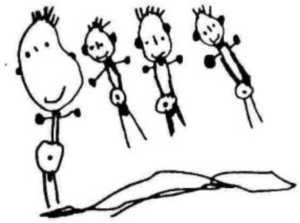
Radiofrequency electromagnetic fields exposure, sleep, and neurodevelopment in preadolescents and adolescents

· Alba Cabré-Riera, 2020 ·

Thesis director: Dr. Mònica Guxens

· Barcelona Institute for Global Health (ISGlobal) · Pompeu Fabra University, Department of Experimental and Health Sciences ·



A la Happy Family

1 Preface

This PhD thesis was written between 2017 and 2020 at Barcelona Institute for Global health (ISGlobal). It was supervised by Dr. Mònica Guxens. This work comprises a compilation of the scientific publications co-authored by the PhD candidate according to the procedures of the Biomedicine PhD program of the Department of Experimental and Health Sciences of University Pompeu Fabra. The research presented in this thesis has been funded by the French Agency for Food, environmental, and occupational Health & Safety within the *Étude Longitudinale à radioFréquences Et problèmes du Sommeil chez les enfants (ELFES) Project* (EST-2016 RF-21), by the European Commission with the *Generalized EMF Research Using Novel Methods (GERoNiMO) Project* (603794), by the Spanish Institute for Health Carlos III with the *Radiofrequency Electromagnetic Fields Exposure and Brain Development (REMBRANDT) Project* (MS13/00054, CP13/00054), the *Association between environmental exposure during pregnancy and the health in the late adolescence (AMICS-INMA-18y) Project* (PI14/00677), and the *Radiofrequency electromagnetic fields, noise, and sleep problems in adolescence (INMA-Ado-Sleep) Project* (PI17/01340), and by the Netherlands Organization for Health Research and Development with the *Radiofrequency electromagnetic fields exposure assessment in children in Generation R (RF-GenR) Project* (85500036).

The thesis includes an abstract in Catalan, Spanish, and English, a general introduction, objectives, methods, results (4 original research articles), a general discussion, and conclusions. The thesis is focused on the associations between radiofrequency electromagnetic fields exposure, sleep, and neurodevelopment in preadolescents and adolescents. The scientific papers included in this thesis are based on data from various European prospective birth cohorts: the Infancia y Medio Ambiente (INMA) Project, the Adolescent Brain Cognitive Development (ABCD) Study, and the Generation R Study.

2 Resum / Resumen / Abstract

Resum

L’ús de dispositius mòbils de comunicació com els telèfons mòbils, tauletes i ordinadors portàtils ha augmentat els darrers anys, especialment en preadolescents i adolescents. Els dispositius mòbils de comunicació utilitzen els camps electromagnètics de radiofreqüència (CEM-RF) per l’intercanvi constant d’informació necessari pel seu funcionament. L’evidència científica dels efectes que té l’exposició de CEM-RF al cervell és limitada i els estudis epidemiològics que avaluaven l’exposició de CEM-RF i la seva relació amb el son i el neurodesenvolupament són escassos.

Aquesta tesi té com a objectiu entendre millor les associacions entre l’exposició a CEM-RF i el son i l’exposició a CEM-RF i el neurodesenvolupament. Per fer-ho: i) hem fet una avaluació completa de l’exposició de CEM-RF al cervell, és a dir, distingint entre fonts de CEM-RF amb diferents patrons d’exposició al cervell com les trucades telefòniques, l’ús d’aparells mòbils de comunicació per activitats amb pantalla i les fonts ambientals, ii) hem estimat la quantitat de CEM-RF que el cervell absorbeix de cada font i en total, iii) hem avaluat el son utilitzant mesures objectives recollides amb actigrafia i iv) hem avaluat el neurodesenvolupament com a funció cognitiva i volums cerebrals.

L’ús d’alguns dispositius mòbils de comunicació com per exemple la tauleta i l’ús problemàtic del telèfon mòbil estan associats amb pitjor qualitat i mesures objectives del son. A més a més, hem trobat una associació entre la dosi de CEM-RF al cervell provinent de les trucades telefòniques al vespre i pitjors mesures objectives del son. En relació amb el neurodesenvolupament, la dosi total de CEM-RF al cervell i la dosi de CEM-RF al cervell provinent de les trucades telefòniques no estan associades amb els volums cerebrals, en canvi, la dosi de CEM-RF al cervell provinent d’usos d’aparells mòbils de comunicaió per activitats amb pantalla està associada amb un volum més petit del nucli caudat. Finalment, la dosi total de CEM-RF al cervell i la dosi de CEM-RF al cervell provinent de les trucades telefòniques estan associades amb pitjor la intel·ligència no verbal.

Tenint en compte que es desconeix el mecanisme biològic que hi ha darrere de les associacions observades entre l'exposició a CEM-RF i el son i l'exposició a CEM-RF i el neurodesenvolupament, que els efectes que hem trobat són petits i que no hem pogut separar completament entre els minuts d'ús dels dispositius mòbils de comunicació i la

dosi de CEM-RF al cervell, els nostres resultats s’han d’interpretar amb precaució. No podem descartar que les troballes siguin casuals, causalitat inversa o que altres factors relacionats amb l’ús de dispositius mòbils de comunicació estiguin darrere de les associacions observades. Per exemple, exposició a la llum blava, addicció als aparells mòbils de comunicació, excitació mental o desplaçament del son.

Resumen

El uso de dispositivos móviles de comunicación como los teléfonos móviles, tabletas y ordenadores portátiles ha aumentado en los últimos años, especialmente en preadolescentes y adolescentes. Los dispositivos móviles de comunicación utilizan los campos electromagnéticos de radiofrecuencia (CEM-RF) para el intercambio constante de información necesario para su funcionamiento. La evidencia científica de los efectos que tiene la exposición a CEM-RF al cerebro es limitada y los estudios epidemiológicos que evalúan la exposición de CEM-RF y su relación con el sueño y el neurodesarrollo son escasos.

Esta tesis tiene como objetivo entender mejor las asociaciones entre la exposición a CEM-RF y el sueño y la exposición a CEM-RF y el neurodesarrollo: i) haciendo una evaluación completa de la exposición de CEM-RF al cerebro, es decir, distinguiendo entre fuentes de CEM-RF con diferentes patrones de exposición al cerebro como las llamadas telefónicas, el uso de aparatos móviles de comunicación para actividades con pantalla y las fuentes ambientales, ii) estimando la cantidad de CEM-RF que el cerebro absorbe de cada fuente y en total, iii) evaluando el sueño utilizando medidas objetivas recogidas con actigrafia y iv) evaluando el neurodesarrollo como función cognitiva y volúmenes cerebrales.

El uso de algunos dispositivos móviles de comunicación como por ejemplo la tableta y el uso problemático del teléfono móvil están associados con peor calidad y medidas objetivas del sueño. Además, hemos observado una asociación entre la dosis de CEM-RF al cerebro proveniente de las llamadas telefónicas por la tarde y peores medidas objetivas del sueño. En cuanto al neurodesarrollo, la dosis total de CEM-RF al cerebro y la dosis de CEM-RF al cerebro proveniente de las llamadas telefónicas no están asociadas con los volúmenes cerebrales, en cambio, la dosis de CEM-RF al cerebro proveniente de usos de aparatos móviles de comunicación para actividades con pantalla está asociada con un volumen más pequeño del núcleo caudado. Finalmente, la dosis total de CEM-RF al cerebro y la dosis de CEM-RF al cerebro proveniente de las llamadas telefónicas están asociadas con peor inteligencia no verbal.

Teniendo en cuenta que se desconoce el mecanismo biológico que hay detrás de las asociaciones observadas entre la exposición a CEM-RF y el sueño y la exposición a CEM-RF y el neurodesarrollo, que los efectos que hemos encontrado son pequeños y que no hemos podido separar completamente entre los minutos de uso y la dosis de

CEM-RF, nuestros resultados deben interpretarse con precaución. No podemos descartar hallazgo casual, causalidad inversa o que otros factores relacionados con el uso de dispositivos móviles de comunicación estén detrás de las asociaciones observadas. Por ejemplo, exposición a la luz azul, adicción a los dispositivos móviles de comunicación, excitación mental o desplazamiento del sueño.

Abstract

The use of mobile communication devices (e.g. mobile phones, tablets, and laptops) increased during the last few years, especially in preadolescents and adolescents. In order to function, mobile communication devices require a constant exchange of information achieved using radiofrequency electromagnetic fields (RF-EMF). Evidence is limited for potential effects of RF-EMF exposure to the brain and epidemiological studies that assessed RF-EMF exposure and its relationship with sleep and neurodevelopment are scarce.

This thesis aimed to better understand the potential association between RF-EMF exposure and sleep, and RF-EMF exposure and neurodevelopment by: i) using a comprehensive RF-EMF exposure assessment (i.e. distinguish between sources with different patterns of RF-EMF exposure to the brain such as phone calls, screen activities, and environmental sources, ii) estimating the amount of RF-EMF the brain absorbs from each source and overall, ii) assessing sleep using objective measures collected with actigraphy, and iii) assessing neurodevelopment as cognitive function and brain volumes.

The use of some mobile communication devices such as the tablet and problematic mobile phone use were associated with poorer sleep quality and less favourable objective sleep measures. Moreover, evening whole-brain RF-EMF dose from phone calls was associated with less favourable objective sleep measures. Regarding neurodevelopment, overall whole-brain RF-EMF dose and whole-brain RF-EMF dose from phone calls were not associated with brain volumes but whole-brain RF-EMF dose from screen activities was associated with smaller caudate volume. Finally, overall whole-brain RF-EMF dose and whole-brain RF-EMF dose from phone calls was associated with non-verbal intelligence.

Given that the biological mechanism behind the observed associations between RF-EMF exposure and sleep, and RF-EMF exposure and neurodevelopment is unknown, that we found small effects sizes, and that we could not entirely disentangle between minutes of use and RF-EMF dose, our results should be interpreted with caution. We cannot discard chance finding, reverse causality, or that other non-RF-EMF factors related to the use of mobile communication devices are behind the observed associations (e.g. blue light, addiction, mental arousal or sleep displacement).

3 Abbreviations

ABCD – Adolescent Brain Cognitive Development Study

DECT - Digital Enhanced Cordless Telecommunications

EEG - electroencephalography

GHz - gigahertz

H - hertz

IARC - WHO/International Agency for Research on Cancer

INMA – Infancia y Medio Ambiente Project

ITU – International Telecommunications Union

J – Joules

Kg - kilogram

kHz - kilohertz

min - minutes

mJ - milijoules

MRI – Magnetic resonance imaging

NREM - non-rapid eye movement sleep

REM – rapid eye movement

RF-EMF – Radiofrequency electromagnetic fields

SAR – Specific absorption rate

W - Watt

WHO - World Health Organization

4 Introduction

Life without mobile phones, tablets, and laptops has become difficult to imagine. The percentage of individuals using mobile communication devices connected to the internet increased 36.8% between 2005 and 2019, when the International Telecommunications Union (ITU) estimated that more than 4.1 billion people were using internet (53.6% of the global population) [1]. In order to function, mobile communication devices require a constant exchange of information achieved using radiofrequency electromagnetic fields (RF-EMF), which leads to a continuous exposure to RF-EMF in the population of the developed countries. In 2011, the World Health Organization (WHO) - International Agency for Research on Cancer (IARC) classified RF-EMF emitted by mobile communication devices (from 3 kilohertz (kHz) to 300 gigahertz (GHz)) as possibly carcinogenic to humans [2]. This, against the background of the rapid increase of mobile communication device use in the last years, especially in preadolescents and adolescents, has raised concern about other potential RF-EMF effects on the developing brain.

