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CLINICAL STUDY – PATIENT STUDY

Association between number of cell phone contracts and brain tumor incidence in nineteen U.S. States

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Abstract Some concern has arisen about adverse health effects of cell phones, especially the possibility that the low power microwave-frequency signal transmitted by the antennas on handsets might cause brain tumors or accelerate the growth of subclinical tumors. We analyzed data from the Statistical Report: Primary Brain Tumors in the United States, 2000–2004 and 2007 cell phone subscription data from the Governing State and Local Sourcebook. There was a significant correlation between number of cell phone subscriptions and brain tumors in nineteen US states ($r = 0.950, P < 0.001$). Because increased numbers of both cell phone subscriptions and brain tumors could be due solely to the fact that some states, such as New York, have much larger populations than other states, such as North Dakota, multiple linear regression was performed with number of brain tumors as the dependent variable, cell phone subscriptions, population, mean family income and mean age as independent variables. The effect of cell phone subscriptions was significant ($P = 0.017$), and independent of the effect of mean family income ($P = 0.894$), population ($P = 0.003$) and age (0.499). The very linear relationship between cell phone usage and brain tumor incidence is disturbing and certainly needs further epidemiological evaluation. In the meantime, it would be prudent to limit exposure to all sources of electro-magnetic radiation.

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Cell phones were introduced to the U.S. in 1984 but were not widely adopted until the mid-1990s. By early 2000, the number of subscribers to cell phone services had grown to an estimated 92 million in the United States and 500 million worldwide. Some concern has arisen about adverse health effects, especially the possibility that the low power microwave-frequency signal transmitted by the antennas on handsets might cause brain tumors or accelerate the growth of subclinical tumors. Inskip et al. performed a case control study and concluded that their data did not support the hypothesis that the recent use of cell phones causes brain tumors, but the data were not sufficient to evaluate the risks among long-term, heavy users [1]. Hardell et al. performed a meta analysis of two cohort studies and 16 case–control studies and reported that long-term use (10 years or more) of cell phones long term use has been associated with increased risk of brain tumors [2]. Myung et al. found possible evidence linking mobile phone use to an increased risk of tumors from a meta-analysis of low-biased case–control studies [3]. A World Health Organization study has shown a significantly increased risk of some brain tumors related to use of cell phones for a period of 10 years or more [4]. The Interphone Study Group found no overall increase in risk of glioma or meningioma with use of mobile phones; but there were suggestions of an increased risk of glioma at the highest exposure levels, though biases and error prevented a causal interpretation [5].

In the current study we examined the relation of cell phone subscriptions to brain tumor incidence by US state.

Methods

The following sources were used:

Reports of brain tumor incidence 2000–2004 and population from 19 U.S. states: Az, Co, Ct, De, Id, Ma, Me, Mn, Mt, NC, ND, NM, NY, RI, SD, Tx, Ut, Va, WV, data from Table 9 of Ref. [6]. These 19 states were chosen because their cancer registries responded to the request of the Central Brain Tumor Registry of the United States for brain tumor data. Brain tumor types are shown in Table 1, which is derived from Table 1 of Ref. [6].

Table 1 Types of brain tumors included in analysis (Information from Table 1 of reference 6)

Tumors of neuroepithelial tissue
Pilocytic astrocytoma
Protoplasmic and fibrillary astrocytoma
Anaplastic astrocytoma
Unique astrocytoma variants
Astrocytoma, not otherwise specified
Glioblastoma
Oligodendroglioma
Anaplastic oligodendroglioma
Ependymoma/anaplastic ependymoma
Ependymoma variants
Mixed glioma
Glioma malignant, not otherwise specified Choroid plexus
Neuroepithelial
Non-malignant and malignant neuronal/glial, neuronal and mixed
Pineal parenchymal
Embryonal/primitive/medulloblastoma
Tumors of cranial and spinal nerves
Nerve sheath, non-malignant and malignant
Other tumors of cranial and spinal nerves
Tumors of meninges
Meningioma
Other mesenchymal, non-malignant and malignant
Hemangioblastoma
Lymphomas and hemopoietic neoplasms
Lymphoma
Germ cell tumors and cysts
Germ cell tumors, cysts and heterotopias
Tumors of sellar region
Pituitary craniopharyngioma
Local extensions from regional tumors
Chordoma/chondrosarcoma
Unclassified tumors
Hemangioma
Neoplasm, unspecified
All other

