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Case-control study of paternal occupation and social class with risk of childhood central nervous system tumours in Great Britain, 1962–2006

T J Keegan*[,1], K J Bunch[2], T J Vincent[2], J C King[2], K A O'Neill[2], G M Kendall[2], A MacCarthy[2], N T Fear[3] and M F G Murphy[2]

[1]*Furness Building, Lancaster Medical School, Lancaster University, LA1 4YG Lancaster, UK;* [2]*Childhood Cancer Research Group, University of Oxford, OX3 7LG Oxford, UK and* [3]*Academic Centre for Defence Mental Health, King's College London, SE5 9RJ London, UK*

Background: Paternal occupational exposures have been proposed as a risk factor for childhood central nervous system (CNS) tumours. This study investigates possible associations between paternal occupational exposure and childhood CNS tumours in Great Britain.

Methods: The National Registry of Childhood Tumours provided all cases of childhood CNS tumours born and diagnosed in Great Britain from 1962 to 2006. Controls without cancer were matched on sex, period of birth and birth registration sub-district. Fathers' occupations were assigned to one or more of 33 exposure groups. A measure of social class was also derived from father's occupation at the time of the child's birth.

Results: Of 11 119 cases of CNS tumours, 5 722 (51%) were astrocytomas or other gliomas, 2 286 (21%) were embryonal and 985 (9%) were ependymomas. There was an increased risk for CNS tumours overall with exposure to animals, odds ratio (OR) 1.40 (95% confidence intervals (CIs) 1.01, 1.94) and, after adjustment for occupational social class (OSC), with exposure to lead, OR 1.18 (1.01, 1.39). Exposure to metal-working oil mists was associated with reduced risk of CNS tumours, both before and after adjustment for OSC, OR 0.87 (0.75, 0.99). Risk of ependymomas was raised for exposure to solvents, OR 1.73 (1.02,2.92). For astrocytomas and other gliomas, risk was raised with high social contact, although this was only statistically significant before adjustment for OSC, OR 1.15 (1.01,1.31). Exposure to paints and metals appeared to reduce the risk of astrocytomas and embryonal tumours, respectively. However, as these results were the result of a number of statistical tests, it is possible they were generated by chance. Higher social class was a risk factor for all CNS tumours, OR 0.97 (0.95, 0.99). This was driven by increased risk for higher social classes within the major subtype astrocytoma, OR 0.95 (0.91, 0.98).

Conclusion: Our results provide little evidence that paternal occupation is a significant risk factor for childhood CNS tumours, either overall or for specific subtypes. However, these analyses suggest that OSC of the father may be associated with risk of some childhood CNS cancers.

*Correspondence: Dr TJ Keegan; E-mail: t.keegan@lancs.ac.uk

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Central nervous system (CNS) tumours are the second most common group of cancers diagnosed in children. They account for around 25% of all new cases of cancer in children aged <15 years in Great Britain. About 360 cases of CNS tumours are registered each year at the National Registry of Childhood Tumours (NRCT), with an annual age-standardised incidence of 34 per million children (Stiller, 2007).

The most common CNS tumour subtypes in childhood are: astrocytomas (around 40% of all CNS tumours), intracranial and intraspinal embryonal tumours (19%), and other specified intracranial and intraspinal neoplasms (around 12%). CNS tumours overall are distributed evenly across the childhood age groups, although ependymomas are more common before age 4, and the incidence of embryonal tumours decreases with increasing age (Stiller, 2007).

Known risk factors for CNS tumours in children are few. Genetic susceptibility is suggested because medulloblastoma is more common in boys, and brain cancers are more common in individuals with certain genetic conditions such as neurofibromatosis (risk increased 50-fold) and tuberous sclerosis (risk increased 70-fold). Therapeutic and diagnostic doses of ionising radiation are also a known risk factor for childhood brain tumours (Gurney *et al*, 1999; Pearce *et al*, 2012). Studies of risk of CNS tumours from a range of other environmental and genetic risk factors have provided only suggestive or inconsistent evidence (Gurney *et al*, 1999), although some childhood subtypes are associated with high birth weight (Harder *et al*, 2008).

The aetiology of childhood CNS cancers is not well understood, but prenatal exposures may be important. There has also been concern that paternal occupational exposures may be risk factors for cancer in the children of workers (Colt and Blair, 1998). Fathers may bring harmful substances home on their clothes to which a child or pregnant woman may be exposed. There is also the possibility that exposure to certain chemicals or radiation could cause genetic changes in sperm, which could predispose a child to cancer (Cordier, 2008).

