Cancer Epidemiology 56 (2018) 6–13

Contents lists available at ScienceDirect

Cancer Epidemiology

journal homepage: www.elsevier.com/locate/canep

Trends in the incidence of primary brain, central nervous system and intracranial tumors in Israel, 1990–2015

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ARTICLE INFO

Keywords:
Brain and central nervous system tumors
Israel
Joinpoint analysis
Time trends

ABSTRACT

Background: The association between cellphone technology and brain, central nervous system (CNS) and intracranial tumors is unclear. Analysis of trends in incidence of such tumors for periods during which cellphone use increased dramatically may add relevant information. Herein we describe secular trends in the incidence of primary tumors of the brain and CNS from 1990 to 2015 in Israel, a period during which cellphone technology became extremely prevalent in Israel.

Methods: All cases of primary brain, CNS and intracranial tumors (excluding lymphomas) diagnosed in Israel from 1990 to 2015 were identified in the Israel National Cancer Registry database and categorized by behavior (malignant; benign/uncertain behavior) and histologic type. Annual age-standardized incidence rates by sex and population group (Jews; Arabs) were computed, and the annual percent changes and 95% confidence intervals per category were calculated using Joinpoint software.

Results: Over 26 years (1990–2015) no significant changes in the incidence of malignant brain, CNS and intracranial tumors were observed, except for an increase in malignant glioma incidence in Jewish women up to 2008 and Arab men up to 2001, which levelled off in both subgroups thereafter. The incidence of benign/uncertain behavior brain, CNS and intracranial tumors increased in most population groups up to the mid-2000s, a trend mostly driven by changes in the incidence of meningioma, but either significantly decreased (Jews) or stabilized (Arabs) thereafter.

Conclusions: Our findings are not consistent with a discernable effect of cellphone use patterns in Israel on incidence trends of brain, CNS and intracranial tumors.

1. Introduction

Over 236,000 new cases of brain and central nervous system (CNS) tumors were diagnosed globally in 2012, a third of them occurring in more developed countries. Israel, with an age-standardized incidence rate of 6.8/100,000 in men and 5.3/100,000 in women, was ranked 20th in the world [1]. Genetic factors and exposure to ionizing radiation are well-known risk factors for both benign and malignant brain and CNS tumors [2] but account for only a small proportion of cases. Public and scientific concerns were raised regarding exposure to non-ionizing radiation associated with cellphone technology as a potential risk factor for brain and CNS tumors, concerns that were fueled in part by the exponential growth in cellphone use worldwide. According to a Deloitte recent report, within four decades since the introduction of the first cellphone, most developed countries have at least 90% cellphone penetration [3]. In Israel, cellphones were firstly introduced in 1986 [4]; in 2000, 63.5% of Israeli households owned at least one cellphone device, increasing to 95% in 2012 [4]. Furthermore, in 2015, 86% of the total Israeli population owned a smartphone, with higher proportions in younger (aged 18–34) (90%), more educated (93%) and higher-incomed (94%) subjects [5].

Unlike ionizing radiation, non-ionizing radiation is incapable of causing DNA damage [4]. Indeed a recent EU report concluded that currently there is no consistent evidence that non-ionizing radiation increases cancer risk [6]. Epidemiological studies, however, have yielded conflicting results. Three large-scale studies reported inconclusive results; the Interphone case-control study, a joint effort of researchers from 13 countries that focused on the association between self-reported cellphone use and benign and malignant brain and CNS tumors occurrence rates, reported no increase in the risk of glioma or

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https://doi.org/10.1016/j.canep.2018.07.003
Received 14 April 2018; Received in revised form 19 June 2018; Accepted 9 July 2018

Table 1
Distribution of malignant brain, CNS and intracranial tumors by histologic group, Israel.1990–2015.

Histological type	N	Percent
Astrocytoma [excluding glioblastoma]	2,219	21.8
Glioblastoma	4,131	40.5
Other glioma	2,297	22.6
Meningioma	199	2.0
Blood vessel tumor	26	0.2
Others	1,311	12.9
Total	**10,183**	**100.0**

