RESEARCH COMMUNICATION

Increasing Incidence of Brain and Nervous Tumours in Urban Shanghai, China, 1983-2007

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Abstract

Background: Wide use of cellular telephones has given rise to concerns about adverse health effects, especially in the brain, which might caused by the low power microwave-frequency signal transmitted by the antennas on handsets. Subscribers to cellular telephone services increased from mid-1990s in Shanghai; time trends in brain and nervous tumour after 2000 may supply information about possible associations between tumour risk and cellular telephones use. Methods: We investigated time trends in the incidence of brain and nervous tumour in urban Shanghai, from 1983 to 2007, applying joinpoint regression models to analyze the annual incidence rates and to predict future trends. Results: from 1983 to 2007, the age-adjusted incidence rate of brain and nervous tumours increased gradually by 1.2% per year (95% confidence interval [CI] = 0.4% to 1.9%) among men and 2.8% per year (95% CI =2.1 to 3.4) among women. Age-adjusted incidences of brain and nervous tumours in urban Shanghai for 2020 were estimated to 7.4 and 10.9 per 100,000 person-years. Conclusion: The study did not support an association between cellular telephone use and increased risk of brain and nervous tumours. However, considering of the increasing incidence rate of brain and nervous tumours now and in the future, in addition to the high prevalence of mobile phone exposure in the population and worldwide, assessment of longer follow-up time trends in brain tumour incidence rates is warranted.

Keywords: Brain tumours - Shanghai, China - cellular telephone - joinpoint regression model

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Introduction

A brain tumour is an intracranial solid neoplasm, a tumour within the brain or the central spinal canal. Aside from exposure to vinyl chloride or ionizing radiation, there are no known environmental factors associated with brain tumours (McKinney, 2004).

Cellular telephones and their base stations transmit and receive radiofrequency (RF) signals in the range between about 800 MHz and 2000 MHz, part of microwave of the electromagnetic spectrum. RF radiation at sufficiently high levels can cause heating by inducing small electric currents and increasing molecular movement (International Commission on Non-Ionizing Radiation Protection, 1998). A cellular phone can result in a specific energy absorption rate of about 1.5 W/kg and rise brain temperature at a maximum of 0.1°C (Van Leeuwen et al., 1999).

Thus, some concern has arisen about adverse health effects, especially tumours of the central nervous system which might caused by the low power microwave-frequency signal transmitted by the antennas on handsets. In a case-control study (Inskip et al., 2001), reported there are not association between the recent use of cell phones and incidence of brain tumours, but the data were not sufficient to evaluate the risks among long-term, heavy users. A World Health Organization study (Beckford and Winnett, 2009) has shown a significantly increased risk of some brain tumours related to use of cell phones for a period of 10 years or more. The Interphone Study (INTERPHONE Study Group, 2010), the largest international case-control study on this topic, reported no overall increase in risk of glioma or meningioma with use of mobile phones; but there were suggestions of an increased risk of glioma (odds ratio 1.40, 95% confidence interval 1.03 to 1.89) at the highest exposure levels. Danish nationwide study, the only cohort study investigating mobile phone use and cancer of all 420 095 people who had signed a mobile phone contract with a phone company (subscribers) from 1982 to 1995, and been followed-up to 1996 (Johansen et al., 2001), 2002 (Schüz et al., 2006) and 2007 (Frei et al., 2001), found no evidence of any increased risk of brain or nervous system tumours or any cancer among mobile phone subscribers.

Cell phones were introduced to the Shanghai in 1987, subscribers to cell phone services reached 100,000 in 1995, 1,000,000 in 1998, and 10,000,000 in 2000. (http://news.xinhuanet.com/fortune/2003-07/20/content_984135.htm). If new risk factors are introduced, the time trend of disease incidence would be expected to change. In this study, we performed a Joinpoint regression analysis to analyze the

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time trends in incidence of brain and nervous tumour, to evaluate whether trends in the incidence of brain and nervous tumour changed in urban Shanghai urban, from 1998 to 2003, before and after the introduction of cell phones.

Materials and Methods

Subjects

Shanghai is the largest city in China, consists of 17 county-level divisions and with a total population of over 23 million as of 2010. Shanghai is the commercial and financial center of mainland China, and ranks fifth in the 2011 edition of the Global Financial Centres Index published by the City of London. Shanghai cancer registry was established in 1963. In accordance with the provisions of Shanghai Bureau of Health, each medical institution, whether inpatient or outpatient department, has the responsibility to report new cases of cancer diagnosed. In the study, urban Shanghai covers about 6 million individuals in 9 county-level divisions (Huangpu, Luwan, Xuhun, Changning, Jing'an, Putuo, Zhabei, Hongkou and Yangpu).

