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REVIEW ARTICLE

The connection between six common air pollution particles and adult brain tumors: a meta-analysis of 26,217,930 individuals

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Abstract

Environmental air pollutants (black carbon (BC), nitrogen oxides (NO_x), particulate matter with diameter < 2.5 μm ($PM_{2.5}$), nitrogen dioxide (NO_2), particulate matter with diameter <10 μm (PM_{10}), and ozone (O_3)) are one of the major menaces to mankind's health globally. This analysis reviews the association between exposure to these air pollutants and the chance of developing brain tumors in adults (total brain tumors, malignant brain tumors, and benign brain tumors). Studies published by April 2022 were searched. Raw effect sizes were converted to standardized effect sizes per 10 μg/m^3 increase. Random effect models were applied to calculate combined effect size and 95% confidence intervals (CIs) were computed. A total of 8 articles were included for meta-analysis. The pooled effect size (ES) for per 10 μg/m^3 BC intake was 1.67 (95% CI: 1.25, 2.22), $P = 0.449$. For every 10 μg/m^3 rise in NO_2 concentration, ES was 1.03 (95% CI: 1.01, 1.05), $P = 0.319$. Meanwhile, there was a boundary association between NO_x and adult brain tumors (ES and 95% CI: 1.01; 1.00, 1.01/10 μg/m^3; $P = 0.716$). While there was no conjunction between $PM_{2.5}$, PM_{10}, O_3 ($PM_{2.5}$: ES and 95% CI: 1.04; 0.99, 1.08/10 μg/m^3; $P = 0.834$; PM_{10}: ES and 95% CI: 1.01; 0.97, 1.04/10 μg/m^3; $P = 0.627$; O_3: ES and 95% CI: 0.97; 0.94, 1.00/10 μg/m^3; $P = 0.253$). This research shows testimony of a significant link between air pollutants and brain tumors in adults, especially when exposed to BC, NO_2, and NO_x. This evidence emphasizes the importance of improving air quality as part of a comprehensive approach to prevent the occurrence and deterioration of brain tumors.

Keywords Adult brain tumors · Air pollution · Benign brain tumors · Malignant brain tumors · Environmental hazards · Epidemiology

Introduction

Brain tumors are one of the universal diseases in the nervous system and are very harmful to the function of the human nervous system. With the rapid growth and aging of the population, as well as changes in environmental and lifestyle factors, the survival rate of middle-aged and elderly patients has significantly decreased, especially the survival rate of patients aged 45 and above has significantly deteriorated. The incidence rate and mortality of brain tumors in middle-aged and elderly people continue to rise globally (Miller et al. 2021). In 2016, there were 330,000 new cases of brain cancers and 227,000 deaths worldwide (Patel et al. 2019). Therefore, in order to promote the development of public health, it is greatly important to determine the modifiable hazard factors for brain tumors in adults. The established risk factors of

Highlights
1. A meta-analysis was conducted to evaluate the association between air pollutants and brain tumors in adults.
2. Ambient air pollution is one of the global challenges. This study covers many air pollutants (BC, $PM_{2.5}$, PM_{10}, NO_2, NO_x, O_3).
3.This study provides a basis for formulating policies to reduce air pollution and provides directions for follow-up research.

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brain tumor in adults are radiation and head genetic risk, but dietary factors, industrial exposure, HIV infection, smoking, and environmental air pollution have been identified as potential hazard factors (McNeill 2016; Ostrom et al. 2019; Ostrom et al. 2014).

Exposure to air contamination is the fourth largest reason of attributable death worldwide in 2019 and one of the challenging issues in the global environmental health sector (Brauer et al. 2016). At present, people have recognized the potential chronic harm of air pollution to mankind's health. Many studies clearly show that there is a strongly correlated material correlation between chronical exposure to air contamination and the increase of incidence rate and mortality, (like gastrointestinal neoplasms (Pritchett et al. 2022), neurodegenerative diseases (Khreis et al. 2022), clinical dementia (Wilker et al. 2023), chronic kidney disease (Ye et al. 2021)). Meanwhile, more and more documents have debated the influence of environmental air pollution exposure on the brain tumors (Chang et al. 2022; Poulsen et al. 2020a). There have been literature studies on environmental pollution elements and the hazard of brain tumors in youngster (Zumel-Marne et al. 2019). However, there is no clear epidemiological evidence regarding long-term exposure to air pollutants (such as black carbon (BC), nitrogen dioxide (NO_2), nitrogen oxides (NO_x), particulate matter with diameter < 2.5 μm ($PM_{2.5}$), particulate matter with diameter <10 μm (PM_{10}), and ozone (O_3) and brain tumors in the adults).

Thus, it is necessary to quantitatively integrate existing epidemiological evidence through a meta-analysis system to assess the influence of exposure to atmospheric pollutants on the risk of brain tumors in adults.

Methods

Literature retrieve strategy

The PubMed, Embase, and Web of Science databases were retrieved for essays on the correlation between air contamination and adult brain tumors including total brain tumors, malignant brain tumors, and benign brain tumors up to April 2022. The final search strategy is described in the supplementary material. EndNote X9 (Clarivate Analytics) was used to collect, manage, and identify duplicate references. Screening was performed independently by two evaluators, and after duplication was removed, titles and abstracts were screened and possible related articles were retrieved as full texts. Any discrepancies are resolved by discussion.

Inclusion and exclusion standard

Documents that met the following standard were brought into the following:(1) to evaluate the effects of prolonged (≥3 years) exposure to atmospheres pollutants (BC, NO_x, NO_2, $PM_{2.5}$, PM_{10}, O_3) on the occurrence of brain tumors; (2) epidemiological studies contain cohort, case-crossover, or case-control studies; (3) for duplicate publications, we included only studies that reported the most recent and detailed information; and (4) the research subjects are all 40 years old or older.

Articles that met the following standard were removed as follows: (1) reviews, letters, comment letters to the editor, case reports, animal studies; (2) assess the influence of exposure and air pollution on the brain tumor mortality; and (3) risk estimates (hazard ratio (HR), relative risk ratio (RR), or odds ratio (OR)) and 95% CI for quantitative increments of pollutant exposure (ppb, ppm, $\mu g/m^3$) were not reported in the original papers.