Radiofrequency Electromagnetic Fields

Radiation is a physical phenomen consisting of the emission, propagation, and absorption of energy by matter, both in the form of waves (electromagnetic radiation), and particles (corpuscular radiation). Electromagnetic radiation refers to the waves of the electromagnetic field, propagating through space, carrying electromagnetic radiant energy. Photons are the elemental particles that compound electromagnetic radiation. Electromagnetic waves are determined by their corresponding frequency (i.e. how many times the waves cycles per second and is referred to as Hertz (Hz)), their wavelength (i.e. the distance between waves), and their wave amplitude, which is directly proportional to the transported energy (Joules (J)). A larger frequency implies shorter wavelength and greater energy. The electromagnetic spectrum ranges from the natural earth magnetic field (low frequencies, large wavelengths) to medical radiation (high frequencies, short wavelengths).

Human-made sources of electromagnetic radiation are divided into ionizing radiation, meaning that individual photons have enough energy to ionize molecules or break chemical bonds, and non-ionizing radiation. Photons of non-ionizing radiation include extremely low frequencies (from 3 Hz to 3 kilohertz (kHz)), radio frequencies

(RF, from 3 kHz to 300 gigahertz (GHz)), and the optical radiation (ultraviolet radiation, visible light, and infrared radiation) and have lower energy than non-ionizing radiation thus do not have the ability to ionize molecules but are related to other biological effects [3]. In particular, RF-EMF exposure has been related to nerve stimulation, temperature rise, and change of permeability of cell membranes in vitro and in animal studies [4].

The main source of RF-EMF exposure to humans is the personal use of mobile communication devices (i.e. near-field sources such phone calls and mobile communication devices use for screen activities). However, humans are also exposed to RF-EMF from a variety of other sources (e.g. environmental or far-field sources such as exposure from mobile phone base stations, FM radio and TV broadcast antennas, mobile phones from other users, and WiFi). There are different approaches to assess RF-EMF exposure. Epidemiological studies have used reported phone calls to assess exposure from near-field sources, and portable exposure meters, spot measurements, or modeling to assess exposure from far-field sources. Few studies have considered characterizing the overall RF-EMF exposure by estimating exposure from all RF-EMF sources together. Moreover, when a biological body is exposed to RF-EMF, some of the energy is reflected away from the body, and some is absorbed by it. This results in complex patterns of electromagnetic fields inside the body that are dependent on the RF-EMF characteristics as well as the physical properties and dimensions of the body. To assess potential RF-EMF health effects, we are interested in how much RF-EMF energy is absorbed by biological tissues. This is typically described as a function of a dosimetric quantity. For example, in terms of the specific absorption rate (SAR). Three studies presented in this thesis apply an innovative and recently developed integrated exposure model to estimate brain RF-EMF doses in population-based samples.

Preadolescents and adolescents

Preadolescents (9-13 years-old) and adolescents (13-18 years-old) are one of the vulnerable populations to the potential effects of RF-EMF exposure to the brain [5]. The absorbed RF-EMF penetrates proportionally deeper into the brain of preadolescents compared to adults’ brain, and the skin and skull layers are thinner so the RF-EMF source is closer to the brain [6]. In addition, preadolescents and adolescents will experience long periods of exposure to RF-EMF because they start using mobile communication devices at an early age and are likely to continue using them through their life. The use of mobile phone for calling increases with age [7], thus, adolescents have potentially higher RF-EMF exposure to the brain than preadolescents. This can also compromise adolescents' brain.

Radiofrequency Electromagnetic fields and sleep

Sleep is not just the absence of waking, but an active neurophysiological process and the primary activity of the developing brain. Consequently, inadequate sleep duration or quality is known to lead to adverse physical and mental health consequences [8]. Despite its importance to health, insufficient sleep duration and resultant daytime sleepiness are prevalent among preadolescents and adolescents [9]. Sleep is regulated by two overlapping but distinct systems: the circadian system and sleep/wake homeostasis. The circadian system endogenously synchronizes biologic rhythms, including sleep, cyclically with the 24h day and is adjusted through the influence of exogenous factors (e.g. light) [10]. Sleep/wake homeostasis describes the body's internal neurophysiologic drive toward either sleep or waking. Thus, sleep and waking are regulated by a circadian process and by a homeostatic process. However, the sleep state itself has a cyclic or rhythmic organization. The sleeping brain alternates between rapid eye movement sleep (REM) and non-rapid eye movement sleep (NREM), in sleep cycles. REM and NREM sleep have defined electroencephalography (EEG) patterns, and neurological and physiological features [11].

There are several hypotheses to why the use of mobile communication devices might disrupt sleep [12]. The exposure to RF-EMF emitted by these devices has been suggested as one of them [13]. Experimental studies in humans showed that RF-EMF exposure has an effect on waking and sleeping EEG [14]–[18] but whether the exposure to RF-EMF alters the circadian rhythm affecting sleep, as it is observed with light exposure, is an open question. In epidemiological studies, the use of mobile communication devices for calling or screen activities during the day was associated with daytime sleepiness and higher symptoms of sleep disturbances [19]–[25] but the RF-EMF exposure from far-field sources at home or school was not [23], [26] in adolescents and young adults at 14-24 years old. Interestingly, the awareness about the importance of reducing the use of mobile communication devices close to bedtime increased during the last years [27], [28]. However, only three cross-sectional studies have assessed evening use of mobile communication devices for activities that lead to RF-EMF exposure to the brain, including phone calls, and sleep. The authors reported that higher evening use was related to more symptoms of sleep disturbances [29], [30] and lower objective sleep efficiency [31] at 12-18 years of age. Only one of them assessed objective sleep measures, and there are no studies assessing all-day RF-EMF exposure and evening RF-EMF exposure independently.

Radiofrequency electromagnetic fields and neurodevelopment

The development of the brain is characterized by numerous vital and often fragile processes beginning early in gestation and continuing into childhood and adolescence, crucial for a proper development, and disruption of any of these processes by external stressors, such as RF-EMF, might lead to irreversible alterations that manifest in later life [32]. Neuroimaging techniques have advanced significantly in the past years and have enabled scientists to learn more about preadolescents' and adolescents' brain. However, few studies have explored potential associations between environmental exposures and brain alterations using neuroimaging. Most epidemiological studies assess the brain performance evaluating the cognitive function or the behaviour problems using neuropsychological tests or questionnaires. Experimental studies in humans showed both positive and negative cognitive effects after or during exposure to RF-EMF [33]–[36]. Moreover, several epidemiological studies have investigated the association between brain RF-EMF exposure using reported phone calls, the primary contributors of RF-EMF exposure to the brain [37], and cognitive function [19], [38]–[42]. Two studies did not observe any relationship of number of phone calls with speed of information processing [39] or minutes of phone calls with inattention [42] in children and preadolescents at 5-13 years of age. But other studies suggested that higher number of phone calls were related to poorer working memory [38], [40], poorer spatial and executive ability [41], and poorer cognitive flexibility [39] in children and preadolescents at 5-13 years of age. The association between number of phone calls and inhibitory control and visual recognition has also been investigated in previous studies and they showed mixed results in children and preadolescents at 5-13 years of age [19], [39]–[41]. Only one study has previously estimated the overall whole-brain RF-EMF dose received from several RF-EMF sources [43]–[45]. This study found that higher overall whole-brain RF-EMF dose was related to lower figural memory [43], [45] but not to concentration capacity [44] at ages between 12 and 17 years. Differences in results between studies might be related to methodological differences (e.g., exposure assessment approach, neuropsychological outcome assessed, or the age of assessment of the outcome of interest).

Scientific gaps

Several studies have found an association of the use of mobile communication devices with sleep and neurodevelopment. However, there are several unanswered questions remaining: i) whether the observed associations between mobile communication devices and sleep, and mobile communication devices and neurodevelopment in previous studies are due to the exposure to the emitted RF-EMF by mobile communication devices; ii) whether the exposure to RF-EMF impairs the morphology of the developing brain (e.g., brain volumes alterations); and iii) whether the evening and night are relevant windows of exposure when assessing associations between mobile communication devices, sleep, and neurodevelopment.

5 Objectives

The aims of this thesis are:

1. To assess the association between the use of mobile communication devices and sleep in adolescents (**Study I**)
2. To assess the association between estimated all-day and evening whole-brain RF-EMF doses and sleep in preadolescents (**Study II**)
3. To assess the association between estimated whole-brain and lobe-specific RF-EMF doses and brain volumes in preadolescents (**Study III**)
4. To assess the association between estimated whole-brain RF-EMF doses and cognitive function in preadolescents and adolescents (**Study IV**)

6 Methods

This section summarizes the design and study population, the RF-EMF exposure, the sleep, and the neurodevelopment assessments. A more detailed explanation is given in each study included in the results chapter.

Design and study population

This thesis included data from three population birth-based cohort studies: i) the Infancia y Medio Ambiente (INMA) Project including four sub-cohorts: Menorca, Valencia, Sabadell, and Gipuzkoa [46], ii) the Adolescent Brain Cognitive Development (ABCD) Study (www.abcd-study.nl), and iii) the Generation R Study [47]. These cohorts were selected because they had detailed information on RF-EMF exposure to the brain, and sleep or neurodevelopment assessments. Each cohort had different periods of recruitment in which pregnant women were invited to participate (Menorca, 1997-1998; Valencia, 2004-2005; Sabadell, 2004-2006; Gipuzkoa, 2006-2008; ABCD, 2003-2004; and Generation R, 2002-2006). Children were followed until 9-12 years old (i.e. preadolescents) in Valencia, Sabadell, Gipuzkoa, Generation R, and ABCD, and until 17-18 years old (i.e. adolescents) in Menorca. In **Study I**, we used data from Menorca. In **Study II**, we used data from Sabadell, Gipuzkoa, and Generation R. In **Study III**, we included only Generation R, and in **Study IV**, we used data from Menorca, Valencia, Sabadell, Gipuzkoa, and ABCD.

RF-EMF exposure

Personal mobile communication devices use

In **Study I, II, III,** and **IV**, information of the minutes of use of mobile communication devices was collected using maternal-reported questionnaires in preadolescents and self-reported questionnaires in adolescents. In **Study II, III,** and **IV**, this information was used to estimate all-day brain RF-EMF doses from personal mobile communication devices use close to the body (i.e. near-field sources). In **Study II**, we also estimated evening whole-brain RF-EMF doses using this information for use after 7 p.m. until falling asleep collected for 7 consecutive days with sleep diaries completed by preadolescents.