For CNS tumours, a number of paternal occupational risk factors have been reported, including exposure to agriculture, aircraft industry paint, solvents and electromagnetic fields (Cordier, 2008). However, these and other associations have not been consistently reported in the ~30 studies carried out since the late 1970s. However, many of these studies have suffered from small numbers and imprecise exposure assessments (Savitz and Chen, 1990; Colt and Blair, 1998; McKinney, 2005; Cordier, 2008). We addressed some of the shortcomings of previous studies by drawing the study population from the NRCT, which holds an almost complete record of all childhood cancers registered in the United Kingdom between 1962 and 2006 (Stiller *et al*, 1998), and which provides sufficient cases to allow analysis of risk by tumour subtype.

The main objective of this study was to investigate possible associations between paternal occupational exposure and CNS tumours overall and tumour subtypes in children in Great Britain, using a matched case-control design. We focus on paternal occupation because it is more completely recorded on birth registrations during our study period than maternal occupation (Fear *et al*, 1999a). Additionally, we use job title to derive an approximate measure of paternal social class and use this to investigate possible associations between paternal occupational social class (OSC) and childhood CNS tumours.

MATERIALS AND METHODS

Cases and controls. The NRCT contained 12 706 registered cases of CNS tumours in children aged <15 years born and diagnosed between 1962 and 2006 in Britain. A total of 465 cases were excluded because they were born overseas or adopted. In addition, 367 case for whom no birth registration could be found were excluded, leaving 11 874 eligible cases for whom a birth record was available.

Control children ($n = 11\,874$) were selected from all birth registrations for Britain, held by the Office for National Statistics (ONS) or the General Register Office for Scotland (GROS). One cancer-free control for each case was selected, matched on sex, date of birth (±6 months) and birth registration sub-district.

The completeness of ascertainment of childhood cancer cases in the NRCT has varied over time, but it contains an almost (>97%) complete record of all registered cases of childhood cancer in Britain from the early 1970s (Stiller, 2007; Kroll *et al*, 2011a).

Oxfordshire Research Ethics Committee (Oxfordshire REC C, Reference 07/Q1606/45) approved the use of these data in 2007.

Coding of occupational groups. In the United Kingdom, paternal occupation is routinely recorded on the publically available section of birth registrations where the father is named. Paternal occupation was abstracted verbatim from the case and control birth records as supplied by ONS and GROS.

Occupations were coded according to the 1980 Office of Population Censuses and Surveys (OPCS) Standard Occupational Classifications (SOC; Office of Population Censuses and Surveys, 1980). Coding was carried out independently by two coders, using the OPCS (now the ONS coding manuals. Where the two coders disagreed, a third coded the occupation. Where the third coder agreed with one of the original coders that agreed code was assigned. Where all three coders disagreed, the occupation was regarded as 'uncodable'. At all stages occupations were coded blind to the case control status of the individuals. The 1980 classifications were converted to the codes used in the 1970 SOC (Office of Population Censuses and Surveys, 1970), using a computer program.

The 1970 codes were subsequently allocated to one or more of 33 occupational exposure groups, which have been described elsewhere (Fear *et al*, 1999a, b). Briefly, the occupational exposure groups were derived by one of the authors (NTF) in conjunction with an occupational hygienist and an occupational researcher. Occupations not appearing in any of the 33 groups were classified 'unexposed' in all groups. For the occupational exposure group, 'social contact', jobs were classified according to a previously used scheme in which occupations were classified by an occupational hygienist according to whether they had higher than average social contact (Fear *et al*, 1999b, 2005). Occupations classified to one or more of the exposure groups were further defined as having either 'definite' (daily contact with the agent, or contact at a high intensity, for example, carpenters and wood dust) or 'possible' (exposure to the agent but not necessarily daily nor necessarily at high intensity, for example, builders and wood dust) exposure in that group (Fear *et al*, 1999a). Job titles could be coded to more than one occupational exposure group for example, bus drivers appear as exposed in 'exhaust fumes', 'inhaled hydrocarbons' and 'social contact'.

Each 1980 occupation code was then assigned to one of six social class codes based on occupation (V unskilled, IV partly skilled, IIIM-skilled non-manual, IIINM-skilled manual, II managerial and technical, I professional) from the 1980 OPCS Classification of Occupations.