Brain tumor definition

According to the International Classification of Diseases, Tenth revision (ICD10): C70.0, C71.0–C71.9, C72.2–C72.5, D32.0, D33.0–D33.3, D33.3, D42.0, D43.0–D43.2, D43.3. Our purpose is to consider the following two outcomes: the total of brain tumors; malignant subtypes of brain tumors: malignant (C70.0, C71.0–C71.9, C72.2–C72.5) and benign (D32.0, D33.0-D33.2, D33.3, D42.0, D43.0-D43.2, D43.3)

Data collection

The following records were collected from the articles that met the inclusion standard: first author, year of publication, year of study, study area, study type, demographic characteristics, air pollutants, and their distribution. All relevant estimates, including fully adjusted ORs, HRs, and 95% CIs for ambient air exposure (for any adults) associated with the risk of brain tumors, were extracted. All effect sizes were on account of a single pollutant model to assess the risk of brain tumors caused by different air pollutants. Records were collected separately by two investigators, and divergences were resolved by discussion.

Quality score evaluation

We utilized Newcastle-Ottawa Quality Assessment Scale (NOS) (Hu et al. 2020) to evaluate the quality of cohort and case-control studies. The NOS evaluates observational studies based on three parameters: option of study groups,

ascertainment of exposure, and outcome. The NOS score for each study ranged from 0 to 9. A score of 7 was sorted out as good quality.

Meta-analysis and statistical analysis

Due to the low occurrence of brain tumors in the population, we believe that the OR and RR reported in the original paper can roughly represent the HR (Hu et al. 2019), which we will refer to as the effect estimate (ES). For consistency, the effect size estimates for $PM_{2.5}$, PM_{10}, NO_x, NO_2, CO, and BC were transformed to increments per 10 μg/m^3. Studies that reported air-pollution concentrations in parts per billion (ppb) or parts per million (ppm) were first converted to per μg/m^3 on the basis of the following equation: 1 ppb NO_2 = 1.88 μg/m^3; 1 ppb NO_x = 1.9125 μg/m^3; 1 ppb O_3 = 1.96 μg/m^3; 1 ppb CO = 1.145 μg/m^3; 1 ppm = 1000 ppb (Fan et al. 2020). Discontinuous estimates of associations were not standardized and are shown in their original format. We converted original reported risk effect size to standardized ES by using the formula (Shah et al. 2013):

$$\text{Effect estimate}_{\text{Standardized}} = e^{\frac{\ln\left(\text{Effect estimate}_{\text{Original}}\right)}{\text{Increment}_{\text{Original}}} \times \text{Increment}_{\text{Standardized}}}$$

We conducted a random effects (RE) meta-analysis applying the Der-Simonian-Laird (DerSimonian and Laird 1986) method to explore the relation between environmental air pollution and the brain tumors. All data analyses were conducted using the Stata 11.2. We utilized a random effects model to merge the standardized effect estimates for every 10 μg/m^3 increase in each pollutant into a summary effect estimate. Cochran's Q test and I^2 index were applied to analyze the heterogeneity of risk estimates. In Cochran's Q test, if $P < 0.05$ or $I^2 > 50\%$, then significant heterogeneity was considered in the combined analysis. We visually examined funnel plots and evaluated possible publication bias using Egger's weighted linear regression (Egger et al. 1997). In addition, to explore possible heterogeneity among study results, we performed meta-regressions using candidate factors (age and mean pollutant concentration).

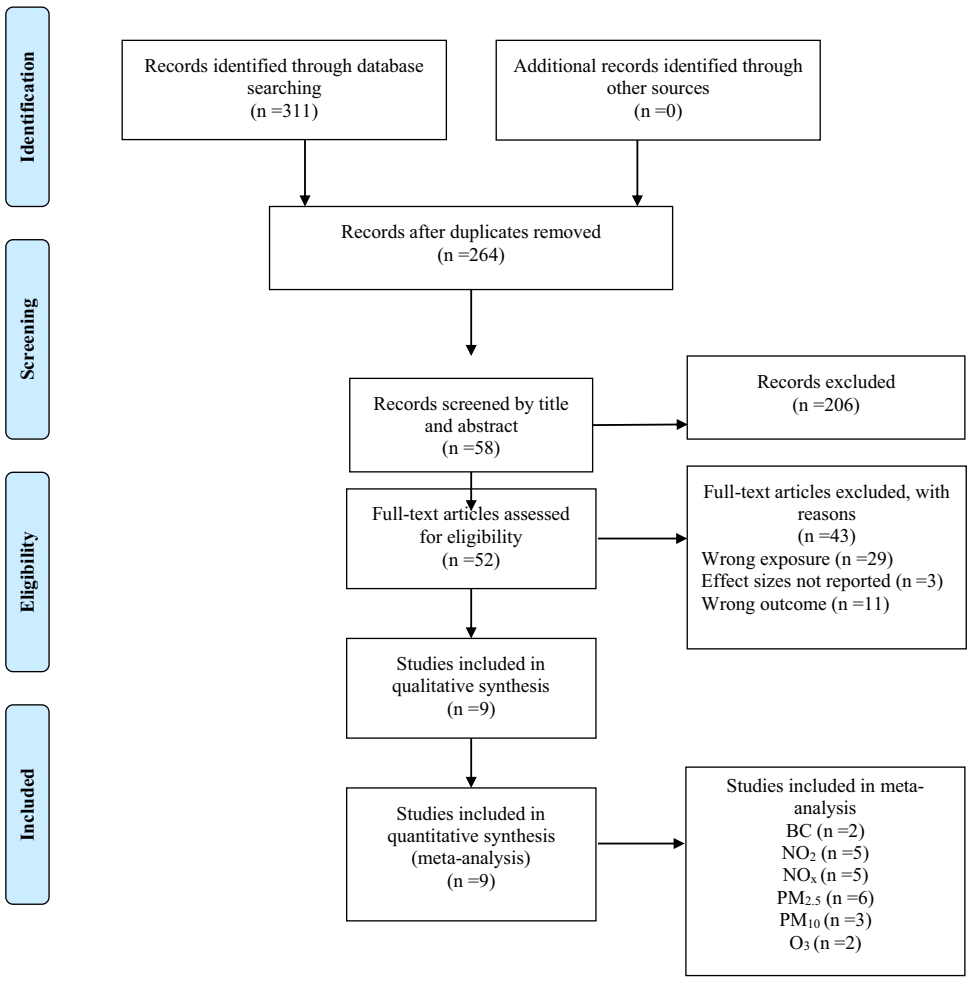


Fig. 1 Flow chart of PRISMA for the systematic review of the correlation between air pollution exposure and the hazard of brain tumors