Environmental exposure

In **Study II, III,** and **IV**, we estimated RF-EMF exposure to different environmental or far-field RF-EMF sources (mobile phone base stations, FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) based on the microenvironments where preadolescents and adolescents spend most of their time such as home, school, commuting, and outdoors. To estimate RF-EMF exposure from mobile phone base stations at home, a validated 3D geospatial radio wave propagation model NISMap was used [48]–[51]. In **Study II**, we additionally assessed evening RF-EMF exposure using the estimations for the home.

RF-EMF exposure from mobile phone base stations in the other microenvironments besides home and RF-EMF exposure from the other far-field sources (FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) in all microenvironments was approximated using the average of the personal RF-EMF measurements of up to 72 hours [37].

Estimated brain RF-EMF doses

In **Study II, III,** and **IV**, we applied an integrative RF-EMF exposure model to estimate brain RF-EMF doses from several RF-EMF exposure sources [52]–[54]. This model is built using information on the personal use of mobile communication devices and estimations of exposure to environmental RF-EMF sources. Briefly, the model combines three types of information: i) the estimated ratio of the absorbed power to the mass in which it is absorbed of each specific RF-EMF source for each brain region, known as specific absorption rate (SAR, in Watts (W) / kilogram (kg)/ W), normalized to 1 W output power, ii) the output power of each RF-EMF source and activity (in W), and iii) the daily duration of use or exposure of each RF-EMF source and activity (in minutes (min)/day). First, for each brain region the model estimated a specific RF-EMF dose (millijoules (mJ)/kg/day) to each RF-EMF source (mobile phone calls, DECT phone calls, other mobile phone uses, tablet use, laptop use, and far-field RF-EMF sources). Second, RF-EMF sources were combined in three groups that lead to different exposure patterns to the brain: i) high RF-EMF doses from peak exposures very close to the head but for short periods of time (i.e. mobile and DECT phone calls), ii) low RF-EMF doses that might mainly represent non-RF-EMF factors related to the use of mobile communication devices (i.e. use of other mobile phone uses, tablet, and laptop while wirelessly connected to the internet), and iii) low RF-EMF doses received continuously throughout the day (i.e. far-field sources such as mobile phone base stations, FM radio and TV broadcast antennas, and WiFi). Third, we summed source-specific RF-EMF doses to obtain overall RF-EMF dose for each brain region. In **Study II**, we estimated overall and source-specific all-day and evening RF-EMF doses to the whole-brain. In **Study III**, we estimated overall and source-specific all-day RF-EMF doses to the whole-brain and to each brain lobe (frontal, parietal, temporal, and occipital). In **Study IV**, we estimated overall and source-specific all-day RF-EMF doses to the whole-brain.

In **Study I**, we did not estimate brain RF-EMF doses. We used mobile and DECT phone calls as proxy of RF-RMF exposure to the brain.

Sleep

Sleep disturbances

Sleep disturbances were assessed using validated sleep questionnaires. In **Study I**, the Pittsburgh Sleep Quality Index was self-reported by adolescents. In **Study II**, the Sleep Disturbance Scale for Children was maternal-reported.

Objective sleep measures

Preadolescents and adolescents wore accelerometers placed on their non-dominant wrist and completed a sleep diary for 7 consecutive days. In **Study I**, adolescents wore the ActiGraph wGT3X-BT and, in **Study II**, preadolescents wore the GENEActiv. Objective sleep measures included were total sleep time, sleep efficiency, sleep onset latency, and wake after sleep onset.

Neurodevelopment

Brain volumes

Preadolescents underwent a magnetic resonance imaging scan to assess brain volumes. Global metrics of cortical and subcortical volumes were extracted. In **Study III**, we included the volumes of the total brain, cortical gray matter, cortical white matter, cerebellar gray matter, and cerebellar white matter as global brain volumes. The volumes of frontal, parietal, temporal, and occipital lobes were included as cortical lobar volumes. The volumes of the hippocampus, amygdala, thalamus, putamen, caudate, nucleus accumbens, and pallidum were considered as subcortical volumes.

Cognitive function

In **Study IV**, cognitive function measured as non-verbal intelligence, speed of information processing, attentional function, cognitive flexibility, working memory, and semantic fluency were assessed in preadolescents or adolescents using a battery of validated neurocognitive tests.

References

[1] ITU, «Facts and figures 2019. Measuring digital development», 2019. [En línea]. Disponible en: https://itu.foleon.com/itu/measuring-digital-development/home/ (accessed june 2020).

[2] L. Hardell, «World Health Organization, radiofrequency radiation and health - a hard nut to crack (Review)», *Int. J. Oncol.*, vol. 51, n.º 2, pp. 405-413, ago. 2017, doi: 10.3892/ijo.2017.4046.

[3] T. Saliev, D. Begimbetova, A.-R. Masoud, y B. Matkarimov, «Biological effects of non-ionizing electromagnetic fields: Two sides of a coin», *Prog. Biophys. Mol. Biol.*, vol. 141, pp. 25-36, ene. 2019, doi: 10.1016/j.pbiomolbio.2018.07.009.

[4] International Commission on Non-Ionizing Radiation Protection (ICNIRP), «Guidelines for Limiting Exposure to Electromagnetic Fields (100 kHz to 300 GHz)»:, *Health Phys.*, vol. 118, n.º 5, pp. 483-524, may 2020, doi: 10.1097/HP.0000000000001210.

[5] R. D. Morris, L. L. Morgan, y D. Davis, «Children Absorb Higher Doses of Radio Frequency Electromagnetic Radiation From Mobile Phones Than Adults», *IEEE Access*, vol. 3, pp. 2379-2387, 2015, doi: 10.1109/ACCESS.2015.2478701.

[6] J. Wiart, A. Hadjem, M. F. Wong, y I. Bloch, «Analysis of RF exposure in the head tissues of children and adults», *Phys. Med. Biol.*, vol. 53, n.º 13, pp. 3681-3695, jul. 2008, doi: 10.1088/0031-9155/53/13/019.

[7] M. Eeftens *et al.*, «Personal exposure to radio-frequency electromagnetic fields in Europe: Is there a generation gap?», *Environ. Int.*, vol. 121, pp. 216-226, dic. 2018, doi: 10.1016/j.envint.2018.09.002.

[8] G. Medic, M. Wille, y M. Hemels, «Short- and long-term health consequences of sleep disruption», *Nat. Sci. Sleep*, vol. Volume 9, pp. 151-161, may 2017, doi: 10.2147/NSS.S134864.

[9] J. Owens, «Insufficient Sleep in Adolescents and Young Adults: An Update on Causes and Consequences», *PEDIATRICS*, vol. 134, n.º 3, pp. e921-e932, sep. 2014, doi: 10.1542/peds.2014-1696.

[10] S. Higuchi, Y. Nagafuchi, S. Lee, y T. Harada, «Influence of Light at Night on Melatonin Suppression in Children», *J. Clin. Endocrinol. Metab.*, vol. 99, n.º 9, pp. 3298-3303, sep. 2014, doi: 10.1210/jc.2014-1629.

[11] E. Bathory y S. Tomopoulos, «Sleep Regulation, Physiology and Development, Sleep Duration and Patterns, and Sleep Hygiene in Infants, Toddlers, and Preschool-Age Children», *Curr. Probl. Pediatr. Adolesc. Health Care*, vol. 47, n.º 2, pp. 29-42, feb. 2017, doi: 10.1016/j.cppeds.2016.12.001.

[12] B. Carter, P. Rees, L. Hale, D. Bhattacharjee, y M. S. Paradkar, «Association Between Portable Screen-Based Media Device Access or Use and Sleep Outcomes: A Systematic Review and Meta-analysis», *JAMA Pediatr.*, vol. 170, n.º 12, p. 1202, dic. 2016, doi: 10.1001/jamapediatrics.2016.2341.

[13] B. Lewczuk, G. Redlarski, A. Żak, N. Ziółkowska, B. Przybylska-Gornowicz, y M. Krawczuk, «Influence of Electric, Magnetic, and Electromagnetic Fields on the Circadian System: Current Stage of Knowledge», *BioMed Res. Int.*, vol. 2014, pp. 1-13, 2014, doi: 10.1155/2014/169459.

[14] A. A. Borbély, R. Huber, T. Graf, B. Fuchs, E. Gallmann, y P. Achermann, «Pulsed high-frequency electromagnetic field affects human sleep and sleep electroencephalogram», *Neurosci. Lett.*, vol. 275, n.º 3, pp. 207-210, nov. 1999.

[15] R. Huber *et al.*, «Exposure to pulsed high-frequency electromagnetic field during waking affects human sleep EEG», *Neuroreport*, vol. 11, n.º 15, pp. 3321-3325, oct. 2000.

[16] D. Henz, W. I. Schöllhorn, y B. Poeggeler, «Mobile Phone Chips Reduce Increases in EEG Brain Activity Induced by Mobile Phone-Emitted Electromagnetic Fields», *Front. Neurosci.*, vol. 12, p. 190, abr. 2018, doi: 10.3389/fnins.2018.00190.

[17] A. Lowden, R. Nagai, T. Åkerstedt, K. Hansson Mild, y L. Hillert, «Effects of evening exposure to electromagnetic fields emitted by 3G mobile phones on health and night sleep EEG architecture», *J. Sleep Res.*, vol. 28, n.º 4, p. e12813, ago. 2019, doi: 10.1111/jsr.12813.

[18] K. Parmar, R. Tandon, N. Kumar, y R. K. Garg, «Variations in electroencephalography with mobile phone usage in medical students», *Neurol. India*, vol. 67, n.º 1, pp. 235-241, feb. 2019, doi: 10.4103/0028-3886.253610.

[19] M. Redmayne *et al.*, «Use of mobile and cordless phones and cognition in Australian primary school children: a prospective cohort study», *Environ. Health Glob. Access Sci. Source*, vol. 15, p. 26, feb. 2016, doi: 10.1186/s12940-016-0116-1.

[20] X. Jiang, L. L. Hardy, L. A. Baur, D. Ding, L. Wang, y H. Shi, «Sleep duration, schedule and quality among urban Chinese children and adolescents: associations with routine after-school activities», *PloS One*, vol. 10, n.º 1, p. e0115326, 2015, doi: 10.1371/journal.pone.0115326.

[21] V. C. Brunetti, E. K. O'Loughlin, J. O'Loughlin, E. Constantin, y É. Pigeon, «Screen and nonscreen sedentary behavior and sleep in adolescents», *Sleep Health*, vol. 2, n.º 4, pp. 335-340, dic. 2016, doi: 10.1016/j.sleh.2016.09.004.