For 622 cases and 703 controls, paternal occupation was missing, and these subjects were excluded from the analysis (Figure 1). For some (82 cases and 95 controls), it was not possible to assign a 1980 occupation code, or it was not possible to convert the 1980 code to a 1970 code (51 cases and 37 controls). In these circumstances, the paternal occupation was coded as if missing. For 1 020 cases and 1 172 controls, social class was

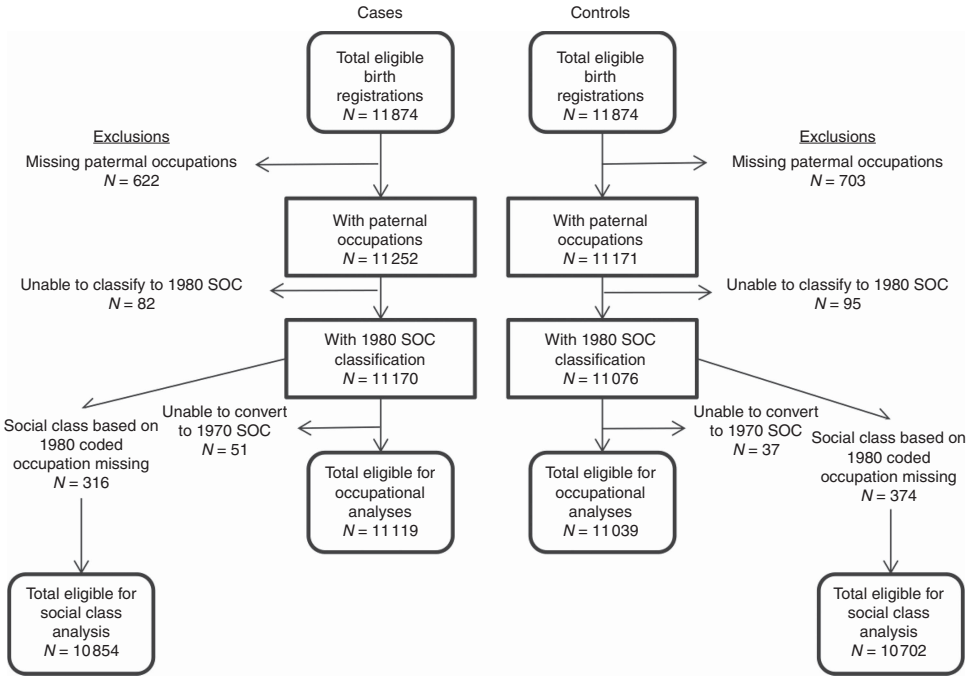

Figure 1. Flow chart showing the numbers of eligible CNS tumour cases and controls included in the analysis.

classified as 'missing' because no occupation was given or the occupation falls outside the ONS social classifications (for example, armed forces, student, independent means or sick). The 51 cases and 37 controls excluded from the occupation analysis, because their 1980 code could not be translated to a 1970 code, were included in the social class analysis and appear in the results shown in Table 5.

A total of 1024 case/control fathers were classified as 'forces', comprising the armed forces, police force, fire service, and guards and related workers not elsewhere classified. Within the 'forces' group, social class code was unavailable for members of the armed forces, approximately half the group, so OSC was not included in the analysis for this exposure group.

Outcomes. All cancers registered in the NRCT are coded to the International Classification of Childhood Cancer, third edition (ICCC-3; Steliarova-Foucher *et al*, 2005). Outcomes of interest in this study were: ependymomas (ICCC-3 31 division 1), astrocytomas (ICCC-3 32) and intracranial and intraspinal embryonal tumours (ICCC-3 33). Astrocytomas and other gliomas together (ICCC-3 32 + 34) were also considered as an outcome group. The group 'total CNS tumours' include these and the following additional categories: choroid plexus tumours (ICCC-3 31 division 2), other specified intracranial and intraspinal tumours (ICCC-3 35), unspecified intracranial and intraspinal neoplasms (ICCC-3 36; Table 2).

Analysis. Odds ratios (ORs) and 95% confidence intervals (95% CIs) for our matched analysis were calculated using conditional logistic regression (Breslow and Day, 1980). Matching factors were: sex, period of birth and birth registration sub-district. ORs and 95% CIs adjusted for social class (I, II, IIINM, IIIM, IV, V) were also generated. Our exposed population for occupational exposure consisted of individuals classified as 'definitely' exposed. The same analyses were repeated, taking the exposed population as those with either 'definite' or 'possible' exposures, although results are not shown because of the potential inclusion of misclassified or non-exposed individuals. Statistically significant results were defined as those where the P value was <0.05.