Data on incidence and age-standardized rates (Segi's population standard by WHO) of thyroid cancer and total cancer for each gender were obtained from official publications of Shanghai Municipal Center for Disease Control and Prevention and Shanghai Cancer Institute (Shanghai Municipal Center for Disease Control and Prevention & Shanghai Cancer Institute, 2010), and Cancer Incidence in Five Continents (Parkin et al., 2005). The number of patients suffering from brain and nervous tumour (based on code 191- 192 in International Classification of Diseases, Ninth Revision [ICD-9] before 1999, and code 70-72 in International Classification of Diseases, tenth Revision [ICD-10]), the proportion of brain and nervous tumour among any tumours, the age-standardized rates of brain and nervous tumour, as well as that of any tumours, expressed as rates/100 000 persons, were used in the trend analysis. The study did not involve direct contact with patients nor were personal identifiers obtained. Therefore, patient consent and ethical approval was not required.

Statistical methods

Joinpoint regression analysis was carried out to identify points where a statistically significant change over time in linear slope of the trend occurred (Kim et al., 2000). In Joinpoint analysis, the best-fitting points where the rate changes significantly (increase or decrease) are chosen. In the final model, each Joinpoint indicates a statistically significant change in trend, and annual percentage change (APC) and average APC (AAPC) is computed for each of those trends by means of generalized linear models assuming a Poisson distribution. In describing long- and short-term trends with estimates of APC and AAPC, the terms "increase" or "decrease" signify that the slope (APC or AAPC) of the trend was statistically significant ($P < 0.05$) using a t test (APC) or Z test (AAPC).

The future burden of brain and nervous tumour was predicated using the modelled incidence rate in 2007 and its annual percentage change (calculated in Joinpoint regression). The age-adjusted incidences and the number of brain and nervous tumour cases were estimated in 2010, 2015 and 2020.

Results

Incidence of brain and nervous tumour from 1983 to 2007

The results are summarized in Figure 1. In the year 1983, there were 128 brain and nervous tumour cases in males and 105 in females in urban Shanghai. This represents 1.5% and 1.8%, respectively, of cases of any tumour (Figure 1a, b). While in the year of 2007, there were 281 brain and nervous tumour cases in males and 396 in females, representing 2.33% and 3.59%, respectively (Figure 1a, b).

On Joinpoint regression, no significant change of trend was observed, either in incidence rate of brain and nervous tumour or age-adjusted incidence rate. The incidence of brain and nervous tumour in male more than duplicated between 1983 and 2007 increased from 4.1 per 100,000 persons in 1983 to 9.1 per 100,000 persons in 2007, with an Annual Percent Change (APC) of 2.7 (95% CI =2.1 to 3.3), while that in female more than tripled, increased from 3.5 per 100,000 persons in 1983 to 12.9 per 100,000 persons in 2007, with an Annual Percent Change (APC) of 4.9 (95% CI =4.3 to 5.5) in females (Figure 1c). For age-adjusted incidence rate of brain and nervous tumour, the annual incidence of brain and nervous tumour increased from 3.7 per 100,000 persons in 1983 to 6.1 per 100,000 persons in 2007, with an Annual Percent Change (APC) of 1.2 (95% CI =0.4 to 1.9) in males, and increased from 2.9 per 100,000 persons in 1983 to 6.9 per 100,000 persons in 2007, with an Annual Percent Change (APC) of 2.8 (95% CI =2.1 to 3.4) in females (Figure 1c).