[22] Y. W. Mak *et al.*, «Association between screen viewing duration and sleep duration, sleep quality, and excessive daytime sleepiness among adolescents in Hong Kong», *Int. J. Environ. Res. Public. Health*, vol. 11, n.º 11, pp. 11201-11219, oct. 2014, doi: 10.3390/ijerph111111201.

[23] R. Durusoy, H. Hassoy, A. Özkurt, y A. O. Karababa, «Mobile phone use, school electromagnetic field levels and related symptoms: a cross-sectional survey among 2150 high school students in Izmir», *Environ. Health*, vol. 16, n.º 1, dic. 2017, doi: 10.1186/s12940-017-0257-x.

[24] S. Liu, Y. K. Wing, Y. Hao, W. Li, J. Zhang, y B. Zhang, «The associations of long-time mobile phone use with sleep disturbances and mental distress in technical college students: a prospective cohort study», *Sleep*, vol. 42, n.º 2, feb. 2019, doi: 10.1093/sleep/zsy213.

[25] A. Cabré-Riera, M. Torrent, D. Donaire-Gonzalez, M. Vrijheid, E. Cardis, y M. Guxens, «Telecommunication devices use, screen time and sleep in adolescents», *Environ. Res.*, vol. 171, pp. 341-347, abr. 2019, doi: 10.1016/j.envres.2018.10.036.

[26] G. Berg-Beckhoff *et al.*, «Mobile phone base stations and adverse health effects: phase 2 of a cross-sectional study with measured radio frequency electromagnetic fields», *Occup. Environ. Med.*, vol. 66, n.º 2, pp. 124-130, feb. 2009, doi: 10.1136/oem.2008.039834.

[27] C. A. Czeisler y T. L. Shanahan, «Problems Associated With Use of Mobile Devices in the Sleep Environment—Streaming Instead of Dreaming», *JAMA Pediatr.*, vol. 170, n.º 12, p. 1146, dic. 2016, doi: 10.1001/jamapediatrics.2016.2986.

[28] J. He, Z. Tu, L. Xiao, T. Su, y Y. Tang, «Effect of restricting bedtime mobile phone use on sleep, arousal, mood, and working memory: A randomized pilot trial», *PLOS ONE*, vol. 15, n.º 2, p. e0228756, feb. 2020, doi: 10.1371/journal.pone.0228756.

[29] S. Lemola, N. Perkinson-Gloor, S. Brand, J. F. Dewald-Kaufmann, y A. Grob, «Adolescents' Electronic Media Use at Night, Sleep Disturbance, and Depressive Symptoms in the Smartphone Age», *J. Youth Adolesc.*, vol. 44, n.º 2, pp. 405-418, feb. 2015, doi: 10.1007/s10964-014-0176-x.

[30] C. J. Calamaro, T. B. A. Mason, y S. J. Ratcliffe, «Adolescents Living the 24/7 Lifestyle: Effects of Caffeine and Technology on Sleep Duration and Daytime Functioning», *PEDIATRICS*, vol. 123, n.º 6, pp. e1005-e1010, jun. 2009, doi: 10.1542/peds.2008-3641.

[31] A. D. Fobian, K. Avis, y D. C. Schwebel, «Impact of Media Use on Adolescent Sleep Efficiency», *J. Dev. Behav. Pediatr. JDBP*, vol. 37, n.º 1, pp. 9-14, ene. 2016, doi: 10.1097/DBP.0000000000000239.

[32] D. Rice y S. Barone, «Critical periods of vulnerability for the developing nervous system: evidence from humans and animal models», *Environ. Health Perspect.*, vol. 108 Suppl 3, pp. 511-533, jun. 2000.

[33] E. Valentini, M. Ferrara, F. Presaghi, L. D. Gennaro, y G. Curcio, «Systematic review and meta-analysis of psychomotor effects of mobile phone electromagnetic fields», *Occup. Environ. Med.*, vol. 67, n.º 10, pp. 708-716, oct. 2010, doi: 10.1136/oem.2009.047027.

[34] A. Verrender, S. P. Loughran, A. Dalecki, R. McKenzie, y R. J. Croft, «Pulse modulated radiofrequency exposure influences cognitive performance», *Int. J. Radiat. Biol.*, vol. 92, n.º 10, pp. 603-610, oct. 2016, doi: 10.1080/09553002.2016.1213454.

[35] A. Barth, I. Ponocny, T. Gnambs, y R. Winker, «No effects of short-term exposure to mobile phone electromagnetic fields on human cognitive performance: A meta-analysis», *Bioelectromagnetics*, vol. 33, n.º 2, pp. 159-165, feb. 2012, doi: 10.1002/bem.20697.

[36] Z. Vecsei, B. Knakker, P. Juhász, G. Thuróczy, A. Trunk, y I. Hernádi, «Short-term radiofrequency exposure from new generation mobile phones reduces EEG alpha power with no effects on cognitive performance», *Sci. Rep.*, vol. 8, n.º 1, dic. 2018, doi: 10.1038/s41598-018-36353-9.

[37] L. E. Birks *et al.*, «Spatial and temporal variability of personal environmental exposure to radio frequency electromagnetic fields in children in Europe», *Environ. Int.*, vol. 117, pp. 204-214, ago. 2018, doi: 10.1016/j.envint.2018.04.026.

[38] S. Thomas *et al.*, «Use of mobile phones and changes in cognitive function in adolescents», *Occup. Environ. Med.*, vol. 67, n.º 12, pp. 861-866, dic. 2010, doi: 10.1136/oem.2009.054080.

[39] M. Guxens *et al.*, «Outdoor and indoor sources of residential radiofrequency electromagnetic fields, personal cell phone and cordless phone use, and cognitive function in 5–6 years old children», *Environ. Res.*, vol. 150, pp. 364-374, oct. 2016, doi: 10.1016/j.envres.2016.06.021.

[40] M. J. Abramson *et al.*, «Mobile telephone use is associated with changes in cognitive function in young adolescents», *Bioelectromagnetics*, vol. 30, n.º 8, pp. 678-686, dic. 2009, doi: 10.1002/bem.20534.

[41] C. R. Bhatt *et al.*, «Use of mobile and cordless phones and change in cognitive function: a prospective cohort analysis of Australian primary school children», *Environ. Health*, vol. 16, n.º 1, dic. 2017, doi: 10.1186/s12940-017-0250-4.

[42] F. Zheng *et al.*, «Association between mobile phone use and inattention in 7102 Chinese adolescents: a population-based cross-sectional study», *BMC Public Health*, vol. 14, p. 1022, oct. 2014, doi: 10.1186/1471-2458-14-1022.

[43] A. Schoeni, K. Roser, y M. Röösli, «Memory performance, wireless communication and exposure to radiofrequency electromagnetic fields: A prospective cohort study in adolescents», *Environ. Int.*, vol. 85, pp. 343-351, dic. 2015, doi: 10.1016/j.envint.2015.09.025.

[44] K. Roser, A. Schoeni, y M. Röösli, «Mobile phone use, behavioural problems and concentration capacity in adolescents: A prospective study», *Int. J. Hyg. Environ. Health*, vol. 219, n.º 8, pp. 759-769, nov. 2016, doi: 10.1016/j.ijheh.2016.08.007.

[45] M. Foerster, A. Thielens, W. Joseph, M. Eeftens, y M. Röösli, «A Prospective Cohort Study of Adolescents' Memory Performance and Individual Brain Dose of Microwave Radiation from Wireless Communication», *Environ. Health Perspect.*, vol. 126, n.º 7, p. 077007, jul. 2018, doi: 10.1289/EHP2427.

[46] M. Guxens *et al.*, «Cohort Profile: The INMA—INfancia y Medio Ambiente—(Environment and Childhood) Project», *Int. J. Epidemiol.*, vol. 41, n.º 4, pp. 930-940, ago. 2012, doi: 10.1093/ije/dyr054.

[47] M. N. Kooijman *et al.*, «The Generation R Study: design and cohort update 2017», *Eur. J. Epidemiol.*, vol. 31, n.º 12, pp. 1243-1264, dic. 2016, doi: 10.1007/s10654-016-0224-9.

[48] A. Bürgi *et al.*, «A model for radiofrequency electromagnetic field predictions at outdoor and indoor locations in the context of epidemiological research», *Bioelectromagnetics*, p. n/a-n/a, 2009, doi: 10.1002/bem.20552.

[49] J. Beekhuizen, R. Vermeulen, H. Kromhout, A. Bürgi, y A. Huss, «Geospatial modelling of electromagnetic fields from mobile phone base stations», *Sci. Total Environ.*, vol. 445-446, pp. 202-209, feb. 2013, doi: 10.1016/j.scitotenv.2012.12.020.

[50] J. Beekhuizen *et al.*, «Modelling indoor electromagnetic fields (EMF) from mobile phone base stations for epidemiological studies», *Environ. Int.*, vol. 67, pp. 22-26, jun. 2014, doi: 10.1016/j.envint.2014.02.008.

[51] A. Huss *et al.*, «Environmental Radiofrequency Electromagnetic Fields Exposure at Home, Mobile and Cordless Phone Use, and Sleep Problems in 7-Year-Old Children», *PLOS ONE*, vol. 10, n.º 10, p. e0139869, oct. 2015, doi: 10.1371/journal.pone.0139869.

[52] Ilaria Liorni, «Approximation Formulas for Evaluation of Specific Absorption Rate in the Far-Field, Near-to-Far Field and Near-Field Regions for Integrative Radiofrequency Exposure Assessment in Epidemiological Studies (under review)».

[53] Luuk van Wel, «Organ-specific integrative exposure assessment: Radio-frequency electromagnetic field exposure and contribution of sources in the general population (under review)».

[54] L. E. Birks *et al.*, «Radiofrequency Electromagnetic Fields from Mobile Communication: Description of Modeled Dose in Brain Regions and the Body in European Children and Adolescents (under review)».

7 Results

In this section, the following studies are presented:

Study I: Telecommunication devices use, screen time, and sleep in adolescents

Study II: Estimated all-day and evening whole-brain radiofrequency electromagnetic fields doses and sleep in preadolescents

Study III: Estimated whole-brain and lobe-specific RF-EMF doses and brain volumes in preadolescents

Study IV: Association between estimated whole-brain RF-EMF doses and cognitive function in preadolescents and adolescents

Study I: Telecommunication devices use, screen time, and sleep in adolescents

Cabré-Riera, A., Torrent, M., Donaire-Gonzalez, D., Vrijheid, M., Cardis, E., Guxens, M., 2019. Telecommunication devices use, screen time and sleep in adolescents. Environmental Research 171, 341–347. https://doi.org/10.1016/j.envres.2018.10.036

Abstract

Purpose: To investigate the association between telecommunication and other screen devices and subjective and objective sleep measures in adolescents at 17-18 years.

Methods: Cross-sectional study on adolescents aged 17-18 years from a Spanish population-based birth cohort established in Menorca in 1997-1998. Information on devices use was collected using self-reported questionnaires. Mobile Phone Problematic Use Scale was used to assess mobile phone use dependency. Pittsburgh Sleep Quality Index was used to assess subjective sleep (n=226). ActiGraph wGT3X-BT for 7 nights was used to assess objective sleep (n=110).

