk by more than 20%. Full models only included subjects with complete information on all covariates.

Dose–response relationships were estimated for quartiles of exposure to pesticides, determined from the distribution of the cumulative index in the whole exposed population. All risk estimates were calculated with the cumulative index equal to

Table 3 General characteristics, lifestyle and potential confounders in cases and controls, CEREPHY study, Gironde, France, 1999–2001

Characteristics	Cases (n = 221) No (%)	Controls (n = 442) No (%)	OR (95% CI)	p Value
Sex (n = 663)				
Men	95 (43.0)	190 (43.0)	1.00	
Women	126 (57.0)	252 (57.0)	1.00	1.00
Marital status (n = 662)				
Married/cohabitant	159 (72.3)	330 (74.7)	1.00	
Widow	27 (12.3)	50 (11.3)	1.19 (0.66 to 2.15)	0.57
Other (separated, etc)	34 (15.4)	62 (14.0)	1.17 (0.70 to 1.94)	0.56
Educational level (n = 662)				
No or primary school	74 (33.5)	122 (27.6)	1.00	
Middle school	82 (37.1)	141 (32.0)	0.91 (0.60 to 1.39)	0.67
High school	33 (14.9)	104 (23.6)	0.47 (0.28 to 0.80)	0.005
University	32 (14.5)	74 (16.8)	0.66 (0.38 to 1.14)	0.14
Smoking (n = 663)				
No	125 (56.6)	249 (56.3)	1.00	
Yes	96 (43.4)	193 (43.7)	0.99 (0.69 to 1.41)	0.95
Alcohol consumption (n = 661)				
No	107 (48.8)	196 (44.4)	1.00	
Moderate	86 (39.3)	173 (39.1)	0.89 (0.62 to 1.28)	0.53
Excessive	26 (11.9)	73 (16.5)	0.61 (0.36 to 1.05)	0.07
Aspartame consumption (n = 621)				
No	147 (82.1)	335 (75.8)	1.00	
Yes	32 (17.9)	107 (24.2)	0.68 (0.42 to 1.09)	0.11
Antecedents of radiotherapy (n = 660)				
No	210 (95.5)	422 (95.9)	1.00	
Yes	10 (4.5)	18 (4.1)	1.13 (0.50 to 2.56)	0.78
Antecedents of head trauma (n = 663)				
No	212 (95.9)	425 (96.2)	1.00	
Yes	9 (4.1)	17 (3.8)	1.06 (0.47 to 2.38)	0.89
Occupational handling of chemical products (n = 663)				
No	164 (74.2)	354 (80.1)	1.00	
Yes	57 (25.8)	88 (19.9)	1.46 (0.97 to 2.19)	0.07
Cellular phone (n = 661)				
No	172 (78.5)	330 (74.7)	1.00	
Yes	47 (21.5)	112 (25.3)	0.78 (0.51 to 1.18)	0.24
Residence near high-tension lines (n = 649)				
No	167 (78.4)	357 (81.9)	1.00	
Yes	46 (21.6)	79 (18.1)	1.24 (0.82 to 1.87)	0.32

zero (subjects never exposed to pesticides) as the reference category. Separate analyses were carried out for gliomas and meningiomas, each using controls associated with those particular cases.

RESULTS

Selection procedure

Cases

During the study period in Gironde, 315 eligible cases of central nervous system tumours were identified. Ninety-four of them (29.8%) were not included for the following reasons: 14 refused to participate, and the remaining 80 were deceased or too ill and an appropriate proxy could not be found or refused to be interviewed. These 94 subjects had a mean age of 64 years, included slightly more men (54%), and included 54 subjects with gliomas (57.4%), 17 with meningiomas (18.1%), 11 with lymphomas (11.7%), 3 with neurinomas (3.2%) and 9 with other tumour types (9.6%). Participating cases were significantly younger and less frequently presented with gliomas and lymphomas but did not differ for rural/urban residence. The final study group comprised the 221 remaining cases. Among them, 8 (3.6%) questionnaires were completed with proxies.

Controls

A total of 796 people were asked to participate in the study as controls. Among them, 7 were deceased, 43 declined owing to health reasons, and 104 were unreachable for undetermined reasons. Among the 642 remaining subjects, 442 (68.8%) agreed to participate and were interviewed. Non-participating controls did not differ significantly from participating controls in age (58.8 vs 57.8 years), sex (48.0% vs 43.0% male) or in rural or urban residence (46.1% vs 53.9% in rural setting).