To assess the impact of multiple statistical testing on the likelihood of any of 33 P values for total CNS tumours being statistically significantly different from those expected by chance should the null hypothesis for each test be true, we plotted the empirical cumulative distribution of P values whose null sampling distribution is assessed as uniform on (0,1). We used a Kolmogorov-Smirnov test to test for significant deviation from linearity.

All analyses were carried out using STATA v. 11 (StataCorp LP 2009).

RESULTS

After exclusions, a total 11 119 cases and 11 039 controls were included in analyses of occupation and CNS cancer risk. There was no significant difference between the birth regions of cases and controls, nor was there a difference in social class or occupational status between the two groups (Table 1). Of the cases, 5 722 (51%) were astrocytomas or other gliomas, 2 286 (21%) were embryonal and 985 (9%) were ependymomas (Table 2). There were no marked differences between the results for definite exposure and definite or possible exposure, so results and discussion that follow are based on definite exposures alone.

Table 3 shows that there was an increased risk for CNS tumours as a whole with paternal occupational exposure to animals, both before and after adjustment for OSC. Paternal occupational exposure to lead showed an increased risk after adjustment for OSC. However, risk of CNS tumours was reduced in children whose fathers were occupationally exposed to metal-working oil mists, both before and after adjustment for OSC.

Analysis by tumour subtype revealed further associations (Table 4). For ependymomas (ICCC-3 31 division 1), there was a significantly raised OR for exposure to solvents before adjustment for social class (falling to borderline significance after adjustment). For astrocytomas (ICCC3 32), there was a borderline significantly reduced OR for exposure to paints, both before and after adjustment for social class. ORs for high social contact were significantly raised for both astrocytoma and astrocytomas and other gliomas taken together, but these risk associations became

Table 1. Childhood CNS cancer cases born and diagnosed in Great Britain between 1962 and 2006 for whom a birth record was available, and their matched controls

	Cases	(%)	Controls	(%)
Sex				
Males	6469	54	6469	54
Females	5405	46	5405	46
Total	11874	100	11874	100
CNS tumour subtype				
Ependymoma	1057	9	1057	9
Choroid plexus	260	2	260	2
Astrocytoma	4678	39	4678	39
Embryonal	2428	20	2428	20
Other gliomas	1430	12	1430	12
Other specified	1213	10	1213	10
Unspecified intracranial	808	7	808	6
Total	11874	100	11874	100
Birth year				
1962–1969	2525	21	2523	21
1970–1979	2654	22	2651	22
1980–1989	3126	26	3137	26
1990–1999	2916	25	2913	25
2000–2006	653	5	650	5
Total	11874	100	11874	100
Social class				
I	760	6	671	6
II	2154	18	2139	18
IIINM	1315	11	1268	11
IIIM	4024	34	3905	33
IV	1871	16	1947	16
V	730	6	772	7
Not known	1020	9	1172	10
Total	11874	100	11874	100
Region				
North	679	6	679	6
Yorkshire and Humberside	1017	9	1004	8
East Midlands	862	7	870	7
East Anglia	424	4	421	4
South East	3637	31	3657	31
South West	957	8	953	8
West Midlands	1152	10	1157	10
North West	1456	12	1442	12
Wales	589	5	591	5
Scotland	1095	9	1095	9
Not known	6	0	5	0
Total	11874	100	11874	100

Abbreviation: CNS = central nervous system.

Table 2. Number of cases and their controls by CNS tumour type included in the occupational exposure analysis (see Figure 1 for details of exclusions)

ICCC-3 division	CNS tumour	Cases	%	Controls	%
31 division 1	Ependymoma	985	8.9	987	8.9
31 division 2	Choroid plexus	243	2.2	231	2.1
32	Astrocytoma	4383	39.4	4330	39.2
33	Embryonal	2286	20.6	2263	20.5
34	Other gliomas	1339	12	1340	12.1
35	Other specified intracranial and intraspinal neoplasms	1125	10.1	1125	10.2
36	Unspecified intracranial and intraspinal neoplasms	758	6.8	763	6.9
31–6	All CNS	11 119	100	11 039	100

Abbreviations: CNS = central nervous syatem; ICCC-3 = International Classification of Childhood Cancer, third edition.

nonsignificant after adjustment for OSC (Table 4). For embryonal tumours (ICCC-3 33) the OR for exposure to metals was significantly reduced, both with and without adjustment for OSC.