Results: One or more cordless phone calls/week was associated with a lower sleep quality [Prevalence Ratio PR 1.30 (95%CI 1.04; 1.62)]. Habitual and frequent problematic mobile phone use was associated with a lower sleep quality [PR 1.55 (95%CI 1.03; 2.33) and PR 1.67 (95%CI 1.09; 2.56), respectively]. Higher tablet use was associated with decreased sleep efficiency and increased minutes of wake time after sleep onset [β -1.15 (95%CI -1.99; -0.31) and β 7.00 (95%CI 2.40; 11.60) per increase of 10 minutes/day of use, respectively]. No associations were found between other devices and sleep measures.

Conclusions: Tablet use, mobile phone use dependency, and frequency of cordless phone were related to an increase of subjective and objective sleep problems in adolescents. These results seem to indicate that sleep displacement, mental arousal, and exposure to blue light emission might play a more important role on sleep than a high RF-EMF exposure to the brain. However, more studies are needed assessing personal RF-EMF levels to draw conclusions.

Introduction

Adequate sleep is necessary for optimal daytime functioning [1]. Adolescents' sleep patterns are determined by maturational changes, often incompatible with societal demands which lead to insufficient sleep. Poor sleep affects around 25–40% adolescents [2], and has been associated with several health related problems [1].

The use of telecommunication and other screen devices, including both passive devices (e.g. television) and interactive devices (e.g. phones, tablets, computers, laptops, or videogame consoles) are detrimental to sleep [3]. Two potential mechanisms have been suggested to explain these associations: i) through the devices use itself (e.g. sleep displacement, mental arousal, and blue light screen emission), and ii) through the exposure to radiofrequency electromagnetic fields (RF-EMF) [3], [4].

Previous studies have related higher use of television to delayed bedtimes and short self-reported sleep duration in children at 4-18 years [3]. Recent studies also found an association between the use of interactive devices and shorter self-reported sleep duration [5]–[11]. However, little is known about the association between the use of these devices and sleep measures other than self-reported sleep duration, and to what extend the timing of their use (daytime vs. bedtime) is relevant. Only two studies have assessed objective sleep measures using actigraphy in adolescents and young adults [8], [11]. Higher mobile phone, television, videogame console, and computer use during bedtime was related to decreased sleep efficiency in adolescents at 14-15 years [8], whereas daytime and bedtime use of mobile phone was not associated with objective sleep measures, while it was associated with subjective sleep in young adults at 18-22 years [11]. Actigraphy provides information on sleep patterns in participants' natural sleep environment and avoids inaccurate findings due to potential information bias in self-reported questionnaires [12].

Therefore, the aim of the present study is to assess the association between the use of telecommunication and other screen devices and subjective and objective sleep measures in adolescents at 17-18 years of age.

Methods

Study design and population

The INMA Project is a population-based prospective birth cohort study established in seven Spanish regions following a common protocol approved by an ethics committee [13]. This analysis uses data from the INMA region of Menorca, a Balearic island in the north western Mediterranean Sea in Spain. A total of 492 mothers seeking antenatal care were recruited in 1997-1998. Children were periodically assessed from birth until 17-18 years. Adolescents with data on at least one device use and one sleep measure at 17-18 years were included (258, 52.4% of the original cohort) (See Supplementary Figure S1). Among the included adolescents, 226 had Pittsburgh Sleep Quality Index data (subjective sleep measures) and 110 had actigraphy data (objective sleep measures).

Telecommunication devices use and screen time

Information on telecommunication devices use was collected with self-reported questionnaires at 17-18 years [14]. Frequency of mobile and cordless phone calls was categorized in no calls, less than 1 call/week, or 1 call/week or more based on the distribution of phone calls variables in our study population. Duration of mobile and cordless phone calls was collected in minutes/day. A short-version of the validated Mobile Phone Problematic Use Scale (MPPUS-10) [15] was used to assess problematic mobile phone use, a measure of mobile phone dependency, and categorized into occasional (<15th percentile), habitual (15th-80th percentile), and frequent (>80thpercentile) problematic use based in a previous study [16]. Duration of other mobile phone uses (i.e. phone use excluding calls and including texting and internet use) and of use of tablets, and laptops was collected in minutes/day. Information on other screen devices use (videogame consoles and television) was self-reported and collected in minutes/day. Total screen time was calculated by summing the duration of use of all devices, except phone use for calls. Information on the presence of a television in the adolescents' bedroom was collected. Bedtime use was assessed and categorized into <1 time/week or ≥1 time/week. Night time use was collected by "Do you normally wake up by any device at night?" and categorized into no (hardly ever) and yes (≥1 time/week).

Subjective and objective sleep measures

Adolescents completed the Pittsburgh Sleep Quality Index (PSQI) [17] when they were 17-18 years (n=226). It is a validated self-reported questionnaire that consists of 19 items which quantify sleep quality over the past month. The items are grouped into seven subscales evaluating different sleep difficulties: sleep quality (very good, good, bad, very bad), daytime sleepiness (no, low, medium, high), sleep disturbances (no, low, medium, high), sleep duration (≥7h, <7-≥6h, <6-≥5, <5h), total sleep efficiency (≥85%, <84.9%-≥75%, 65%-74.9%, <65%), sleep latency (no, low, medium, high), and sleep medication (no, yes). Total score was calculated adding the seven subscales and higher score indicates poorer sleep.

Subjects wore an ActiGraph wGT3X-BT placed on their non-dominant wrist for seven consecutive days and completed a sleep diary. Nights with movement artifacts and other technical failures were removed and subjects with data on at least one entire night (mean=6 nights, interquartile range=6-7) were included and analysed using the Actilife software version 6.11.9. Subjects who wore the accelerometer and could be included were 110 (70% of the initial sample) [18]. Objective sleep measures included total sleep time (time between falling asleep and final awakening from which the time spent awake in between is subtracted), sleep efficiency (total sleep time divided by total time in bed, in %), sleep onset latency (time between lying down in bed and falling asleep), and wake after sleep onset (time awake between falling asleep and final awakening).

Potential confounding variables

In order to decide a priori which potential confounding variables needed to be included in our models, we drew a direct acyclic graph (DAG) according to current knowledge from the scientific literature (See Supplementary Material, Figure S2). Maternal and paternal social class based on occupation, maternal and paternal education level based on the Spanish education system, and maternal age were obtained with questionnaires completed by the mother during pregnancy and at child's birth. Adolescents' characteristics and lifestyle variables (sex, age, body mass index (normal weight (<25kg/m^2), overweight (25-30 kg/m^2), obese (>30 kg/m^2)), hours of physical activity per week (no, <4 hours, 4-6 hours, >6 hours), caffeinated drinks intake, and tobacco consumption), adolescents' current working situation (working and/or studying), adolescents' bedroom size (number of people sleeping in the adolescent's bedroom), household size (number of people living in the house), and family structure (living with mother and father, only mother or father, others) were collected from a self-reported questionnaire at 17-18 years. Chronotype was assessed with the question: "Do you consider yourself a morning or an evening type person?" from the validated Munich

ChronoType Questionnaire [19]. Adolescents' self-perceived health-related quality of life was assessed using the validated Kidscreen-27 [20] which contains five subscales: physical well-being, psychological well-being, financial autonomy and parents relation, peers and social support, and school environment. Higher scores indicate better quality of life.

Statistical analysis

Among adolescents with available data on at least one device use and one sleep measure (n=258), we performed multiple imputation of missing potential confounding variables using chained equations where 25 completed datasets were generated and analysed (Table S1). The percentage of missing values was <8.5% depending on the variable and distributions in imputed datasets were very similar to those observed (data not shown). Adolescents not included in the study due to lost to follow-up (n=224) were more likely to have parents from lower socioeconomic status compared to those included (n=258) (See Supplementary Material, Table S2). Thus, we performed inverse probability weighting to correct for lost to follow-up, i.e. to account for potential bias when including only participants with available data as compared to the full cohort recruited at pregnancy. The variables used to create these weights are in Supplementary Tables S3.

Poisson regression models with robust variance were used to examine the association between use of each device and sleep quality (very good vs. good/bad/very bad), daytime sleepiness (no/low vs. medium/high), sleep disturbances (no vs. low/medium/high), sleep duration (≥7h vs. <7h), sleep efficiency (≥85% vs. <85%), and sleep latency (no/low vs. medium/high). We could not analyze sleep medication subscale because only 1% of the adolescents reported to take medication to sleep. Prevalence ratios (PR) were calculated instead of odd ratios due to the potential overestimation of the odd ratios when the prevalence of the outcome is high (>10%) in cross-sectional studies [21]. Linear regression models were used to assess the association between use of each device and PSQI total score, and each objective sleep measure (total sleep time, sleep efficiency, sleep onset latency, and wake time after sleep onset). Models were adjusted for all potential confounding variables described previously. All analyses were performed using Stata version 14 (StataCorp, College Station, Texas, USA).

Results

Adolescents' characteristics are described in Table 1. Adolescents reported a higher frequency of calls with the mobile phone than the cordless phone (e.g. 60.2% vs. 26.9% for >1 call/week, respectively) and 23.2% reported frequent problematic mobile phone use (Table 2). On average, adolescents reported spending 3 hours and 30 minutes per day in a screen activity; television was the device with longest duration. Around 87.1% of the adolescents reported using a device before going to sleep at least once per week and 90.0% reported not to wake up by any device at night. Relationships between devices use variables are shown in Supplementary Material, Table S4 and Table S5.

Only 31.4% of adolescents reported having a very good sleep quality while around 10% reported bad or very bad sleep quality (Table 3). On average adolescents went to bed at 11:56 pm and woke up at 7:57 am. Adolescents woke up 3 hours later in weekend days compared to weekdays (10:00 am vs. 7:00 am, respectively). Mean adolescents' amount of sleep was 6 hours 48 minutes, sleep efficiency was 83.6%, sleep onset latency was 7 minutes, and wake time after sleep onset was 1 hour 11 minutes, with little difference between week days and weekends. Daytime sleepiness was positively correlated with sleep quality (0.34) and negatively correlated with total sleep time (-0.14) (See Supplementary Material, Table S6). Objective sleep measures showed a low correlation with subjective sleep measures (<0.22). Distribution of adolescents' characteristics and their association with subjective and objective sleep measures are shown in Supplementary Material, Table S7 and Table S8.

Adolescents with habitual or frequent problematic mobile phone use were more likely to have a lower sleep quality compared to those with occasional problematic mobile phone use [PR 1.55 (95%CI 1.03; 2.33) and PR 1.67 (95%CI 1.09; 2.56), respectively] (Table 4). Adolescents who reported making one or more cordless phone calls per week were more likely to have a lower sleep quality compared to those who did not make cordless phone calls [PR 1.30 (95%CI 1.04; 1.62)]. No clear associations were found between daytime or bedtime use of other devices and subjective sleep measures (See Supplementary Material, Table S9).