2007 Cell phone subscriber data from the *Governing State and Local Sourcebook* (http://sourcebook.governing.com).

Mean population age and income by state 2004–2006 from www.census.gov.

Results

There was a significant correlation between number of cell phone subscriptions and brain tumors ($r = 0.950$, $P < 0.001$, Fig. 1). Because increased numbers of both cell phone subscriptions and brain tumors could be due solely to the fact that some states, such as New York, have much larger populations than other states, such as North Dakota, multiple linear regression was performed with number of brain tumors as the dependent variable, cell phone subscriptions, population, mean income (i.e socioeconomic status) and mean age as independent variables. The effect of cell phone subscriptions was significant ($P = 0.017$), and independent of the effect of mean income ($P = 0.894$), population ($P = 0.003$) and age (0.499).

Discussion

The association of cell phones and brain tumors remains controversial. The only documented adverse effect from cell phones is an increased risk of automobile crashes when the phones are used while driving. Moreover, the lack of ionizing radiation and the low energy level emitted from cell phones and absorbed by human tissues have led many investigators to doubt that these devices cause cancer [7].

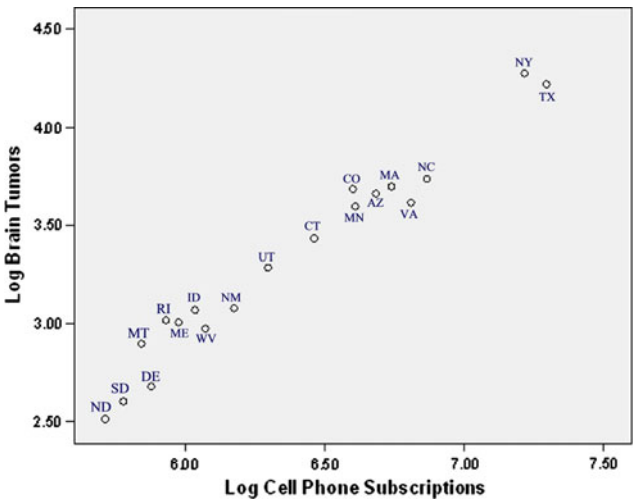

Fig. 1 Log US cell phone subscriptions 2007 versus log brain tumors reported to the Central Brain Tumor Registry of the United States (2000–2004) in 19 U.S. states. There is a significant correlation ($r = 0.950$, $P < 0.001$)

However, several animal studies have shown dysfunction of the blood–brain barrier caused by radiofrequency fields [8, 9]. Leakage of albumin into the brain has been demonstrated. The blood brain barrier consists of endothelial cells and the end-feet of astrocytes. Thus, one mechanism might be that microwaves induce blood brain barrier dysfunction so that carcinogenic substances may leak into the brain; the astrocytes especially might be exposed. There is some support for this mechanism in the study of Hardell and Carlberg, who found an increased risk for astrocytoma but not other types of malignant brain tumors [2]. An interaction with microwaves themselves might exist, since microwaves have been shown to induce several non-thermal effects in experimental studies, including free radicals [10, 11].

A weakness in the analysis that we have presented here is that tumor type was not taken into account. Indeed, Ahlbom et al., suggest that the risk associated with cell phone use may differ with tumor type [12]. Similarly, a meta-analysis by Khurana et al. demonstrated a significant cell phone effect when gliomas and acoustic neuromas were considered, but the observed effect did not extend to meningiomas [13].