Results

Literature characteristics and quality assessment

In document retrieval, a preliminary search of 311 relevant articles was conducted, and after strict screening, 8 studies (Brauner et al. 2013; Chang et al. 2022; Jorgensen et al. 2016; Poulsen et al. 2020a; Poulsen et al. 2020b; Poulsen et al. 2016; Raaschou-Nielsen et al. 2011; Weichenthal et al. 2020; Wu et al. 2020) were ultimately included (Fig. 1). This study ultimately identified 26,217,930 patients with an average age of over 40 years diagnosed with brain tumors, including 161,213 from Taiwan, 25,707,900 from Canada, 103,098 from Latin America, and 245,719 from Denmark (Table 1). All research data contained in this meta-analysis are quantitative data, and the standard effect magnitude data after summary analysis and conversion are shown in Table 2.

By the NOS scale, two studies were elected as very high quality (case-control study—8 stars), and three studies were elected as high quality (cohort or case-control study—7 stars). The Newcastle-Ottawa scores for all the articles in the meta-analyses are shown in Table 1.

Relationship between air pollutants and adult brain tumors

BC

Meta-analysis shows that BC are significantly related to the occurrence of total brain tumors and malignant tumors. The pooled effect size (95% CI) of total brain tumors per 10 μg/m^3 exposure was 1.66 (1.11, 2.48); $P = 0.549$, and the ES (95% CI) of malignant tumors per 10 μg/m^3 exposure was 2.42 (1.42, 2.10); $P = 0.927$ (Fig. 2). The study also discovered a statistically meaningless positive correlation between benign brain tumors and BC (ES and 95% CI: 1.01; 0.55, 1.88/10 μg/m^3; $P = 0.934$) (Fig. 2). There was no proof of heterogeneity in this study. There was no significant publication bias in the funnel plot (Fig. 3). Egger's test showed no evidence of publication bias ($t = 0.21$; $P = 0.846$). Meanwhile, in the sensitivity analysis of BC with brain tumors, the combined estimates did not change (Fig. 4).

NO_2

Although the upper limit of the 95% CI was 1.00, there was a marginal correlation between NO_2 and total brain tumors. NO_2 per 10 μg/m^3 increases in exposure (total brain tumors: ES = 1.03; 95% CI = (1.00–1.06); $P = 0.472$; benign brain tumors: ES = 1.05; 95% CI = (1.00, 1.10); $P = 0.153$) (Fig. 2). Mean-while, NO_2 had no significant effect on the development of malignant tumors (1.01 (0.97, 1.05); $P = 0.320$) (Fig. 2). This discovery has not been proven to be heterogeneous, and the funnel plot does not show asymmetry (Fig. 3). Egger's test presents no testimony of publication bias ($t = 0.37$; $P = 0.724$). Meanwhile, the sensitivity analysis of NO_2 with brain tumors indicates the robustness of the outcomes (Fig. 4). In the meta-regression analysis, the age of the participants and the mean NO_2 concentration did not remarkably affect the correlation between NO_2 and brain tumor incidence (Figure S4).

NO_x

Based on 4 studies (Jorgensen et al. 2016; Poulsen et al. 2020b; Poulsen et al. 2016; Raaschou-Nielsen et al. 2011; Wu et al. 2020), the pooled effect of each 10 μg/m^3 increase in NO_x on the incidence of total brain tumors and malignant tumors was 1.01 (95% CI: 1.00–1.03; $P = 0.271$) and 1.01 (95% CI: 1.00–1.02; $P = 0.798$), respectively. An analysis of three studies of the correlation between NO_x and benign brain tumor risk was performed, and a pooled effect of 1.00 (95% CI: 0.99 to 1.01; $P = 0.694$) was observed (Fig. 2). This discovery has not been proven to be heterogeneous. However, the funnel plot was a little unsymmetric (Figure S2). Egger's test presents no proof of publication bias ($t = 1.04$; $P = 0.324$). The meta-regression analysis of NO_x and brain tumor incidence showed that none of the covariates investigated was the main sources of heterogeneity (Figure S5). Sensitivity analyses excluding each study did not change the overall estimates (Figure S3).