Description of cases and controls

Among the 221 patients with tumours, 95 were in men (43.0%) and 126 in women (57.0%). The majority had gliomas (47.5%), meningiomas (30.3%), neurinomas (14.9%) and lymphomas (3.2%) (table 2). Histological diagnoses were available for

Table 4 Adjusted brain tumour risks for occupational and environmental exposure to pesticides, CEREPHY study, Gironde, France, 1999–2001

	All brain tumours (n = 221)			Gliomas (n = 105)			Meningiomas (n = 67)		
	Cases (n)	Controls (n)	Adjusted OR (95% CI)	Cases (n)	Controls (n)	Adjusted OR (95% CI)	Cases (n)	Controls (n)	Adjusted OR (95% CI)
Occupational exposure to pesticides									
No	113	245	1.00	51	114	1.00	36	77	1.00
Yes	66	113	1.29 (0.87 to 1.91)	31	50	1.47* (0.81 to 2.66)	21	37	1.26 (0.61 to 2.64)
Cumulative index of occupational exposure to pesticides†‡									
Unexposed	113	245	1.00	51	114	1.00	36	77	1.00
First quartile	10	28	0.77 (0.36 to 1.65)	7	12	1.23* (0.43 to 3.53)	3	8	0.89 (0.22 to 3.58)
Second quartile	19	35	1.18 (0.63 to 2.20)	7	17	0.89* (0.32 to 2.45)	9	10	2.18 (0.76 to 6.25)
Third quartile	18	31	1.28 (0.69 to 2.40)	6	14	1.31* (0.46 to 3.76)	6	10	1.57 (0.48 to 5.15)
Fourth quartile	19	19	2.16 (1.10 to 4.23)	11	7	3.21* (1.13 to 9.11)	3	9	0.65 (0.16 to 2.55)
Residence in rural area									
No	78	125	1.00	41	56	1.00	21	44	1.00
Yes	143	317	0.72 (0.51 to 1.02)	64	154	0.56 (0.34 to 0.93)	46	90	1.07 (0.57 to 2.01)
Treatment of house plants									
No	195	409	1.00	92	194	1.00	52	100	1.00
Yes	19	17	2.24 (1.16 to 4.30)	9	7	2.57 (0.96 to 6.91)	3	7	0.79 (0.20 to 3.09)

*Conditional regression (sex, age), adjusted for consumption of aspartame.
†Cut-off points for quartiles were the following: for all tumours Q1 (0–3), Q2 (3–9), Q3 (9–34), Q4 (34–158); for gliomas Q1 (0–3), Q2 (3–13), Q3 (13–46), Q4 (46–156), for meningiomas Q1 (0–3), Q2 (3–6.5), Q3 (6.5–22), Q4 (22–158).
‡Trend test for all brain tumours, p = 0.038; for gliomas, p = 0.074; for meningiomas, p = 0.74.

87.3% of cases. Concordance between the two pathologists was 96.8%. The mean time between diagnosis and interview was 57 days.

The mean age was 57.0 years for cases and 57.8 for controls. Educational level was higher for controls: 40.4% had a secondary level versus 29.4% of cases. A similar proportion of cases and controls reported smoking or an excessive consumption of alcohol.

Exposure to pesticides

Occupational exposure

Analysis of occupational histories showed that among the 663 subjects, 232 (35.0%) had a history of pesticide exposure (79 cases and 153 controls). There was no difference in the proportion of occupational exposure to pesticides in cases (35.7%) and controls (34.6%) (crude OR = 1.05, 95% CI 0.75 to 1.49). The duration of occupational exposure to pesticides exceeded 7 years in half of the exposed subjects and 20 years in a quarter of them. The latent period between the first occupational exposure to pesticides and the interview exceeded 38 years in half of the subjects (53.2% in cases and 49.6% of controls), and 52 years in a quarter of them (22.8% of cases and 26.1% of controls). A minority of exposed workers (n = 37) mixed or sprayed pesticides during at least one job and a large number of subjects were exposed through working in treated fields. Their proportion was slightly higher in cases (5.9%) than in controls (5.4%), but not significantly (crude OR = 1.09, 95% CI 0.54 to 2.24).

Environmental exposure

Slightly fewer cases (64.7%) than controls (71.7%) had always lived in a rural area, resulting in a crude OR of 0.72 (95% CI 0.51 to 1.02). Other measurements of environmental pesticide exposure (living in an area planted with vines, gardening, and use of home insecticides) were also associated with a lower risk of brain tumour. More cases (8.9%) than controls (4.1%) used pesticides on house plants (OR = 2.24; 95% CI 1.16 to 4.30).

Other potential risk factors

Table 3 gives details of other potential risk factors.

More cases than controls reported occupational handling of chemical products, living near power lines or having a personal history of radiotherapy, but no difference appeared to be statistically significant. On the other hand, fewer cases than controls reported using cellular phones or consuming aspartame, and a comparable proportion of cases and controls reported a history of head trauma.