The predicated future burden of brain and nervous tumour

The predicted incidences of brain and nervous tumour

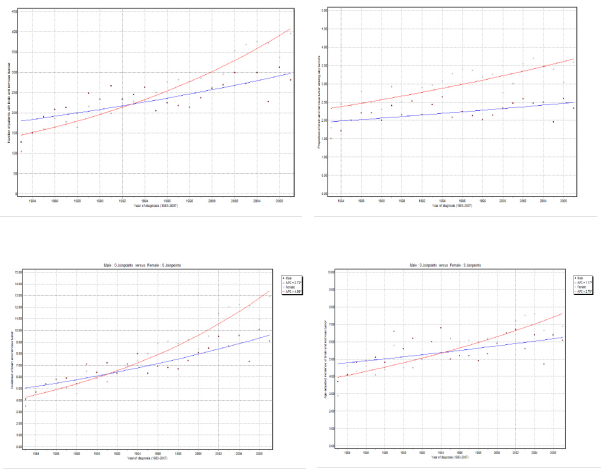

Figure 1. Trends in the Incidence of Brain and Nervous Tissue Cancer sin Male and Females. (A) Number of patients with brain and nervous tumour in male (red) and female (green), (B) Proportion of brain and nervous tumour among any tumours in male (red) and female (green), (C) Joinpoint regression of incidence of brain and nervous tumour in male (red) and female (green), (D) Joinpoint regression of age-adjusted incidence of brain and nervous tumour in male (red) and female (green)

Table 1. The Estimated Age-adjusted Incidences of Brain and Nervous Tumor

Gender	Modeled age-adjusted incidence in 2007 (per 100,000 persons)	Average percent change (1983 to 2007)	Estimated age-adjusted incidence (per 100,000 persons)		
			2010	2015	2020
Male	6.3	1.2	6.5	6.9	7.4
Female	7.6	2.8	8.3	9.5	10.9

were summarized in Table 1. In 2020, the annual age-adjusted incidence of brain and nervous tumour was estimated to reach at 7.4 and 10.9 per 100, 1000 persons in male and female, respectively.

Discussion

Jin et al. (1999) have reported that incidence of brain and nervous system tumour in urban Shanghai increased at APC of 3.7 in male and 3.4 in female, respectively, from 1972 to 1999. The present study demonstrated that the annual age-adjusted incidence of brain and nervous tumour continuously increased at an APC of 1.2 (95% CI =0.4 to 1.9) in males, and at APC of 2.8 (95% CI =2.1 to 3.4) in females from 1983 to 2007 (Figure 1c). Neither the APC from 1983 to 2007 is more than that of previous analysis, nor APC were significantly changed after the introduction of cell phones, suggesting that using of cell phones did not contribute to the increasing incidence of brain and nervous system tumours in Shanghai, China.

Our finding that brain tumour incidence rates were continued a gradual increase that started before the introduction of cell phones is consistent with cell phone use having no observable effect on brain and nervous system tumour incidence in this period. The finding is consistent with two long-term time-trend analysis using jointpoint regression model. Deltour et al. (2009) analyzed incidence of glioma and meningioma using joinpoint regression models in Denmark, Finland, Norway, and Sweden from 1974 to 2003, and concluded there were no change in incidence trends from 1998 to 2003, the time when possible associations between mobile phone use and cancer risk would be informative about an induction period of 5-10 years. In USA, the incidence of brain and other nervous system decreased at APC of 0.6 and 0.2 in male and female respectively, from 1992 and 2007 (Kohler et al., 2011).

The observed patterns of brain and nervous system tumour incidence are consistent with the results of World Health Organization study (Beckford & Winnett, 2009), the Interphone Study (INTERPHONE Study Group, 2010), Danish nationwide cohort study (Johansen et al., 2001; Schüz et al., 2006; Frei et al., 2011), and USA case-control study (Muscat, 2000), demonstrating no overall increase in brain and nervous system tumour risk. Our results are contrasted to Swedish case–control study series (Hardell et al., 2006), which suggested substantially increased risks for glioma among both short- and long-term users of mobile phones. No detectable trend change in incidence rates up to 2007 in this study suggests three possibilities: that the induction period for brain and nervous system tumours associated with mobile phone use exceeds 5- 10 years, that the increased risk of brain tumours associated with mobile phone use in urban Shanghai population is too small to be observed, or there is no increased risk associated with mobile phone use.

In the study, the incidence of brain and nervous tumour in male more than duplicated from 1983 to 2007, with an APC of 2.7 (95% CI = 2.1 to 3.3), while that in female more than tripled, with an Annual Percent Change (APC) of 4.9 (95% CI = 4.3 to 5.5) in females. The increase of incidence of brain and nervous tumour can partly explained by the aging of the population, because that the annual age-adjusted incidence of in male less than duplicated, (APC = 1.2, 95% CI: 0.4 - 1.9), and those in female less than tripled (APC = 2.8, 95% CI: 2.1 - 3.4).