$PM_{2.5}$ and PM_{10}

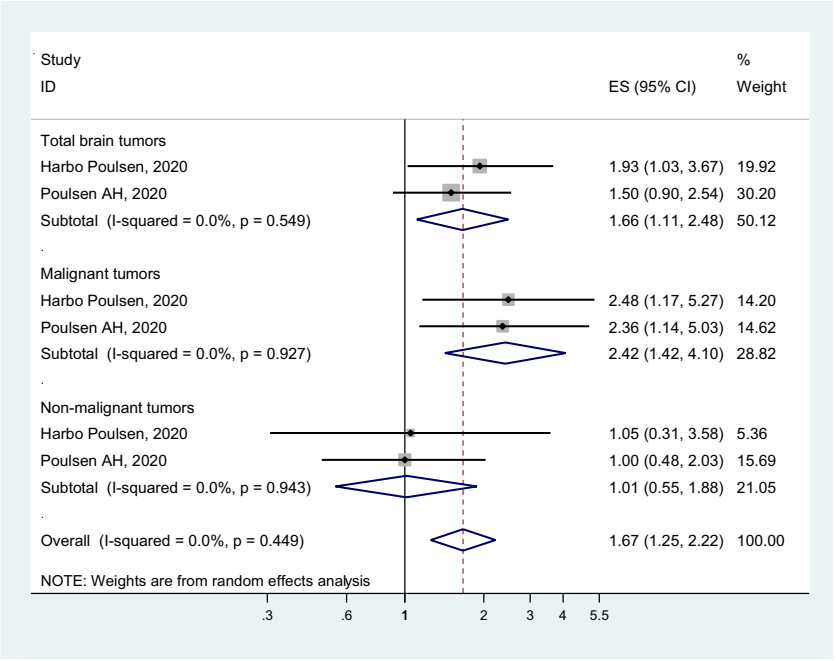
From our analysis, $PM_{2.5}$ and PM_{10} were found to be not statistically significant with brain tumor development. The pooled effect size (95% CI) of total brain tumors per 10 μg/m^3 exposure in $PM_{2.5}$ was 1.00 (0.91, 1.10), $P = 0.827$, and per 10 μg/m^3 exposure in PM_{10} was 0.80 (0.34, 1.88). No prominent correlation was detected between $PM_{2.5}$ and PM_{10} exposure and malignant brain tumors ($PM_{2.5}$: ES per 10 μg/m^3 increase = 1.03, 95% CI = (0.91, 1.17), $P = 0.789$; PM_{10}: ES per 10 μg/m^3 increase = 0.95, 95% CI = (0.37, 2.42), $P = 0.193$) (Figure S1). There was also no prominent correlation between $PM_{2.5}$ and PM_{10} exposure and benign brain tumors ($PM_{2.5}$: ES per 10 μg/m^3 increase = 1.02, 95% CI = (0.93, 1.13), $P = 0.280$; PM_{10}: ES per 10 μg/m^3 increase = 1.01, 95% CI = 0.97, 1.04,

Table 1 Features of the primary documents about the correlation between air contaminants and brain tumors

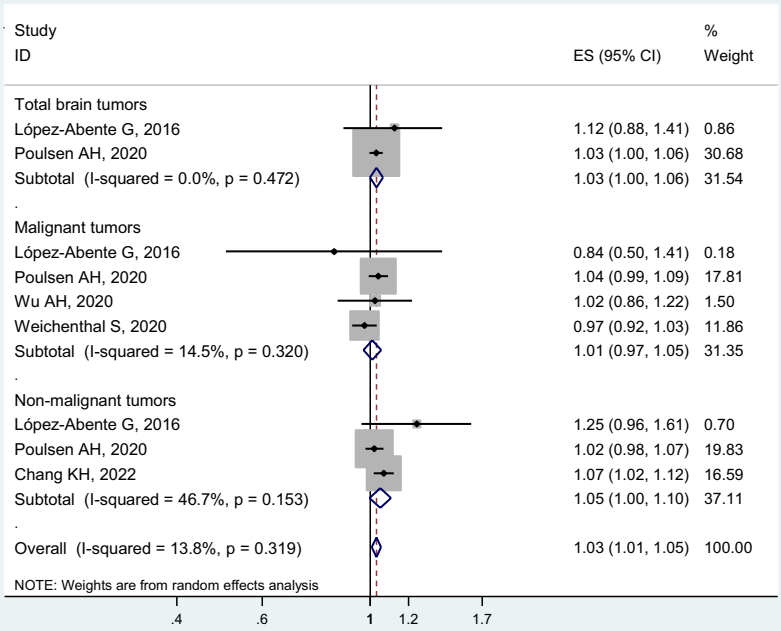
First author, year	Country	Study design	Study period	Study population	Age (year)	Gender (F/M)	Exposure types	Air pollutant and distribution	NOS
Chang et al. 2022	Taiwan, China	Cohort study	1996–2011	161,213	40.4	90,300 /70,913	NO_2 PM_{10} $PM_{2.5}$	Median (IQR) NO_2 (ppm): 23.7 (28.2, 27.5) PM10 (μg/m^3): 55.9 (51.6, 68.6) $PM_{2.5}$ (μg/m^3): 33.3 (29.5, 41.2)	7
Weichenthal et al. 2020	Canada	Cohort study	1991–2006	25,707,900	57	11,889,100/13,818,800	NO_2 $PM_{2.5}$	Mean (SD) NO_2 (ppb): 20.2 (8.43) $PM_{2.5}$ (μg/m3): 8.68 (2.42)	7
Wu et al. 2020	Latino	Case-control study	1993–2013	103,098	64.5	43,880 /59,218	NO_x NO_2 $PM_{2.5}$ O_3 PM_{10}	IQR NO_x (ppb): 41.7 NO_2 (ppb): 18.2 $PM_{2.5}$ (μg/m3): 3.8 O_3 (ppb): 9.3 PM_{10} (μg/m^3): 9	6
Poulsen et al. 2020	Denmark	Case-control study	1989–2014	35,889	62.5	16,613 /19,276	$PM_{2.5}$ BC	IQR $PM_{2.5}$ (μg/m^3): 5.39 BC (μg/m^3): 0.38	8
Poulsen et al. 2020	Denmark	Case-control study	1989–2014	58,425	62.5	NR	$PM_{2.5}$ NO_x NO_2 O_3 BC	IQR $PM_{2.5}$ (μg/m^3): 5.39 NO_x (μg/m^3): 18.86 NO_2 (μg/m^3): 10.78 O_3 (μg/m^3): 9.72 BC (μg/m^3): 0.39	7
Jorgensen et al. 2016	Denmark	Case-control study	1993–2013	25,143	54	NR	NO_2 NO_x $PM_{2.5}$ PM_{10}	Mean (SD) NO_2 (μg/m3): 12.6 (8.1) NO_x (μg/m3): 19 (24.3) $PM_{2.5}$ (μg/m3): 19.7 (3.5) PM_{10} (μg/m3): 23.6 (3.9)	7
Poulsen et al. 2016	Denmark	Case-control study	2000–2009	12,156	51.5	5039 /6892	NO_x	Mean/median NO_x (μg/m^3): 22/17	8
Raaschou-Nielsen et al. 2011	Denmark	Cohort study	1993–2006	57,053	56.7	25,869 /28,435	NO_x	Mean/median (5th–95th percentile) NO_x (μg/m^3) 4.7/2.6 (0.28–15.5)	7