Multivariate analysis

Table 4 presents adjusted odds ratios for exposure to pesticides, for all brain tumours together, and for gliomas and meningiomas separately.

All brain tumours

Subjects with occupational exposure to pesticides had a 1.29-fold increased odds of brain tumour when potential confounders were controlled (95% CI 0.87 to 1.91). When the quartiles of the cumulative index were considered, a statistically significant increase was observed in the highest quartile (OR = 2.16, 95% CI 1.10 to 4.23). This quartile comprised a large proportion of subjects directly involved in pesticide treatment (50.9%) over a number of years, most of them exclusively in vineyards (53.6%), and others in mixed farming (vineyard, corn, wheat). Other cases in the highest quartile were exposed indirectly, except for five who were exposed through applying wood preservatives. Indirect exposure occurs during re-entry into treated vineyards for various tasks, and sometimes even during treatment days or periods.

Latency and duration of occupational exposure were higher in the highest quartile than in the other quartiles and averaged respectively 47 and 35 years.

The risk of brain tumours remained non-statistically significant lower for people who had lived in a rural area (OR = 0.72; 95% CI 0.51 to 1.02). Odds ratio for treatment of house plants remained significantly high (OR = 2.24; 95% CI

Main messages

- This case–control study demonstrates an increase in the risk of brain tumour in farmers, especially for gliomas and for the highest occupational exposures.
- A trend was also seen for treatment of home plants, but this result requires replication.

1.16 to 4.30) in multivariate analysis. There was a non-significant association with use of insecticides indoors.

For all analyses, controlling for matching variables (age and sex) did not change the results.

Gliomas

For gliomas, the unadjusted risk related to occupational exposure to pesticides increased to 1.42 (95% CI 0.80 to 2.53) and the adjusted OR was 1.47 (95% CI 0.81 to 2.66), but was still not statistically significant. When considering the fourth quartile of the cumulative index, the crude OR was 3.46 (95% CI 1.25 to 9.60) and the adjusted OR was 3.21 (95% CI 1.13 to 9.11). The proportion of subjects involved in treatment tasks was 51.9% (n = 14) in this quartile.

The risk of glioma when treating house plants was 2.57 (95% CI 0.96 to 6.91).

Meningiomas

For meningiomas, no statistically significant increase in risk was observed with occupational exposure to pesticides (OR = 1.26; 95% CI 0.61 to 2.64), not even when the most exposed subjects were considered.

DISCUSSION

In a study conducted in Gironde, France, no significant increase in the risk of brain cancer was seen when no versus any occupational exposure to pesticides was considered. However, a significant increase was observed among the most exposed subjects (OR = 2.16, 95% CI 1.10 to 4.23). A 47% non-statistically significant increase in risk was observed when gliomas were considered separately, becoming significant in the most exposed subjects (OR = 3.21, 95% CI 1.13 to 9.11). We also found an increased risk of brain tumour for subjects treating house plants (OR = 2.24, 95% CI 1.16 to 4.30).

Our population-based case–control study is one of the largest specifically exploring the role of occupational and environmental pesticides. The participation rate in the study was high, but non-participating cases were older and more frequently presented gliomas or lymphomas than the participating cases. Elderly people might have been more frequently exposed to pesticides as the part played by agriculture was greater in previous decades in France. Their underparticipation would decrease our risk estimates. The lower participation of subjects with gliomas and lymphomas would have the same impact if we consider that the higher risks were observed for these histological types.

Our study design enabled accurate data on pesticide use to be obtained but did not provide information about the specific pesticides responsible. Unfortunately, because of trade interests, information on the use of specific pesticides in a given area is not available in France. The reliability of farmers' pesticide use report is debatable as the number of pesticides used in vineyards is large, approaching 20 in a single treatment period, and an even larger number during a farmer's whole life Moreover, the brain injury and memory impairment of some of the subjects precluded asking for accurate details of pesticide names. This is why pesticide assessment relied on expertise. However, because interviewers were not blinded to the disease status, it might be argued that they probed more deeply into the exposure of cases than of controls. This bias was minimised by using well-trained interviewers, a standardised questionnaire and by the fact that the distribution of subjects among interviewers was not dependent on the case–control status.

However the index exposure we used has some limitations: it is a generic index, not taking into account differences between classes of pesticides (formulation, volatility, dermal penetration, etc) specificities of use like the type of equipment, the duration of the treatment days, the use of protective equipment, etc. Our approach only enables us to differentiate between users and non-users, and to rank users according to their frequency and duration of use to different gradients of pesticide exposure.