Longer use of tablets was related to decreased sleep efficiency and increased number of minutes of wake time after sleep onset [β -1.15 (95%CI -1.99; -0.31) and β 7.00 (95%CI 2.40; 11.60) per Δ10 minutes/day of use, respectively] (Table 4). No clear associations were found between daytime or bedtime use of other devices and objective sleep measures.

Table 1. Distribution of adolescents and family characteristics (n=258).

Adolescents' characteristics and lifestyle		
Sex (female vs. male)		52.3
Age		17.6 (0.2)
Body mass index	Normal weight	83.9
	Overweight	11.8
	Obese	4.3
Physical activity	No	4.1
	< 4 hours/week	37.0
	4-6 hours/week	21.9
	>6 hours/week	37.0
Caffeinated drinks intake	≤1 drink/week	46.5
	2-4 drinks/week	18.5
	≥5 drinks/week	35.0
Tobacco consumption	Never	71.1
	Yes, but not every day	16.6
	Every day	12.3
Chronotype	Morningness	23.1
	Intermediate	16.3
	Eveningness	60.6
Adolescents' current working situation		
	Only working	7.0
	Only studying	47.3
	Studying and working	45.7
Adolescents' self-perceived health-related quality of life		
Physical well-being		43.1 (9.3)
Psychological well-being		35.7 (3.2)
Financial autonomy and parents relation		50.8 (8.7)
Social support and peers		52.8 (8.5)
School environment		49.4 (8.4)
Adolescents' bedroom environment		
Bedroom size	1 person	86.06
	≥2 persons	13.94
Adolescents' family characteristics		
Household size	1-2 persons	7.8
	3 persons	36.4
	≥4 persons	55.8
Family structure	Living with mother and father	74.4
	mother or father	15.7
	others	9.9
Maternal educational level	University	16.4
	Secondary	32.0
	Primary or lower	51.6
Paternal educational level	University	9.8
	Secondary	27.2
	Primary or lower	63.0
Maternal social class	I/II managers/technicians	15.1
	IIIa/IIIb skilled non-manual and manual	41.1
	IV/V semiskilled/unskilled	8.5
	Unemployed or housewife	35.3
Paternal social class	I/II managers/technicians	19.1
	IIIa/IIIb skilled non-manual and manual	63.4
	IV/V semiskilled/unskilled	10.9
	Unemployed	6.6

Values are percentages for categorical variables and mean (SD) for continuous variables

Table 2. Distribution of telecommunication and other screen devices use (n=258).

Daytime use		
Mobile phone calls		
Frequency	No calls	7.5
	≤ 1 call/week	32.3
	> 1 call/week	60.2
Duration	time/day	2 min (0.7min - 5.7min)
Problematic mobile phone use		
	Occasional	14.2
	Habitual	62.6
	Frequent	23.2
Cordless phone calls		
Frequency	No calls	46.1
	≤ 1 call/week	27.0
	> 1 call/week	26.9
Duration	time/day	2 min (1min - 5min)
Screen time		
Mobile phone use excluding phone calls	Yes vs. no	89.5
	time/day of the users	0h 30min (11min -1h 02min)
Tablet	Yes vs. no	21.5
	time/day of the users	0h 30min (15min -0h 42min)
Laptop	Yes vs. no	67.3
	time/day of the users	1h 08min (30min -2h 15min)
Video game console	Yes vs. no	19.9
	time/day of the users	0h 39min (17min -1h 17min)
Television	Yes vs. no	97.6
	time/day of the users	1h 15min (45min -2h 04min)
Total screen time	time/day	3h 04min (1h 37min -4h 38min)
Bedtime and night time use		
Television in adolescents' bedroom	Yes vs. No	30.4
Telecommunication and screen devices use before going to sleep	≥1 time/week vs. <1 time/week	87.1
Do you normally wake up by any device?	Yes vs. No	10.0

Percentage for categorical variables and median (interquartile range) for continuous variables.

Table 3. Distribution of sleep measures.

Subjective sleep measures (n=226)			
Sleep quality, %	Very good	31.4	
	Good	58.0	
	Bad	9.8	
	Very bad	0.8	
Total score		5.0 (4.0-7.0)	
Objective sleep measures (n=110)			
	Total week	**Weekdays**	**Weekend days**
Bedtime	11:56 pm (11:23 pm-00:26 am)	11:30 pm (11:00 pm-00:30 am)	01:00 am (00:00 am-01:30 am)
Wake-up time	07:57 am (07:32 am-08:35 am)	07:00 am (06:50 am-07:30 am)	10:00 am (09:00 am-10:30 am)
Sleep duration	6h 48min (6h 18min -7h 11min)	6h 39min (6h 09min - 7h 10min)	7h 09min (6h 22min - 07h 57min)
Sleep efficiency, %	83.6 (79.2-86.9)	83.7 (79.2 - 88.2)	81.6 (76.7 - 87.4)
Sleep onset latency	07min 17s (04min 09s -12min 26s)	6min 55s (2min 45s -12min 24s)	7min 30s (0min 0s - 12min 00s)
Wake after sleep onset	1h 11min (0h 56min -1h 40min)	1h 08min (0h 47min -1h 30min)	1h 29min (0h 58min - 1h 53min)

Percentage for categorical variables and median (interquartile range) for continuous variables.

Table 4. Adjusted association between telecommunication and other screen devices use and subjective and objective sleep measures in adolescents at 17-18 years old.

		Subjective sleep measures (n=226)		Objective sleep measures (n=110)			
		Total score β (CI 95%)	Sleep quality (very good vs. good/ bad/very bad) PR (CI 95%)	Total Sleep Time (in minutes) β (CI 95%)	Sleep efficiency (%) β (CI 95%)	Sleep onset latency (in minutes) β (CI 95%)	Wake after sleep onset (in minutes) β (CI 95%)
Mobile phone calls							
Frequency	No calls	0		0	0	0	0
	< 1 call/week	0.05 (-1.17;1.27)	1.13 (0.62; 2.06)	10.71 (-26.55; 47.96)	4.48 (-1.16; 10.13)	1.64 (-4.95; 8.24)	-26.85 (-57.96; 4.25)
	≥1 call/week	0.07 (-1.10;1.25)	1.58 (0.90; 2.78)	2.45 (-35.94; 40.84)	2.01 (-3.82; 7.83)	1.83 (-4.95; 8.60)	-14.20 (-46.27; 17.87)
Duration (per Δ1 minute/day)		-0.01 (-0.01;0.01)	1.00 (0.99; 1.01)	-0.01 (-0.34; 0.31)	-0.02 (-0.08; 0.03)	0.01 (-0.05; 0.07)	0.14 (-0.13; 0.41)
Problematic mobile phone use							
	Occasional	0	1		0	0	0
	Habitual	0.75 (-0.13;1.64)	**1.55 (1.03; 2.33)**	8.58 (-16.30; 33.46)	0.47 (-3.34; 4.27)	-2.82 (-7.20; 1.56)	5.46 (-15.51; 26.44)
	Frequent	0.64 (-0.40; 1.68)	**1.67 (1.09; 2.56)**	14.89 (-14.96; 44.74)	0.43 (-4.14; 4.99)	-2.21 (-7.45; 3.03)	4.07 (-21.15; 29.30)
Cordless phone calls							
Frequency	No calls	0			0	0	0
	< 1 call/week	0.42 (-0.27;1.13)	1.22 (0.98; 1.52)	-1.71 (-20.49; 17.08)	-1.39 (-4.23; 1.44)	0.04 (-3.30; 3.38)	8.38 (-7.26; 24.03)
	≥1 call/week	0.28 (-0.43;0.99)	**1.30 (1.04; 1.62)**	4.09 (-16.74; 24.92)	0.55 (-2.60; 3.70)	0.33 (-3.41; 4.07)	-3.06 (-20.46; 14.35)
Duration (per Δ1 minute/day)		-0.03 (-0.08;0.02)	1.00 (0.97; 1.03)	0.25 (-2.35; 2.84)	0.07 (-0.36; 0.49)	-0.19 (-0.57; 0.19)	-0.20 (-2.64; 2.24)

PR = prevalence ratio, β = beta coefficient. IC 95% = 95% confidence interval. Models adjusted for maternal and paternal social class, maternal and paternal education level, maternal age, adolescents' characteristics and lifestyle variables (sex, age, body mass index, hours of physical activity per week, caffeinated drinks intake, tobacco consumption), adolescents' current working situation (working and/or studying), adolescents' bedroom size, household size, and family structure, adolescent's chronotype, adolescents' self-perceived health-related quality of life (physical well-being, autonomy and parents, peers and social support, psychological well-being, and school environment). **Bold:** p-value<0.05.

Table 4 continuation. Adjusted association between telecommunication and other screen devices use and subjective and objective sleep measures in adolescents at 17-18 years old.

	Subjective sleep measures (n=226)		Objective sleep measures (n=110)			
	Total score β (CI 95%)	**Sleep quality (low vs. high) PR (CI 95%)**	**Total Sleep Time (in minutes) β (CI 95%)**	**Sleep efficiency (%) β (CI 95%)**	**Sleep onset latency (in minutes) β (CI 95%)**	**Wake after sleep onset (in minutes) β (CI 95%)**
Screen time						
Mobile phone use excluding phone calls (per Δ10 minutes/day)	-0.01 (-0.049;0.022)	0.99 (0.98; 1.00)	0.35 (-0.41; 1.11)	0.02 (-0.09; 0.14)	0.06 (-0.07; 0.20)	-0.11 (-0.76; 0.54)
Tablet (per Δ10 minutes/day)	0.01 (-0.196;0.206)	1.00 (0.95; 1.06)	-1.15 (-6.84; 4.55)	**-1.15 (-1.99; -0.31)**	0.23 (-0.78; 1.25)	**7.00 (2.40; 11.60)**
Laptop (per Δ10 minutes/day)	0.01 (-0.026;0.031)	1.00 (0.99; 1.01)	0.31 (-0.85; 1.46)	0.06 (-0.11; 0.24)	-0.03 (-0.23; 0.18)	-0.33 (-1.31; 0.64)
Video game console (per Δ10 minutes/day)	0.01 (-0.094;0.121)	1.02 (0.99; 1.05)	0.84 (-2.51; 4.19)	-0.14 (-0.65; 0.37)	0.13 (-0.46; 0.73)	0.61 (-2.22; 3.44)
Television (per Δ30 minutes/day)	-0.07 (-0.223;0.083)	0.98 (0.93; 1.03)	2.78 (-1.32; 6.88)	0.04 (-0.60; 0.67)	-0.38 (-1.12; 0.36)	0.45 (-3.06; 3.95)
Total screen time (per Δ30 minutes/day)	-0.02 (-0.072;0.040)	0.99 (0.97; 1.01)	1.11 (-0.43; 2.65)	0.04 (-0.20; 0.28)	0.03 (-0.24; 0.31)	-0.08 (-1.40; 1.24)
Television in adolescents' bedroom						
Yes vs. no	0.269 (-0.408; 0.947)	1.04 (0.85; 1.28)	4.08 (-15.91; 24.08)	-0.17 (-3.21; 2.87)	-0.18 (-3.72; 3.37)	0.43 (-16.44; 17.30)
Telecommunication and screen devices use before going to sleep						
<1 time/week vs. ≥1 time/week	0.813 (-0.209;1.834)	1.02 (0.74; 1.41)	-0.51 (-32.86; 31.84)	3.51 (-1.52; 8.53)	-0.62 (-6.29; 5.05)	-22.31 (-49.88; 5.27)

PR = prevalence ratio, β = beta coefficient. IC 95% = 95% confidence interval. Models adjusted for maternal and paternal social class, maternal and paternal education level, maternal age, adolescents' characteristics and lifestyle variables (sex, age, body mass index, hours of physical activity per week, caffeinated drinks intake, tobacco consumption), adolescents' current working situation (working and/or studying), adolescents' bedroom size, household size, and family structure, adolescent's chronotype, adolescents' self-perceived health-related quality of life (physical well-being, autonomy and parents, peers and social support, psychological well-being, and school environment). **Bold:** p-value<0.05.