It would be worthwhile to see if a linear relationship exists between cell phone subscriptions in each state and brain tumor incidence. Also, it might be possible to identify the type of tumors that have increased with cell phone subscriptions. Moreover, the cell phone-brain tumor relationship would be strongly supported if the numbers from each individual state showed similar linear relationships (thus ruling out, for example, that the increased number of brain tumors might be a disproportionate and disparate increase in the state of NY only).

Increased cell phone subscriptions may be a consequence of more and more children using these devices, while the number of adult users may not have increased at all. Indeed, Hardell and Carlberg found that the highest risk of astrocytoma and acoustic neuroma was in persons with first cell phone use under 20 years of age. This result is of biological significance, since a developing organ is more sensitive to carcinogenic agents, and the brain continues to develop until age twenty [2].

The linear relationship between cell phone usage and brain tumor certainly needs further epidemiological evaluation. In the meantime, it would be prudent to limit exposure to all sources of electro-magnetic radiation.

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LETTER TO THE EDITOR

Re. Lehrer S, Green S, Stock RG (2011) Association between number of cell phone contracts and brain tumor incidence in nineteen U.S. States. J Neurooncol 101:505–507

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To the Editor:

The methodology employed in recent article Lehrer et al. [1] raises significant cause for concern. The authors present data which tends to indicate that cell phone use (or at least a contract for a cell phone) is associated with the incidence of brain tumors. The methodology is significantly flawed and the conclusions impossible to accept based on this analysis. In actual fact, the data presented by Lehrer et al. simply show that numbers of cell phone contracts and numbers of brain tumors in 19 U.S. States are both independently related to the population size of these States.

Any statistic related to the population size would also appear related to the number of brain tumors. There is a strong positive association ($R^2 = 0.84$) between the number of brain tumors and number of hospitals in these 19 States (http://www.census.gov/econ/census02/guide/EC02_62.HTM) (Fig. 1a). Even adjustment for population size shows a significant contribution of number of hospitals as predictive factor for number of brain tumors ($P = 0.027$). Figure 1b shows a strong positive association ($R^2 = 0.85$) between the number of brain tumors and number of beauty salons in these States (from the U.S. Census Bureau, 2007 Economic Census). Even adjustment for population size shows a significant contribution of the number of beauty salons as predictive factor for number of brain tumors ($P < 0.001$).

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Of course, neither implies a causal association and nor does the data about the number of cell phone contracts. This is typically an example of "stork epidemiology": the correlation between numbers of pairs of breeding storks and number of births in West Germany does not imply a causal relationship [2].

Should the age-standardized incidence rate of brain tumors have been considered, then it is unlikely that a correlation with cell phone contracts would have emerged. In 13 of the 19 States considered (AZ,CO,CT,ID,ME,MA,MT,NM,NY,RI,TX,UT,WV), the age standardized incidence rate of brain and nervous system tumors, calculated from the last edition of Cancer Incidence in Five Continents volume 9, varies between 5.1 and 6.9 cases per 100,000 person-years. This rate is independent of population size e.g. the largest State, Texas, has a rate of 5.55 whereas the smallest, Montana, has a rate of 5.95.

Data collected by the Surveillance, Epidemiology, and End Results (SEER) Program indicate declining or stable age-adjusted brain cancer incidence rates between 1975 and 2006 [3] and a recent analysis by Inskip et al. [4] of these incidence data do not provide support to the view that cellular phone use causes brain cancer [4].

While the original publication and this rebuttal appear at first glance to be amusing, there is a serious message behind this. The recent publication by Volkow et al. [5] demonstrating an increased in glucose activity following cell phone, includes a statement that the evidence linking cell phone use and brain cancer as being controversial and then cite three publications in favour of such an association and three against. Citing Lehrer et al. [1] among the evidence of an association between cell phone use and brain cancer demonstrates the how studies with an erroneous methodology can be used to support important Public Health claims and also demonstrates the weakness of the evidence