Another need to be addressed is that the APC in age-adjusted incidence of brain and nervous tumour is more than that of North Europe countries (APC of incidence of glioma is 0.5 [95% CI = 0.2 to 0.8] and 0.2 [95% CI = 0.1 to 0.5] in males and female respectively, 1974 to 2003, and that of meningioma is 0.8 [95% CI = 0.4 to 1.3] among men, and 3.8 [95% CI=3.2 to 4.4] among women after the early 1990s) (Deltour et al., 2009), Australia (no significant linear increase) (Dobes et al., 2011), and USA (APC of incidence of brain tumour is - 0.6 and - 0.2 in male and female respectively, from 1992 and 2007) (Kohler et al., 2011). Based on the APC of the incidence of brain and nervous tumour, the age-adjusted incidences were estimated to reach at 7.4 and 10.9 per 100,000 person-year in 2020 for male and female, respectively.

In conclusion, the study presented the increasing incidence of brain and nervous tumour, in the recent decades; and estimates the future burden of brain and nervous tumour in 2010, 2015 and 2020. The study did not support the association between cell phone use and increased risk of brain and nervous tumour. However, considering of high increasing incidence rate of brain and nervous tumour at now or in the future, in addition to the high prevalence of mobile phone exposure in the population and worldwide, longer follow-up of time trends in brain and nervous tumour incidence rates are urgent.

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References

Beckford M, Winnett R (2009). Long-term use of mobile phones may be linked to cancer. Daily Telegraph (London), Oct 24.

Deltour I, Johansen C, Auvinen A, et al (2009). Time Trends in Brain Tumor Incidence Rates in Denmark, Finland, Norway, and Sweden, 1974-2003. *J Natl Cancer Inst*, **101**, 1721–4.

Dobes M, Shadbolt B, Khurana VG, et al (2011). A multicenter study of primary brain tumor incidence in Australia (2000–2008). *Neuro-Oncology*, **13**, 783–90.

Frei P, Poulsen AH, Johansen C, et al (2011). Use of mobile phones and risk of brain tumors: update of Danish cohort study. *Brit Med J*, **343**, d6387.

Hardell L, et al (2006). Tumor risk associated with use of cellular telephones or cordless desktop telephones. *World J Surg Oncol*, **4**, 74.

Inskip PD, Tarone RE, Hatch EE, et al (2001). Cellular-telephone use and brain tumors. *N Engl J Med,* **344**, 79–86.

International Commission on Non-Ionizing Radiation Protection, 1998. Guidelines for limiting exposure to time-varying electric, magnetic, and electromagnetic fields (up to 300 GHz). *Health Phys*, **74**, 494–522.

INTERPHONE Study Group, 2010. Brain tumor risk in relation to mobile telephone use: results of the INTERPHONE international case-control study. *Int J Epidemiol*, **39**, 675–94.

Jin F, Devesa SS, Chow WH, et al (1999). Cancer incidence trends in urban Shanghai, 1972-1994: an update. *Int J Cancer*, **83**, 435-40.

Johansen C, Boice J Jr, McLaughlin J, Olsen J (2001). Cellular telephones and cancer-a nationwide cohort study in Denmark. *J Natl Cancer Inst*, **93**, 203-7.

McKinney PA (2004.) Brain tumors: incidence, survival, and aetiology. *J Neurol Neurosurg Psychiatry*, **75**, ii12- 7.

Kim HJ, Fay MP, Feuer EJ, Midthune DN (2001). Permutation tests for Joinpoint regression with applications to cancer rates. *Stat Med*, **19**, 335-51.

Kohler BA, Ward E, McCarthy BJ, et al (2011). Annual report to the nation on the status of cancer, 1975-2007, featuring tumors of the brain and other nervous system. *J Natl Cancer Inst*, **103**, 714-36.

Muscat JE, Malkin MG, Thompson S, et al (2000). Handheld Cellular Telephone Use and Risk of Brain Cancer. *J Am Med Assoc*, **284**, 3001-7.

Parkin DM, et al (2005). Cancer Incidence in Five Continents, Volumes I to VIII. IARC CancerBase, No. 7, Lyon.

Schüz J, Jacobsen R, Olsen JH, et al (2006). Cellular telephone use and cancer risk: update of a nationwide Danish cohort. *J Natl Cancer Inst*, **98**, 1707-13.

Shanghai Municipal Center for Disease Control and Prevention & Shanghai Cancer Institute (2010). The incidence of malignant tumor in urban Shanghai, 1983-2007. *Tumor*, **30**, 595.

Van Leeuwen GM, Lagendijk JJ, Van Leersum BJ, et al (1999). Calculation of change in brain temperatures due to exposure to a mobile phone. *Phys Med Biol*, **44**, 2367–79.