meningioma associated with use of cellphones, although an increased risk of glioma at the highest exposure levels was suggested [7,8]. An ongoing population-based Danish cohort study that linked all Danish citizens to cellphone subscription data and to the national cancer registry database to identify rates of tumors of the CNS is noteworthy. The last update published in 2011 spanned 3.8 million person-years from 1990 to 2007 and indicated no association between ever or heavy cellphone and incidence of CNS tumors [9]. The British Million Women Study assessed the risk for brain tumors associated with self-reported use of cellphones. No association was found between ever (vs. never) use of cellphones and increased risk for glioma, meningioma or non-CNS cancers. A significant increase in risk of acoustic neuroma was identified among long term cellphone users [10], but further expanded analyses did not confirm this association [11]. Smaller-scale studies mostly reported no associations, although one French case-control study reported an increased risk for glioma and meningioma among the heaviest cellphones users [12] and a pooled meta-analysis of two Swedish case-control studies observed statistically significant trends of increasing brain cancer risk with longer cellphone use, particularly among subjects who began to use cellphones before age 20 [13]. These inconsistent findings may result from biases inherent in such studies; for example, selection bias such as participation bias in both cohort and case-control studies; information bias when exposure (i.e., use of cellphones) is self-reported (inaccurate reporting in cohort studies, recall bias in case-control studies). In addition, the rapidly changing technologies may have also interfered with accurate measuring of the exposure. However, the potentially increased brain tumor risk in certain users, combined with the large scale population exposure involved, led the International Agency for Research on Cancer (IARC) of the World Health Organization (WHO) in 2011 to classify cellphone use as possibly carcinogenic to humans (Group 2B), and to pursue the implementation of the precautionary principle regarding cellphone use [14].

In light of the uncertainty of the association, analyses of incidence trends conducted to determine whether the incidence of brain or other cancers has changed during the time that cellphone use has increased significantly, may also be informative in shedding light on the issue of possible carcinogenicity of cellphone exposure. The aim of the current study was to describe the temporal trends in the incidence of primary brain, CNS and intracranial tumors from 1990 through 2015 in Israel, a period during which cellphone use dramatically increased.

2. Methods

The Israel National Cancer Registry (INCR), established in 1960, is a population-based, passive, national registry, which collects information on all uncertain behavior, in-situ and invasive malignant tumors, as well as benign tumors of the brain and CNS, diagnosed in Israel. The INCR covers the total population of Israel (currently 8.5 million, 75% Jews, 21% Arabs and 4% others). Report to the INCR is compulsory by law since 1982, and the INCR completeness regarding solid (97%) and hematopoietic (88%) tumors is high. Specifically, for malignant brain tumors the completeness is 95% whereas for benign/uncertain behavior CNS tumors it is lower (61%) [15].

For the current analysis, we selected from the INCR database all cases meeting the following criteria: (i) Primary tumors, diagnosed in 1990 through 2015; (ii) with ICD-O-3 topography codes C70.* (meninges), C71.* (brain), C72.* (spinal cord, cranial nerves and other parts of central nervous system), C75.1 (pituitary), or C75.2 (craniopharyngeal duct); (iii) all tumor behaviors (benign, uncertain, in situ or malignant). Lymphomas diagnosed at these sites were excluded from the study dataset.

Relevant brain, CNS and intracranial tumors were categorized by behavior (malignant, invasive and in-situ; benign/uncertain behavior) as well as by histologic type (see Appendix A Table A1). Even though glioblastoma is in fact a subtype of astrocytic tumors, in this report we studied the two entities separately.

For each behavior and histologic group, we computed annual age-

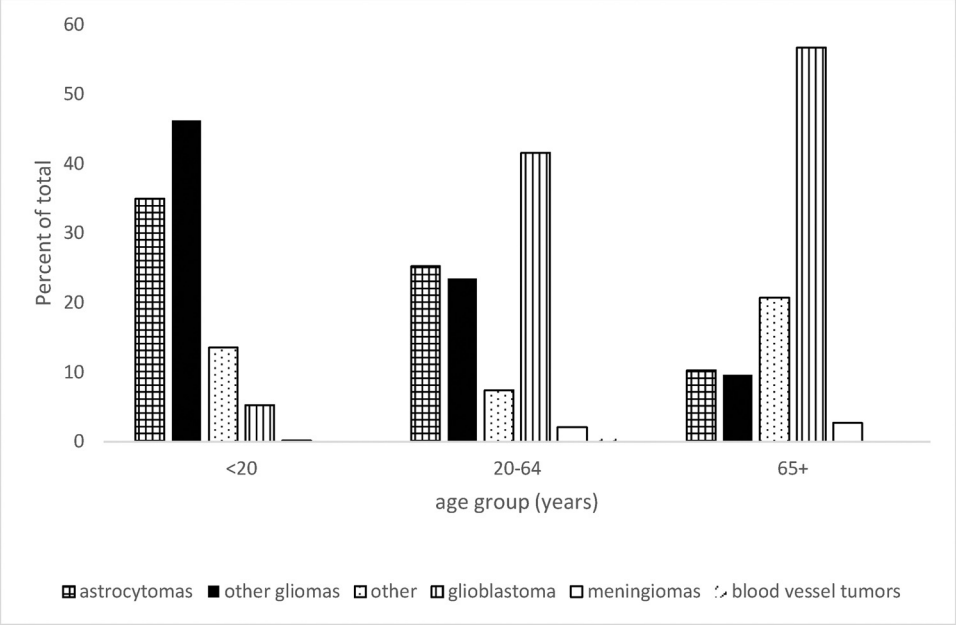

Fig. 1. Distribution of malignant brain, CNS, and intracranial tumors, by age and histologic group, Israel 1990–2015 (% of total).