Table 2 Data synthesized for meta-analysis

Exposure types	First author, year	Measure of association	Types of brain tumors	Reported outcome estimate (95% CI)	Standardized estimate (95% CI)
BC	Poulsen et al. 2020	OR per 0.39 μg/m^3	Total brain tumors	1.03 (1.00–1.05)	1.93 (1.03–3.67)
		OR per 0.39 μg/m^3	Malignant tumors	1.04 (1.01–1.07)	2.48 (1.17–5.27)
		OR per 0.39 μg/m^3	Non-malignant tumors	1.00 (0.96–1.05)	1.05 (0.31–3.58)
	Poulsen et al. 2020	OR per 0.39 μg/m^3	Total brain tumors	1.02 (1.00–1.04)	1.50 (0.90–2.54)
		OR per 0.39 μg/m^3	Malignant tumors	1.03 (1.01–1.07)	2.36 (1.14–5.03)
		OR per 0.39 μg/m^3	Non-malignant tumors	1.00 (0.97–1.03)	1.00 (0.48–2.03)
NO_2	Jorgensen et al. 2016	HR per 7.47 μg/m^3	Total brain tumors	1.09 (0.91–1.29)	1.12 (0.88–1.41)
		HR per 7.47 μg/m^3	Malignant tumors	0.88 (0.60–1.29)	0.84 (0.50–1.41)
		HR per 7.47 μg/m^3	Non-malignant tumors	1.18 (0.97–1.43)	1.25 (0.96–1.61)
	Poulsen et al. 2020	OR per 10.78 μg/m^3	Total brain tumors	1.03 (1.00–1.07)	1.03 (1.00–1.06)
		OR per 10.78 μg/m^3	Malignant tumors	1.04 (0.99–1.10)	1.04 (0.99–1.09)
		OR per 10.78 μg/m^3	Non-malignant tumors	1.02 (0.98–1.07)	1.02 (0.98–1.06)
	Wu et al. 2020	HR per 20 ppb	Malignant tumors	1.09 (0.56–2.11)	1.02 (0.86–1.2)
	Chang et al. 2022	HR per 27.48 ppm	Non-malignant tumors	1.40 (1.09–1.79)	1.07 (1.02–1.12)
	Weichenthal et al. 2020	HR per 10 ppb	Malignant tumors	0.95 (0.85, 1.06)	0.97 (0.92–1.03)
NO_x	Raaschou-Nielsen et al. 2011	IRR per 100 μg/m^3	Total brain tumors	1.89 (1.07–3.36)	1.07 (1.01–1.13)
	Poulsen et al. 2016	OR per 100 μg/m^3	Total brain tumors	1.11 (0.84–1.46)	1.01 (0.98–1.04)
		OR per 100 μg/m^3	Malignant tumors	1.10 (0.81–1.50)	1.01 (0.98–1.04)
		OR per 100 μg/m^3	Non-malignant tumors	1.15 (0.62–2.10)	1.01 (0.95–1.08)
		OR per 100 μg/m^3	Glioma	0.84 (0.58–1.23)	0.98 (0.95–1.02)
	Jorgensen et al. 2016	HR per 10.22 μg/m^3	Total brain tumors	1.02 (0.93–1.12)	1.02 (0.93–1.12)
		HR per 10.22 μg/m^3	Malignant tumors	0.98 (0.82–1.18)	0.98 (0.82–1.18)
		HR per 10.22 μg/m^3	Non-malignant tumors	1.04 (0.93–1.15)	1.04 (0.93–1.15)
	Poulsen et al. 2020	OR per 18.86 μg/m^3	Total brain tumors	1.011 (0.99–1.03)	1.01 (1.00–1.02)
		OR per 18.86 μg/m^3	Malignant tumors	1.03 (1.00–1.06)	1.01 (1.00–1.03)
		OR per 18.86 μg/m^3	Non-malignant tumors	1.00 (0.97–1.03)	1.00 (0.98–1.01)
		OR per 18.86 μg/m^3	Glioma	1.02 (0.98–1.05)	1.01 (0.99–1.03)
	Wu et al. 2020	HR per 50 ppb	Malignant tumors	0.87 (0.51–1.51)	0.99 (0.93–1.04)
$PM_{2.5}$	Jorgensen et al. 2016	HR per 10 μg/m^3	Total brain tumors	1.18 (0.51–2.73)	1.19 (0.52–2.71)
		HR per 10 μg/m^3	Malignant tumors	0.95 (0.22–4.20)	0.94 (0.22–4.19)
		HR per 10 μg/m^3	Non-malignant tumors	1.31 (0.47–3.62)	1.29 (0.41–2.83)
	Poulsen et al. 2020	OR per 5.39 μg/m^3	Total brain tumors	1.01 (0.94–1.08)	1.02 (0.90–1.15)
		OR per 5.39 μg/m^3	Malignant tumors	1.02 (0.93–1.13)	1.04 (0.87–1.25)
		OR per 5.39 μg/m^3	Non-malignant tumors	1.00 (0.91–1.10)	1.00 (0.84–1.19)
		OR per 5.39 μg/m^3	Glioma	0.94 (0.84–1.05)	0.89 (0.72–1.10)
	Chang et al. 2022	HR per 41.22 μg/m^3	Non-malignant tumors	1.29 (1.02–1.65)	1.06 (1.00–1.13)
	Poulsen et al. 2020	OR per 5.39 μg/m^3	Total brain tumors	0.99 (0.91–1.07)	0.97 (0.83–1.14)
		OR per 5.39 μg/m^3	Malignant tumors	1.03 (0.93–1.13)	1.05 (0.88–1.26)
		OR per 5.39 μg/m^3	Non-malignant tumors	0.89 (0.75–1.04)	0.80 (0.58–1.08)
		OR per 5.39 μg/m^3	Glioma	1.27 (1.05–1.52)	1.55 (1.10–2.18)
	Wu et al. 2020	HR per 10 μg/m^3	Malignant tumors	1.27 (0.49–3.30)	1.27 (0.49–3.30)
	Weichenthal et al. 2020	HR per 3 μg/m^3	Malignant tumors	0.91 (0.76, 1.08)	0.72 (0.40–1.29)
PM_{10}	Jorgensen et al. 2016	HR per 10 μg/m^3	Total brain tumors	0.81 (0.35–1.89)	0.80 (0.34–1.87)
		HR per 10 μg/m^3	Malignant tumors	0.40 (0.08–2.11)	0.40 (0.08–2.11)
		HR per 10 μg/m^3	Non-malignant tumors	1.09 (0.41–2.90)	1.09 (0.40–2.88)
	Wu et al. 2020	HR per 10 μg/m^3	Malignant tumors	1.24 (0.84–1.82)	1.24 (0.84–1.82)
	Chang et al. 2022	HR per 68.57 μg/m^3	Non-malignant tumors	1.04 (0.82, 1.33)	1.01 (0.97–1.04)
O_3	Wu et al. 2020	HR per 10 ppb	Malignant tumors	1.54 (1.00–2.51)	1.25 (0.97–1.60)
	Poulsen et al. 2020	OR per 9.72 μg/m^3	Total brain tumors	0.97 (0.93–1.00)	0.97 (0.93–1.00)
		OR per 9.72 μg/m^3	Malignant tumors	0.96 (0.91–1.01)	0.96 (0.91–1.01)
		OR per 9.72 μg/m^3	Non-malignant tumors	0.97 (0.93–1.02)	0.97 (0.92–1.02)
		OR per 9.72 μg/m^3	Glioma	0.97 (0.92–1.03)	0.97 (0.91–1.03)