There was a significant effect of OSC on risk of both astrocytoma and astrocytomas and other gliomas taken together (Table 5). For both these groupings there was a clear and significant trend of increased risk in the higher social classes and decreased risk in the lower social classes. For embryonal tumours no clear relationship between social class and risk of disease was discernible. For ependymomas, there was some indication of an inverse relationship between social class and risk of disease, in that the risk was lower in the higher social classes (significantly so for social class II), although the overall test for trend was non-significant. For CNS tumours overall, the risk was significantly reduced in social class V, and a weaker but still significant trend of increasing risk with higher social class was visible.

We assessed the results for the effect of multiple statistical testing, using a Kolmogorov-Smirnov test on the 33 P values generated in the analysis of paternal occupational exposure groups and childhood CNS tumours. Results showed that the distribution was not different from normal that is, the 33 P values were compatible with a distribution that has arisen by chance (results not shown).

DISCUSSION

Summary. In our analysis of risk of all childhood CNS tumours with paternal occupational exposures, the findings for most exposure groups were unremarkable, with most ORs around 1, both before and after adjustment for OSC. Risk was significantly >1 in two exposure groups; animals and to lead, although this latter group only after adjustment for social class. It remained significantly <1 for exposure to metal oils. In the CNS tumour subgroup analyses, the findings for most exposure groups were also unremarkable, although five associations were significant before adjustment for social class. In particular, social contact was a risk factor for both astrocytoma and astrocytomas and other gliomas taken together, and exposure to solvents was a risk for ependymomas. However, these relationships did not persist after adjustment for social class. Two risk estimates were significantly <1; exposure to paints for astrocytomas and to metals for embryonal tumours. Of the risk associations observed for each CNS tumour subtype, the only one that remained significant after adjustment for social class was that between exposure to metal and embryonal tumours.

We found a significant trend in the association between childhood CNS tumours and social class. There was an increased risk of childhood CNS tumours in the higher social classes and a decreased risk in the lower social classes. This effect was driven principally by the association between risk of astrocytomas and social class, where a clear and highly significant trend was

Table 3. Paternal occupational exposures and ORs with 95% CIs for total CNS tumours

	Exposure group	Exposed cases	%	Exposed controls	%	Informative pairs	OR[a]	95% CI	OR[b]	95% CI
1	Agriculture	228	1.9	251	2.1	431	0.92	0.76–1.11	0.88	0.73–1.07
2	Agrochemical	320	2.7	346	2.9	592	0.93	0.80–1.10	0.91	0.77–1.08
3	Animals	94	0.8	69	0.6	149	**1.40**	1.01–1.94	**1.40**	1.01–1.96
4	Ceramics/glass	47	0.4	35	0.3	78	1.36	0.87–2.14	1.45	0.92–2.30
5	Coal dust	101	0.9	107	0.9	179	0.92	0.69–1.24	0.94	0.70–1.27
6	Construction	839	7.1	826	7.0	1416	1.02	0.92–1.13	1.04	0.93–1.15
7	EMFs	645	5.4	628	5.3	1099	1.04	0.93–1.17	1.04	0.92–1.17
8	Exhaust fumes	931	7.8	887	7.5	1510	1.05	0.95–1.16	1.06	0.96–1.18
9	Fishing	20	0.2	22	0.2	35	1.06	0.55–2.05	1.04	0.53–2.04
10	Foodstuffs	360	3.0	376	3.2	632	0.91	0.78–1.06	0.90	0.77–1.05
11	Forces	502	4.2	522	4.4	863	0.96	0.84–1.10		
12	Heat (prolonged exposure)	228	1.9	215	1.8	387	1.04	0.85–1.27	1.02	0.84–1.25
13	Hydrocarbons (inhaled)	1741	14.7	1748	14.7	2443	0.97	0.89–1.05	0.98	0.90–1.07
14	Hydrocarbons (dermal)	818	6.9	864	7.3	1326	0.92	0.83–1.03	0.94	0.84–1.05
15	Ionising radiation	7	0.1	7	0.1	14	1.00	0.35–2.85	0.97	0.34–2.78
16	Lead	376	3.2	319	2.7	613	1.14	0.97–1.33	**1.18**	1.01–1.39
17	Leather	20	0.2	17	0.1	34	1.43	0.72–2.83	1.45	0.73–2.87
18	Medical/health care	205	1.7	200	1.7	359	0.98	0.80–1.21	0.93	0.75–1.15
19	Metal	1669	14.1	1728	14.6	2505	0.95	0.88–1.03	0.96	0.89–1.05
20	Metal acid mists	6	0.1	8	0.1	12	1.00	0.32–3.10	1.03	0.31–3.55
21	Metal fumes	145	1.2	139	1.2	237	1.04	0.81–1.35	1.00	0.78–1.30
22	Metal working (oil mists)	459	3.9	514	4.3	857	**0.86**	0.75–0.98	**0.87**	0.75–0.99
23	Mining	116	1.0	116	1.0	202	1.00	0.76–1.32	1.03	0.77–1.36
24	Paints	231	1.9	207	1.7	387	1.11	0.91–1.36	1.13	0.92–1.38
25	Paper production	3	0.0	4	0.0	7	0.75	0.17–3.35	0.77	0.17–3.43
26	Plastics	23	0.2	19	0.2	39	1.17	0.62–2.19	1.16	0.61–2.19
27	Printing	103	0.9	112	0.9	203	0.90	0.68–1.18	0.91	0.69–1.20
28	Rubber	23	0.2	19	0.2	42	1.21	0.66–2.22	1.24	0.67–2.31
29	Social contact	1461	12.3	1371	11.5	1767	1.08	0.98–1.18	1.05	0.95–1.16
30	Solvents	355	3.0	342	2.9	559	1.03	0.87–1.22	1.05	0.88–1.24
31	Textile dust	125	1.1	132	1.1	230	0.92	0.71–1.19	0.94	0.73–1.22
32	Tobacco dust	2	0.0	4	0.0	6	0.50	0.09–2.73	0.52	0.10–2.85
33	Wood dust	332	2.8	294	2.5	553	1.12	0.95–1.32	1.14	0.96–1.35