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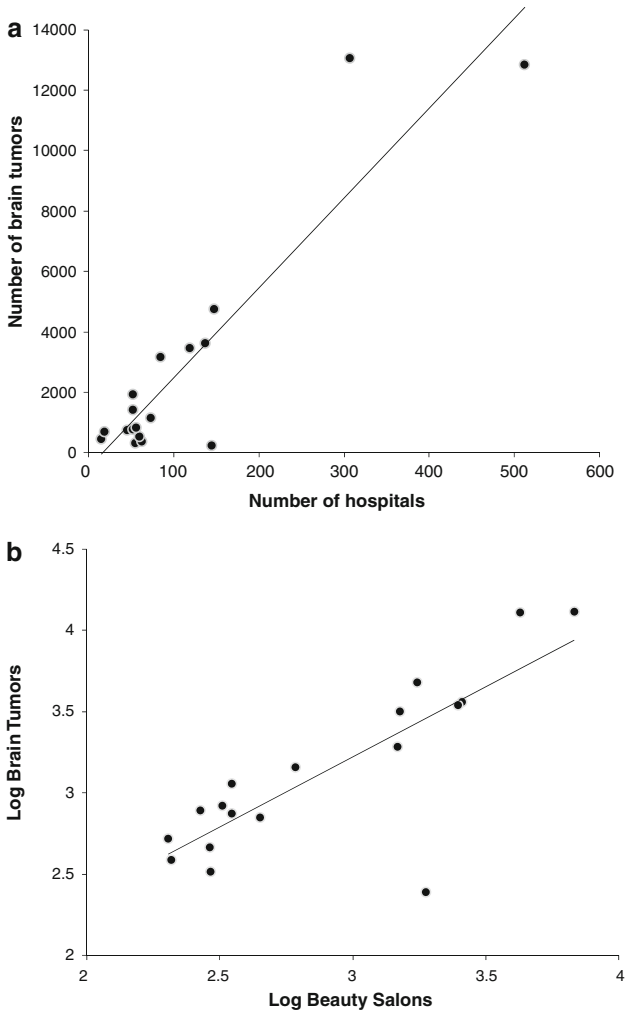

Fig. 1 **a** Correlation of number of hospitals versus number of brain tumors in 18 United States. There is a significant correlation ($r = 0.92$, $P < 0.001$). **b** Plot of Log (number of beauty salons) versus log (number of brain tumors) reported to the Central Brain Tumor Registry of the United States (2000–2004) in 18 U.S. states. There is a significant correlation ($r = 0.92$, $P < 0.001$)

purporting to demonstrate an association between cell phone use and brain tumour risk.

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RESPONSE

Response to Boniol et al.

Steven Lehrer

Boniol et al. [1] suggest that our analysis of the relation of cell phone contracts and brain tumors is erroneous, because both cell phones and brain tumors are associated with population. We agree with important points Boniol et al. make about interpretation of correlational studies, but not with their evaluation of our methodology.

There is no doubt that it is necessary to control for population when comparing variables, such as numbers of brain tumors and cell phones, to avoid spurious associations. In our study, the association was still statistically significant after controlling for population and two other confounders by multiple regression analysis. To illustrate that controlling for population in this way is not sufficient, Boniol et al. present examples of hospitals and beauty salons, both of which had significant associations with brain tumors even after controlling for population. If variables other than population are also associated with both cell phones and brain tumors, they would similarly generate spurious associations. Thus controlling only for population cannot be expected to eliminate all spurious association. The problem is how to distinguish spurious associations from real but subtle ones. In Boniol et al.'s example of beauty salons, prolonged use of dark-colored permanent hair dyes may have a relationship to the genesis of brain tumors [2]. Similarly, the association between number of hospitals and brain tumors also may have a biological basis, since many forms of cancer, including brain tumors, have been attributed to medical radiation [3].

Even if the evidence for a real association between cell phone use and brain tumor risk—based on other studies in addition to ours—is weak, as Boniol et al. assert, it is prudent to err on the side of caution until additional studies indicate more clearly the reason for the apparent association. Thus, we conclude that that there is a need for more evaluation.

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