(A)

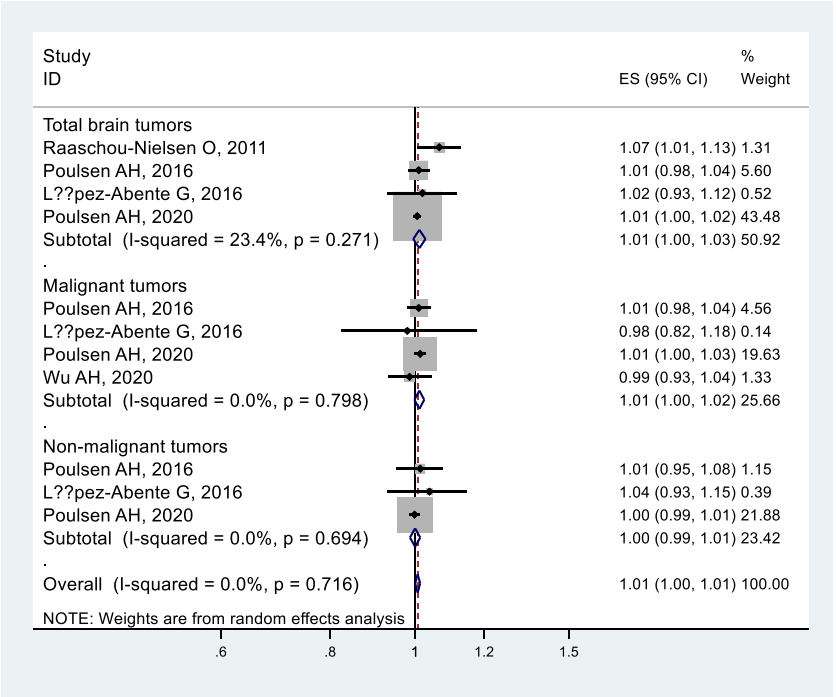


(B)

Fig. 2 Forest plot of the correlation between each type of air pollutant exposure and hazard of brain tumors. **A** BC; **B** NO_2; **C** NO_x

$P = 0.869$) (Figure S1). Meanwhile, there was no proof of heterogeneity according to this research outcomes. The funnel plot was symmetric (Figure S2). Analysis of the sensitivity of $PM_{2.5}$ and the combined estimates did not change significantly (Figure S3). In the meta-regression analysis, the age of the participants and the average $PM_{2.5}$ concentration did not noteworthily affect the correlation between $PM_{2.5}$ and brain tumors (Fig. 5).

Fig. 2 (continued)



(C)

O_3

The number of researches on O_3 was too few for explanation. but no noteworthy relation was indicated between O_3 and total brain tumors, malignant brain tumors, and benign brain tumor incidence by meta-analysis (malignant tumors: ES per 10 μg/m^3 increase = 1.06, 95% CI = (0.83, 1.36); total brain tumors ES per 10 μg/m^3 increase = 0.97, 95% CI = (0.93, 1.00); benign brain tumors: ES per 10 μg/m^3 increase = 0.97, 95% CI = (0.94, 1.00) (Figure S1)). The funnel plot visualized no asymmetry (Figure S2). Egger's test indicated no proof of publication bias ($t = 3.5$; $P = 0.073$).

Discussion

Main outcomes

Environmental air pollution is becoming increasingly grave, and the adverse effects on brain tumors are receiving increasing attention. This meta-analysis explores the correlation between prolonged exposure to environmental air pollution and middle-aged and elderly brain tumors. But the correlation between the two is not always statistically significant. The conclusion of this study is that prolonged exposure to BC and NO_2 significantly increases the hazard of brain tumors, while prolonged exposure to NO_x is slightly connected with the risk of developing brain tumors. However, prolonged exposure to PM_{10}, $PM_{2.5}$, and O_3 is not statistically correlated with the brain tumor development. According to the sensitivity analysis results of this study, the merger effect is robust.

The published studies have analyzed studies on lead exposure, radon exposure, petrochemical air pollution and agricultural exposure, and the incidence rate of brain tumor (Liu et al. 2008; Palmer et al. 2023; Van Maele-Fabry et al. 2017; Wu et al. 2012). All these published literatures have recorded that long-term exposure has a weak positive relationship with brain tumors. At the same time, a meta-analysis also investigated the hazard of brain tumors in nurses exposed to air pollution exposure (Jorgensen et al. 2016), and the results were consistent with this meta-analysis.