Abbreviations: CIs = confidence intervals; CNS = central nervous system; EMF = Electromagnetic fields; OR = odds ratio.
[a]OR is presented as unadjusted for social class.
[b]OR is presented as adjusted for social class, ORs in bold are significant, $P<0.05$.

Table 4. Significant associations between paternal occupational exposures for CNS subtypes

Outcome	Exposure group	Exposed cases (%)	Exposed controls (%)	Informative pairs	OR[a]	OR[b]
Ependymoma	Solvents	44 (4.2)	27 (2.6)	60	**1.73** (1.02–2.92)	1.71 (0.99–2.93)
Astrocytoma	Paints	74 (1.6)	94 (2)	148	**0.72** (0.52–1.00)	0.72 (0.51–1.00)
	Social contact	616 (13)	544 (12)	698	**1.16** (1.00–1.35)	1.13 (0.97–1.33)
Embryonal CNS tumours	Metal	338 (14)	387 (16)	542	**0.82** (0.70–0.98)	**0.83** (0.69–0.98)
Astrocytomas and other gliomas	Social contact	790 (13)	701 (12)	912	**1.15** (1.01–1.31)	1.13 (0.98–1.29)

Abbreviations: CNS = central nervous system; OR = odds ratio.
[a]OR is presented as unadjusted for social class.
[b]OR is presented as adjusted for social class, ORs in bold are significant, $P<0.05$.

Table 5. Childhood CNS tumour risk by paternal occupationally derived social class

		Ependymoma		Astrocytoma		Embryonal		Astrocytoma and other glioma		CNS tumours	
Social class of father	Controls	Cases	OR (95% CI)[a]	Cases	OR (95% CI)[a]	Cases	OR (95% CI)[a]	Cases	OR (95% CI)[a]	Cases	OR (95% CI)
I	671	59	0.82 (0.44, 1.53)	296	1.10 (0.81,1.49)	162	1.12 (0.76, 1.65)	397	1.20 (0.92, 1.57)	760	1.13(0.94, 1.37)
II	2139	173	**0.64** (0.45, 0.91)	908	**1.20** (1.01, 1.43)	441	0.95 (0.75, 1.20)	1159	1.13 (0.97, 1.31)	2154	0.95 (0.86, 1.06)
III Non-manual	1268	115	0.92 (0.58, 1.46)	557	1.10 (0.89, 1.37)	259	0.88 0.65, 1.19)	709	1.14 (0.95, 1.37)	1315	1.04 (0.91, 1.19)
III Manual	3905	374	1.00	1533	1.00	850	1.00	2012	1.00	4024	1.00
IV	1947	177	1.09 (0.76, 1.58)	681	**0.81** (0.68, 0.97)	380	0.85 (0.67, 1.07)	896	**0.81** (0.70, 0.95)	1871	0.92 (0.83, 1.03)
V	772	65	1.00 (0.57, 1.76)	295	0.77 (0.58, 1.02)	143	0.93 (0.63, 1.36)	399	0.84 (0.66, 1.07)	730	**0.83** (0.70, 0.99)
Unknown	1172	94		408		193		536		1020	
Total	11874	1057		4678		2428		6108		11874	
Trend analysis[b]			1.05 (0.98, 1.13)		**0.95** (0.91, 0.98)		0.97 (0.93, 1.02		**0.96** (0.93, 0.99)		**0.97** (0.95, 0.99)