Discussion

We investigated the association between the use of telecommunication and other screen devices and subjective and objective sleep measures in adolescents at 17-18 years. Higher frequency of cordless phone calls was associated with lower sleep quality. Higher tablet use was related to decreased sleep efficiency and increased wake time after sleep onset, and problematic mobile phone use was associated with lower sleep quality. Daytime use of other devices was not associated with any subjective or objective sleep variable and bedtime use was not associated with any sleep variable. In addition, objective sleep measures including wake time after sleep onset and sleep efficiency were below the recommended values, which are ≤40 minutes and ≥85%, respectively, in adolescents [1]. The gap of three hours of wakeup times between weekdays and weekend days suggests a sleep debt on weekdays.

Strengths of this study are: i) the assessment of multiple devices, looking at daytime and bedtime use; ii) the classification of devices use variables in different groups to try to disentangle between the two different potential mechanisms described in the literature that can be behind the studied association; and iii) the assessment of sleep using objective measures (i.e. actigraphy in the wrist) for a full week in 110 adolescents, which represents a larger sample compared to previous studies [8], [11].

Our study has some limitations. Due to its cross-sectional design we cannot discard the possibility of reverse causality meaning that adolescents with sleep problems could have a higher use of telecommunication devices and longer screen times. Although we do not expect our findings on the cordless phone use for calling to be affected by reverse causality, reverse causality could affect the findings on problematic mobile phone use and tablet use since adolescents often use these devices as a sleep aid before going to sleep [22]. This practice may exacerbate existing sleep problems as previous studies have shown a relationship between bedtime use and short sleep duration, long sleep onset latency, and decreased sleep efficiency [7], [23]. We did not find an association between bedtime use and sleep measures. This could be due to the low statistical power to detect an association since the majority of adolescents (87%) regularly used a device during bedtime. As we did not observed an association between willingness to use actigraph and use of telecommunication and other screen devices (data not shown), the sample and the results of the objective sleep measures analysis do not seem to be biased. We could not analyse devices use after falling sleep because most of the adolescents reported not to wake up by any device (90%). A recent study has pointed out the importance of distinguish between bedtime (i.e. going to bed) from shuteye time (i.e. time from lights off) [22]. According to the standards for sleep medicine and sleep research time in bed is defined as the time from lights off until lights on. However, further studies should include the assessment of bedtime and shuteye time because adolescents with higher use can have delayed shuteye times once in bed in addition to the already described delayed bedtimes. Another limitation of our study is that we did not have information on personal RF-EMF exposure from these devices. We considered that those adolescents calling more frequently and longer times with both mobile or cordless phone had a higher RF-EMF exposure to the brain, while other uses (e.g. texting, data, internet, tablet, and laptop) and television viewing led to low or null RF-EMF exposure to the brain, respectively [4]. It is currently difficult to disentangle between the associations related to the RF-EMF exposure from these devices and the association related to the use itself although work is underway to better assess the exposure from different devices. We think that similar effect estimates between mobile and cordless phone calls and stronger effect estimates for mobile and cordless phone calls than for screen time in relation to sleep would suggest effects due to RF-EMF exposure to the brain. No effects for phone calls and associations with screen time in relation to sleep would indicate that associations may be driven by screen-time related problems (e.g. sleep displacement, mental arousal, or blue light screen emission).

We found an increased frequency of lower sleep quality related to higher frequency of cordless and mobile phone calls, although this association only reached statistically significance for cordless phones. Both mobile and cordless phone use for calling represent the main exposure source of RF-EMF to the brain and one would expect similarities of its association with health outcomes [4], [24]. However, we did not find any association with mobile or cordless mobile phone calls duration. Thus, the association between higher frequency of cordless phone calls and lower sleep quality could be due to mental arousal or sleep displacement instead of RF-EMF exposure to the brain. Most previous studies also used self-reported questionnaires to collect information on frequency and duration of mobile and cordless phone calls. One of these studies showed results similar to those of our study in children 10-14 years [25] while other studies found no association with cordless phones but showed that high mobile phone use for calling was associated with daytime sleepiness and sleep disturbances (e.g. difficulties falling asleep or maintaining sleep) in children 5-17 years [5], [26]–

[29]. Three studies assessed the relationship between different objective RF-EMF exposure measures and sleep disturbances in children at 5-16 years showing no association [28]–[30]. In these studies, the assessed measures of RF-EMF exposure did not capture the RF-EMF exposure to the brain, which is considerably higher than the whole-body exposure. Although inconclusive data was found from epidemiological studies, experimental studies showed that RF-EMF exposure affect brain activities. However, the relevance of the small physiological changes remains unclear and mechanistic explanations are still lacking [31]. Further epidemiological studies assessing personal RF-EMF exposure levels more accurately, including exposure levels to the brain, are needed to disentangle whether the potential association between the use of telecommunication devices and sleep is due to the exposure to RF-EMF.

We included both passive and interactive type of devices and we did not find the same pattern of association with sleep measures. Higher tablet use was associated with decreased sleep efficiency and increased wake time after sleep onset, indicating poorer sleep and higher sleep fragmentation. No previous studies have assessed the association between tablet use separately from other devices and sleep in adolescents. Tablet use, which represents a high exposure to blue light, might affect sleep differently than other devices such as television or video games consoles directly connected to television screens because adolescents are more likely to use the tablet closer to their eyes and in bed. It has been shown that blue light screen emission alters sleep patterns through the suppression of melatonin release [32], [33]. Although we did not find any association with other mobile phone uses and laptop use, we would expect to observe similar results because these devices might have similar usage patterns than tablets. While no previous studies have assessed laptop use in relation with sleep, mobile phone use in bedtime has been associated with poor sleep measures in adolescents and young adults at 11-21 years [6], [7], [9]. We could not separate between daytime and bedtime of each device use which will be of great interest for future studies. Although there is a general consensus that screen time affects sleep [4], [34], little information is available on the type of device that is behind this association.

Problematic mobile phone use was associated with lower sleep quality, which indicates that mobile phone dependency could disrupt sleep by exposure to blue light from mobile phone screens, mental arousal, or sleep displacement. Previous studies that investigated the relationship between problematic mobile phone use and sleep found similar results in adolescents and young adults at 11-28 years [35]–[37]. Mobile phone dependency have been also related to mental problems [36], which can be caused by sleep problems [38]. Thus, if problematic mobile phone use affects sleep, it could exacerbate existing mental problems in those with higher phone dependency. The ownership and use of mobile phones increases from childhood to adolescence. About 25% of the children had a mobile phone at 10 years and 94% at 15 years in a Spanish population in 2017 [39] and in Germany the use increased from 25% at 8-10 years to 88% at 12-13 years in 2014 [40]. Therefore, mobile phone dependency might become a relevant public health problem.

Two studies have previously assessed telecommunication and other screen devices use and sleep using actigraphy in children and young adults at 14-22 years and they found inconsistent results [8], [11]. Self-reported questionnaires underestimate wake time after sleep onset and overestimate sleep duration [12] but are also important for reporting subjective sleep dimensions that cannot be measured objectively, such as the perceived sleep quality. We did not find any association with total sleep score but with the sleep quality subscale, which might indicate that device use might be harmful for some sleep dimensions but not for others. Further studies should include both subjective, subscales and total score, and objective sleep measures to have a more comprehensive assessment of sleep.

Conclusion

In summary, tablet use, phone use dependency, and frequency of cordless phone calls were related to an increase of subjective and objective sleep problems in adolescents. These results seem to indicate that sleep displacement, mental arousal, and exposure to blue light emission might play a more important role on sleep than a higher RF-EMF exposure to the brain. Recommendations on telecommunication and other screen devices use should be a public health priority to prevent health-related problems including sleep. Studies assessing both subjective and objective sleep, disentangling between different devices use, assessing more precisely the timing of devices use in relation to sleep, and better estimating personal RF-EMF levels are needed to more accurately understand how new technology disrupt adolescents' sleep.

Acknowledgements

The authors would like to thank all of the participants in this study for their generous collaborative efforts.

Source of financial support

This study was funded by grants from Instituto de Salud Carlos III (Red INMAG03/176; CB06/02/0041; 97/0588; 00/0021-2; PI061756; PS0901958; MS13/00054, CP13/00054, PI14/00677 incl. FEDER funds), CIBERESP, Beca de la IV convocatoria de Ayudas a la Investigación en Enfermedades Neurodegenerativas de La Caixa CIBERESP, Beca de la IV convocatoria de Ayudas a la Investigación en Enfermedades Neurodegenerativas de La Caixa, EC Contract No. QLK4-CT-2000-00263, French Agency for Food, Environmental and Occupational Health & Safety (under the grant agreement number EST-2016 RF-21 – the ELFES Project), European Community's Seventh Framework Programme (FP7/2007-2013) under grant agreement no. 603794 – the GERONIMO Project. ISGlobal is a member of the CERCA Programme, Generalitat de Catalunya.

Supplementary material

Figure S1. Flowchart of participants in the study.