Potential biological mechanisms

Currently, Although the exact relationship between air pollution and brain tumors is not yet clear, it can lead to the disruption of the blood–brain barrier, mediated

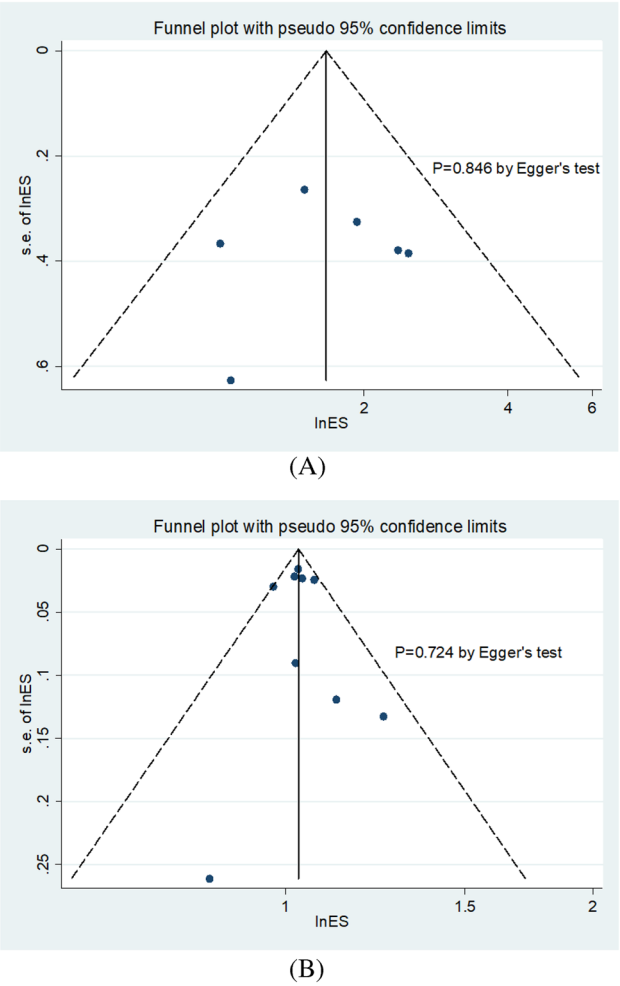


Fig. 3 Funnel chart preforming publication biases of studies on each type of air contaminant. **A** BC; **B** NO_2

by oxidative stress and neuroinflammation pathways, leading to changes in the brain and the occurrence of tumors (Genc et al. 2012; Turner et al. 2017). Exposure to NO_X levels reduces the CD4+t lymphocyte subpopulation in AKR/cum mice (Richters and Damji 1990). These outcomes offer supports that human exposure to conventional NO_2 density in the environment can have a negative effect on the immune system and promote the progression of cancer.

Animal experiments have shown that exposure to PM in the air can cause changes in the expression of specific genes in brain tissue, which may lead to some precancerous lesion (Ljubimova et al. 2013). Exposure to PM2.5 induces the secretion of IL-1 by neurons and reactive astrocytes β and interferon-γ (IFN-γ), thus promoting the infiltration of microglia into the M1 phenotype. M1 microglia release pro-inflammatory mediators and nitric oxide, exacerbating neuronal damage (Kang et al. 2021). Studies have shown that exposure to PM10 for 1–3 months in rats can trigger inflammatory stress and the expression of tumor corresponding biomarkers, including upregulation of Ra1 and EGR2 genes in IL-16 and IL-13 (Ljubimova et al. 2018). Therefore, reducing the level of $PM_{2.5}$ is conducive to reducing the incidence rate of cancer (Lequy et al. 2019).

Studies have shown that inhaling O_3 may be related to an increase in circulating pro-inflammatory mediators. These inflammatory mediators can cross the membrane into the blood–brain barrier of the central nervous system (Erickson et al. 2017), mainly inducing inflammation inside and outside the airway through local production of lipid ozone products, and leading to extrapulmonary inflammatory reactions.

Significance and prospect

This research offers a comprehensive understanding of the relationship between environmental air contamination and the threat of adult brain tumors through a retrospect of 9 studies, which is of great significance. This study provides a basis for formulating environmental air pollution standards and is of great significance for the development of public health. This study is beneficial for helping healthcare professionals and brain tumor patients understand the acute effects of air pollution exposure on brain tumors. Call on relevant departments to develop specific policies to improve targeted strategies for air quality (such as stricter air pollution standards, air quality control measures, and personal protective behavior). At the same time, specific policies should be formulated to improve air quality (such as actively promoting tourism and expanding urban green spaces), with a focus on heavily polluted areas, where pollution is often more severe in impoverished areas (Jerrett 2009).

Air pollution is a ubiquitous exposure, so a small increase in risk may have a weighty impact on public health. Future research needs to elucidate the dose–effect relationship between air pollution and brain tumors, as well as the impact of some indoor air pollutants and explore how air pollution control strategies can reduce the burden of brain tumor diseases to what extent. Brain tumors are a serious ramification that has undue influence of human mortality and future life. At the same time, the comprehensive impact of inhalation allergens, smoking, and environmental air pollution on the incidence rate of brain tumors should be evaluated in the future, because there is evidence that smoking and inhalation allergens can also cause brain tumors (Schlehofer et al. 2011; Vida et al. 2014).