Abbreviations: CIs = confidence intervals; CNS = central nervous system; OR = odds ratio. The table includes 51 cases and 37 controls who had a social class code assigned, but who had no 1970 occupation code assigned and were excluded from the occupation analysis. ORs in bold are significant $P<0.05$; in bold and single underlined $P<0.01$.
[a]OR for the indicated ONS Social class(es) with III manual taken as the reference category.
[b]OR for each increase in OSC.

observed. For the other major CNS subgroup, ependymomas, a nonsignificant inverse relationship was observed.

Comparison with previous studies. Previous epidemiological studies have identified a number of possible paternal occupational risk factors for childhood CNS tumours. These include working in the aircraft industry; electronics, petroleum industry, paper mill worker, printer, metal-related occupations, paint, solvents, ionising radiation and electromagnetic fields (Gurney *et al*, 1999). Subsequent epidemiological research has failed to replicate most of these consistently excepting paternal exposure to paints, and to hydrocarbons or exhaust fumes, which have shown consistently raised risks (Colt and Blair, 1998; Cordier, 2008) as, to a lesser extent, have pesticides (Infante-Rivard and Weichenthal, 2007).

Our findings for all CNS tumours are not in keeping with these results; our ORs for paints, solvents, hydrocarbons and exhaust fumes were all around 1. We did, however, see a raised risk for fathers who work with animals. It is possible that this work is agricultural and was thereby associated with exposure to pesticides, which would align this result with those that have shown an association between paternal exposure to pesticides and risk of childhood CNS tumours (Cordier *et al*, 2001; Infante-Rivard and Weichenthal, 2007). However, we observed no association with exposure to agriculture or agrichemicals, which may argue against an involvement of pesticide exposure. For exposure to EMFs, our ORs were also around 1, in keeping with a recent case-control study of paternal occupational exposure and childhood cancer (Hug *et al*, 2010).

Although we see an apparently protective effect of exposure to paints on risk of astrocytomas, our results for risk of ependymoma from paternal occupational exposure are in accordance with studies that have showed an association between exposure to solvents and risk of CNS tumours (Colt and Blair, 1998). However, loss of significance of results upon adjustment for OSC suggests that social class may be responsible for these associations. The risk for social contact and astrocytomas or astrocytomas and other gliomas was raised, but nonsignificant after adjustment for OSC. This relationship is consistent with results from another UK-based study, which saw no relationship between paternal social contact and CNS tumours in children (Fear *et al*, 2005).

Socioeconomic status. When we examined the risk of CNS tumours in children by the OSC of the father, we found that for all CNS tumours, astrocytomas alone and astrocytomas and other gliomas taken together, there was an increased risk in the higher social classes, with the relationship driven by astrocytomas. In contrast, risk of ependymoma was greater in social class IV and least in social class II, but the trend was not significant.

The relationship between risk of astrocytomas and paternal social class is consistent with evidence from studies of paternal SES and other types of childhood cancer for example, childhood leukaemia (Borugian *et al*, 2005; Poole *et al*, 2006; Kroll *et al*, 2011b). There is also some evidence that higher social class maybe associated with increased risk of brain cancer in adults (Preston-Martin *et al*, 1993). However, there is little direct evidence in the literature to suggest that an increased risk of childhood CNS tumours with higher social class of the father is likely. There are some limited indications that exposure of the mother and to the child to common viral infections may result in a higher risk of childhood brain tumours (Fear *et al*, 2001; McNally *et al*, 2002b; McKinney, 2005); if these exposures themselves are associated with paternal social class, the link might be plausible. Either way, the association would benefit from further investigation.