More than 70% of exposed cases in the highest quartile were exposed in the years 1965 to 1985 and half of them or fewer were exposed before 1950 or after 1985. Therefore, if the association we observed is genuine, it might be suggested that the exposure leading to the occurrence of brain tumour may be the pesticides used in the 1965–85 period. In vineyards, pests controlled by the majority of pesticide applications are fungi such as mildew, black-rot and oidium. In this time period, inorganic substances (copper, sulphur), dithiocarbamates (mancozeb, mancopper, maneb, propineb, zineb) and phthalimides (captafol, folpet, captan) were recommended for use on these fungi.

After 5.3 years of follow-up, no increase in the brain cancer incidence and mortality was observed in the Agricultural Health Study cohort (private applicators, commercial applicators, spouses of private applicators) in comparison with those of the general population of Iowa and North Carolina.[16 17] But the numbers of brain cancer cases may increase with the follow-up. Further analysis will be possible taking into account exposures and confounders. Our results are in accordance with the ecological study by Viel *et al*, who found that mortality from brain cancer was significantly higher in areas planted with vines.[18] Our results are also consistent with the study by Musicco *et al* in Italy, who found an increase in the risk of glioma for farmers, especially for those using chemicals (RR = 1.6, 95% CI 1.06 to 2.42).[19] This study could not dissociate the role of specific families of pesticides, but the use of ''insecticides and fungicides'' considered together was associated with a significant increase in risk (RR = 2.0, 95% CI 1.22 to 3.23). No consistent trend was found with duration of exposure, but the level of exposure was not assessed. The consistency between Musicco's results and our own study is of particular interest, because both regions are predominantly involved in viniculture.

Consumption of aspartame was associated with a decrease in risk. The role of aspartame in brain tumour was suggested from equivocal experimental studies dealing with its carcinogen effects on rodent brain and from the observation that aspartame might be metabolised in nitrosurea-like molecule. From an epidemiological perspective, only one ecological study

Policy implication

- Better understanding of pesticide exposures in farmers is needed to improve prevention.
- Additional studies in other agricultural settings and on pesticide home exposure are needed to confirm these results.

examined the question,[20] but could not reach definitive conclusions. Treatment of house plants was also associated with an increase in risk of brain tumour. The question about such exposure was rather limited in our study and recall bias cannot be ruled out. This is why this subject warrants further research, because exposure to pesticides for such purposes is acknowledged to be far lower than in agricultural settings, and because similar results have never been reported in previous studies. None of the other measures collected in our study appeared to be related to this variable or could signify a confounding effect. It is not completely clear what types of pesticide are being, and have been, sold in the past for use on house plants, but as the general population does not easily identify specific pests, ''total treatment'' (insecticides and fungicides) are commonly purchased. It is a matter of concern that they are sprayed in closed dwellings and that they are recommended for use every week. As in our study, treatment of house plants was mainly by women in urban surroundings, we cannot rule out the role of certain characteristics of this population, which were not explored in our study, such as lifestyle including diet, or domestic exposure to other chemicals.

Living in a rural area tended to be associated with a decrease in risk. Even if not significant, this result could appear inconsistent with the close relationship between ''agriculture'' and ''rural setting''. However, 60.7% of subjects in rural settings were not classified as being occupationally exposed to pesticides in our study. The lower risk in rural areas, together with the slight decrease for subjects living in a district planted with vineyards, does not favour a role of environmental exposure to pesticides near treated areas in the occurrence of brain tumours. This is not consistent with the study by Aschengrau *et al*, who found an association between residence near cranberry bog fields and the risk of astrocytomas (OR = 6.7; 95% CI 1.6 to 27.8).[21] Ahlbom *et al* also found that having lived in the vicinity of a farm increased the risk of astrocytoma (OR = 1.7, 95%CI 1.0 to 2.8), but no detail was given on what was meant by ''vicinity'' and on the type of agricultural setting.[22]

In conclusion, our study supports the role of pesticides in brain tumours but only for high levels of occupational exposure, in treatment tasks and also in re-entry conditions, in an agricultural setting where fungicides are predominantly used. Further studies on larger samples are needed to determine if the risk is more specifically associated with gliomas, and to investigate a possible association with specific families of pesticides. A higher risk for gliomas, the histological subtype consistently more common in men than in women, would suggest that differences in occupational exposure between men and women could contribute to the differences in rates between them. In addition, the treatment of house plants seemed to be associated with the risk of brain tumours, although it was not possible to determine the role of other factors in the domestic setting.

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Brain tumours and exposure to pesticides: a case–control study in southwestern France

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Occup Environ Med 2007 64: 509-514 originally published online May 30, 2007
doi: 10.1136/oem.2006.028100