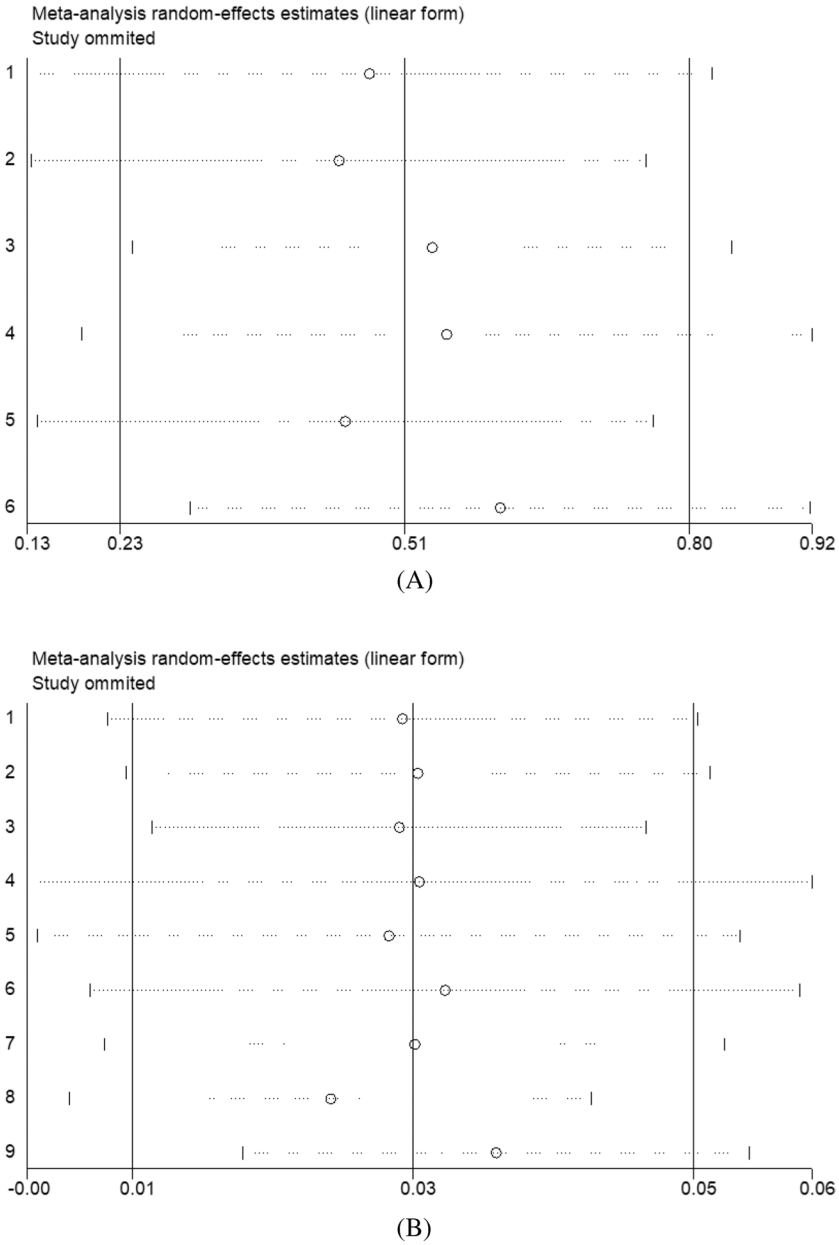


Fig. 4 Analysis of sensitivity was performed on the variable impact of the relationship between each type of air pollutant and brain tumor incidence. **A** BC; **B** NO_2

Limitations

Several limitations need to be recognized. First, the number of studies contained is relatively small, and most of the literature included comes from developed countries. This may lead to deviations due to differences in climate, geography, socioeconomic conditions, and air quality (Witkowska et al. 2016) Therefore, when more studies are published under this title, this will need to be updated. Secondly, because the occurrence and deterioration of cancer is a gradual process, given that the spatial variability of long-term exposure is greater than the temporal variability, the subjects will change with spatial patterns and time (Shekarrizfard et al. 2016).

Conclusion

Overall, the meta-analysis provides epidemiological evidence. There is a dominant correlation between prolonged exposure to BC and NO_2 and the occurrence of brain tumors in adults, and a statistically significant positive

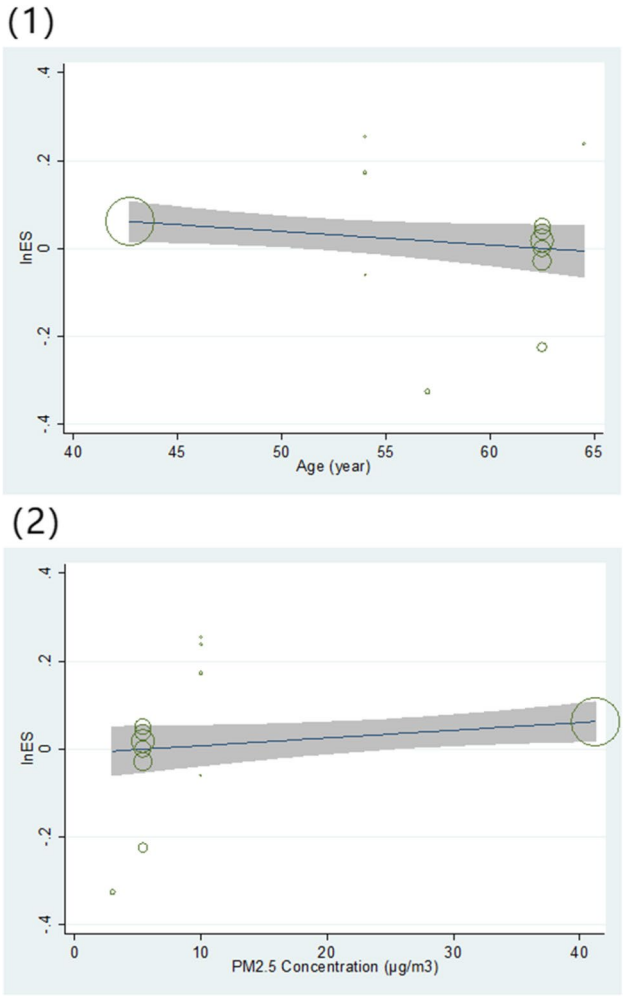


Fig. 5 Meta-regression analyses of the effects of $PM_{2.5}$ on the brain tumor incidence. Meta-regression analysis of the variable effect of the association between brain tumor incidence and $PM_{2.5}$. **1** Age; **2** the mean concentration of $PM_{2.5}$

correlation was discovered in this analysis. Furthermore, we found out a weak correlation between prolonged NO_x exposure and the occurrence of brain tumors in adults. However, the correlation between prolonged exposure to $PM_{2.5}$, PM_{10}, and O_3 and the occurrence of brain tumors did not reach statistical significance. Due to limited existing research, it is currently not possible to draw a very strong conclusion. Therefore, future studies should make more comprehensive adjustments.

Author contribution All the authors contributed to the conception and design of the study. Data collection and analysis were performed by Lu-Ting Shen and Meng-Wei Ge. The first draft of the manuscript was written by Lu-Ting Shen, and all authors commented on previous versions of the manuscript. All the authors read and approved the final manuscript.

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Data availability None.

Declarations

Ethical approval This is a meta-analysis; no specific population is involved; no ethical issues.

Consent to participate and publish All authors listed have agreed to participate and have published the attached manuscript.

Competing interests The authors declare no competing interests.

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