Strengths and limitations. The strengths of this study are that the analysis is based on the case data drawn from the NRCT, which has, over the period studied here, consistently high levels of case ascertainment (Kroll *et al*, 2011a), and thus can be considered almost complete. Of the previous epidemiological studies that have investigated paternal occupational exposure and CNS cancer risk in children, few have been able to examine risks by CNS subtypes (McKinney, 2005). We have data spanning 40 years and over 10 000 cases of CNS tumours, with nearly 1 000 cases of the smallest subtype considered separately.

Frequent problems with interview-based case-control studies are recall and participation bias. This is not a consideration in the present study as we used routinely collected data, and occupation

was documented before diagnosis. The exposure assessment used a well-established occupational and exposure classification (Fear *et al*, 1999a) to which father's occupation was coded blind to case-control status. However, our method used occupation recorded at time of birth, and this might differ from the occupation held during a more aetiologically important time period. We also recognise that the use of occupational title to capture occupational exposure is controversial (Schuz *et al*, 2003). However, using this method does allow comparison with a number of previous studies in this field that have used this method of classifying occupational exposures (McKinney *et al*, 2003; Fear *et al*, 2005).

In our study, we have examined exposures from paternal occupations only. Although maternal exposures of potential carcinogens to their children may have an important role in the development of childhood cancer, fathers' occupations are more completely recorded on birth registrations than they are for mothers. In our study, father's occupation was available for 94% of registrations and for mothers it was 23%. This may result in some misclassification with respect to unmeasured exposure to carcinogens via the mothers' work, but we expect that in the analysis of social class and brain tumour risk, fathers' OSC classification is as appropriate an exposure measure as would be one based on mothers' OSC.

Interpretation. In our analysis we carried out multiple comparisons, which may have resulted in a number of associations having arisen by chance. Our analysis of the likelihood of these arising by chance showed that the significant *P* values, both raised and lowered, are unlikely to be real. Consequently, our results should be interpreted with caution. In addition, other, unmeasured risk factors may also explain any apparent association between OSC and childhood CNS tumours.

The aetiology of childhood cancers, including CNS tumours, is not well understood, and there is continuing debate about the role of occupational and environmental exposures (Belson *et al*, 2007). The importance of the exposure route and timing is also relevant (McKinney *et al*, 1991; Roman *et al*, 2005). Exposures to the mother may be relevant during the intrauterine period and to the father pre-conceptually, when germ cells may be affected and, for both parents, postnatally when residues from work may be brought into the home. As we have no information on the frequency or duration of exposure and occupational practices, and exposures may have changed during the long study period, we cannot exclude the possibility of exposure misclassification. It is also possible that during our long study period some cases of childhood cancer were not diagnosed or registered. If those cases were more likely to be from the lower social classes, there could be fewer cases of CNS cancers in the lower-social class groups relative to the higher-class groups, and this might possibly explain the social class effect we detected, although this is an unlikely explanation, given the size of our data sets.

In this study we have analysed risk of CNS tumours by paternal occupational exposure for each major diagnostic subgroup. This is important as each may have a different aetiology (Ross *et al*, 1994; McKinney *et al*, 2003). However, once paternal social class was accounted for we did not see any notable relationships between paternal occupation and increased risk of CNS tumours. The finding that astrocytomas are apparently most common in social class II and least common in social class V, however, may warrant further investigation. The relationship between paternal social class and risk of leukaemia is thought to reflect the likelihood of encountering common infections. Whether this hypothesis may also apply to the relationship with astrocytomas is unclear. Our results for risk of astrocytoma, and astrocytoma and other gliomas with exposure to 'social contact' showed a (nonsignificant) excess. Although there are well-developed arguments for a role of infection contact in the aetiology of childhood leukaemia (Kinlen *et al*, 2002; McNally and Eden, 2004), the role of infection in the aetiology of childhood CNS tumours is uncertain. There is limited evidence that maternal viral infection during pregnancy might be a risk for tumours of the brain or nervous system (Fear *et al*, 2001). Analysis of space-time clustering has indicated that unspecified infection in the child (or mother) might be relevant (McNally *et al*, 2002a). It is possible that high paternal occupational social contact leads to more frequent exposure to viruses to pregnant women and children at home.

In conclusion, this paper does not add to evidence for paternal occupation as a risk factor for childhood CNS tumours, either overall or for specific subtypes, although it suggests that OSC of the father may be associated with risk of childhood CNS cancers, in particular astrocytomas and other gliomas.

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