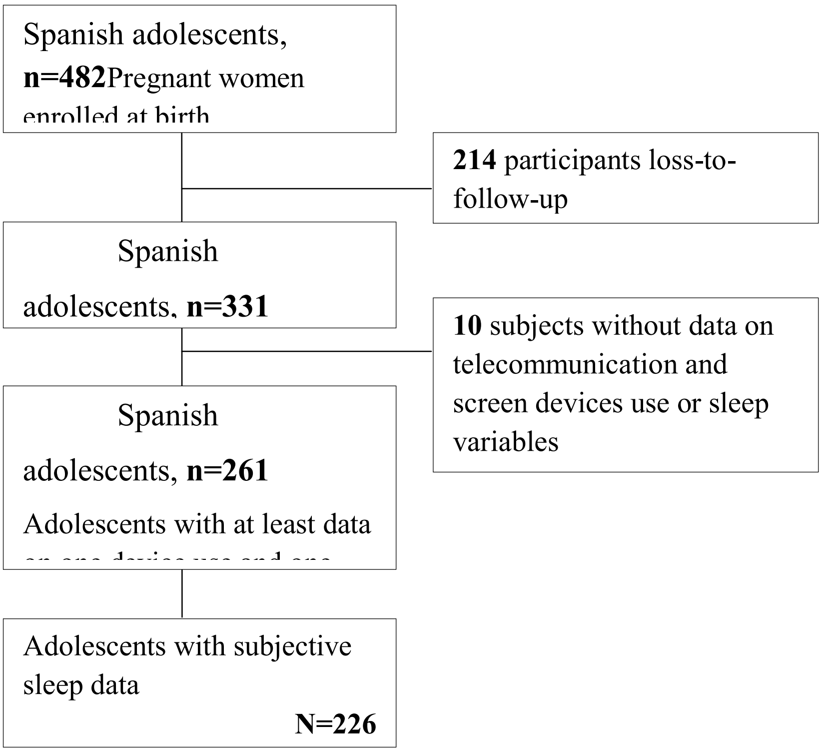
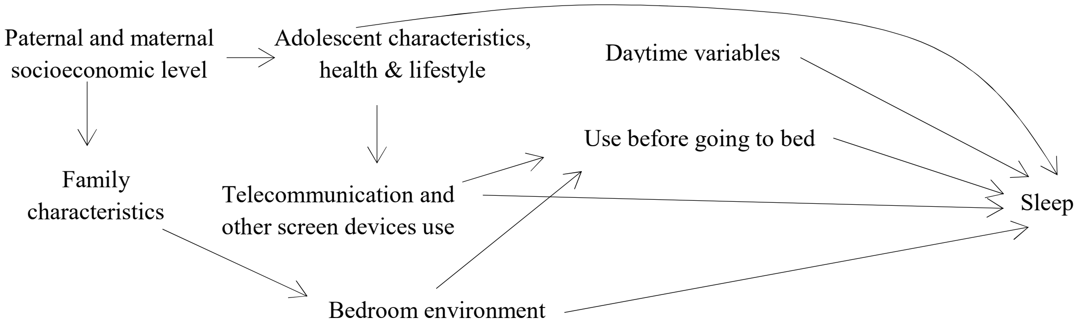


Figure S2. Direct Acyclic Graph (DAG) illustrating the conceptual framework of the potential association between telecommunication and other screen devices use and sleep at 17-18 years old.



Our exposure is daytime and bedtime use of telecommunication and other screen devices (mobile and cordless phone calls, other mobile phone uses than calling, laptop use, tablet use, video console gaming, television, and total screen time). The outcome is sleep (subjective and objective sleep measures). Potential confounding variables are: paternal and maternal socioeconomic level (occupation, education level, and country of birth); family characteristics (household size, and family structure); adolescent's characteristics, health & lifestyle (sex, age, body mass index, physical activity, caffeinated drinks intake, tobacco consumption, chronotype, current working situation, self-perceived health-related quality of life), daytime variables (unmeasured), and bedroom environment (bedroom size).

Table S1. Details of the imputation modelling.

Software used and key settings: STATA 14.0 Software (Stata Corporation, College Station, Texas) - Ice Command (10 cycles)
Number of imputed datasets created: 25
Variables included in the imputation procedure: variables included in the main analysis (telecommunication and screen devices use variables, sleep variables and potential confounding variables). Maternal and paternal social class, maternal and paternal education level, maternal age at pregnancy, adolescents' characteristics and lifestyle variables (sex, age, body mass index, hours of physical activity per week, caffeinated drinks intake, tobacco consumption), adolescents' current working situation (working and/or studying), adolescents' bedroom size, household size and family structure, chronotype, adolescents' self-perceived health related to physical well-being, autonomy and parents, peers and social support, and school environment.
Treatment of categorical variables: logistic and multinomial models
Statistical interactions included in imputation models: none

Table S2. Comparison of maternal, paternal, and individual characteristics of included vs. non-included adolescents.

		Included (n=258)	**Not included (n=224)**	**P-value**
Maternal characteristics				
Social class	I/II managers/technicians	15.1	7.2	**0.004**
	IIIa/IIIb skilled non-manual	41.1	47.6	
	IV/V semiskilled/unskilled	8.5	16.1	
	Unemployed or housewife	35.3	29.1	
Educational level	University	16.4	9.3	**0.004**
	Secondary	32.0	24.5	
	Primary or lower	51.6	66.2	
Country of birth	Spain	97.6	95.0	0.281
	Europe	2.0	2.7	
	Others	0.4	2.3	
Age at child's birth		30.2	29.6	0.181
Parity	0	37.2	47.3	**0.048**
	1-2	55.8	44.7	
	3 or more	7.0	8.0	
Alcohol use during pregnancy	Yes vs. No	10.9	7.1	0.158
Tobacco use during pregnancy	Yes vs. No	32.6	43.8	**0.011**
Pre-pregnancy body mass index	Underweight	2.8	8.4	**0.021**
	Normal	75.9	74.4	
	Overweight	17.3	11.6	
	Obese	4.0	5.6	
Paternal characteristics				
Social class	I/II managers/technicians	19.1	12.2	**0.032**
	IIIa/IIIb skilled non-manual	63.4	72.3	
	IV/V semiskilled/unskilled	10.9	13.2	
	Unemployed or housemen	6.6	2.3	
Educational level	University	9.8	6.4	0.131
	Secondary	27.2	22.1	
	Primary or lower	63.0	71.5	
Country of birth	Spain	97.6	96.8	0.362
	Latin America	0.4	1.8	
	Europe	1.6	1.4	
	Others	0.4	0.0	
Age at child's birth		33.4	32.3	**0.015**
Body mass index at child's 4-years-visit	Normal	43.7	48.6	0.578
	Overweight	48.0	42.9	
	Obese	8.3	8.5	
Adolescent characteristics				
Sex (female vs. male)		52.3	60.0	0.633
Child's birth weight(in grams)		3198 (469)	3173 (537)	0.599

Percentages for categorical variables and mean (SD) for continuous variables. Values are percentages. P-values are based on chi-square and t-student. **Bold:** p-value<0.05.

Table S3. Variables used in forward selection logistic regression model to calculate inverse probability of attrition weights.

Variables	Explored	Included
Maternal social class	X	
Maternal educational level	X	X
Maternal country of birth	X	X
Maternal age at child's birth	X	X
Maternal parity	X	
Maternal alcohol use during pregnancy	X	X
Maternal tobacco use during pregnancy	X	X
Maternal body mass index at the beginning of pregnancy	X	
Paternal social class	X	
Paternal educational level	X	
Paternal country of birth	X	
Paternal age at child's birth	X	X
Paternal body mass index at child's 4-years old	X	
Child's sex	X	X
Child's birth weight	X	

Table S4. Spearman correlations between telecommunication and other screen devices use variables.

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)
Frequency of mobile phone calls (1)	1.00										
Duration of mobile phone calls (2)	**0.63**	1.00									
Problematic mobile phone use (3)	0.21	0.12	1.00								
Frequency of cordless phone calls (4)	0.23	0.06	0.03	1.00							
Duration of cordless calls (5)	**0.49**	**0.65**	0.05	0.28	1.00						
Other mobile phone uses (6)	0.10	0.14	0.30	-0.20	0.25	1.00					
Tablet use (7)	-0.28	-0.17	-0.07	0.07	-0.17	-0.18	1.00				
Laptop use (8)	0.05	-0.07	-0.23	-0.04	-0.19	0.03	-0.13	1.00			
Video console use (9)	-0.05	-0.13	-0.12	0.09	-0.01	0.02	-0.08	-0.14	1.00		
Television (10)	-0.12	-0.17	0.25	-0.02	-0.07	**0.36**	-0.02	**0.33**	0.07	1.00	
Total screen time (11)	0.03	0.01	0.16	-0.01	0.06	**0.55**	-0.05	**0.53**	0.23	**0.77**	1.00

Bold: p-value<0.05.

Table S5. Pearson chi-squared and T-student tests between telecommunication and other screen devices use variables.

	Television in bedroom			Bedtime use			Nigh time use		
	Yes	No		≥1 time/week v	<1 time/week		Yes	No	
	Mean (SD) / %	Mean (SD) / %	p-value	Mean (SD) / %	Mean (SD) / %	p-value	Mean (SD) / %	Mean (SD) / %	p-value
Frequency of mobile phone calls			0.289			0.440			0.380
no calls	5.2	8.5		8.2	3.1		5.4	7.9	
< 1 call/week	27.3	34.1		33.2	28.1		24.3	34.0	
≥1 call/week	67.5	57.4		58.6	68.8		70.3	58.1	
Duration of mobile phone calls	11.3 (26.7)	8.1(20.2)	0.313	9.1 (22.9)	8.9 (19.0)	0.970	14.2 (32.4)	8.2 (20.1)	0.139
Problematic mobile phone use			0.599			**0.023**			21.7
Occasional	14.3	14.2		11.8	29.0		5.6	15.3	
Habitual	58.4	64.2		63.8	58.1		63.9	62.9	
Problematic	27.3	21.6		24.4	12.9		30.5	21.8	
Frequency of cordless phone calls			0.426			**0.011**			0.219
no calls	41.0	48.6		42.1	69.7		36.1	47.3	
< 1 call/week	26.9	26.5		28.5	18.2		38.9	25.2	
≥1 call/week	32.1	24.9		29.4	12.1		25.0	27.5	
Duration of cordless calls	4.1 (4.8)	3.3 (4.9)	0.595	3.6 (4.9)	3.8 (2.0)	0.947	2.8 (2.0)	3.7 (5.1)	
Other mobile phone uses	58.9 (104.8)	50.4 (84.1)	0.489	57.2 (95.8)	28.5 (40.6)	0.091	48.9 (56.8)	54.2 (95.7)	0.741
Tablet use	8.1 (17.3)	6.4 (16.2)	0.479	6.9 (16.2)	6.8 (18.6)	0.975	5.0 (14.7)	7.2 (16.8)	0.490
Laptop use	58.2 (84.9)	75.3 (112.7)	0.271	75.2 (107.3)	39.3 (82.4)	0.091	60.8 (98.6)	71.7 (105.9)	0.621
Video console use	18.5 (44.0)	8.1 (24.8)	**0.024**	11.7 (33.1)	8.3 (24.1)	0.583	8.0 (25.6)	11.8 (32.9)	0.539
Television	103.6 (73.0)	80.7 (52.9)	**0.005**	88.1 (56.8)	86.9 (85.2)	0.917	91.1 (66.6)	87.4 (59.9)	0.737
Total screen time	236.9 (163.7)	201.1 (155.4)	0.096	220.9 (161.4)	157.2 (130.1)	**0.031**	191.7 (135.1)	216.2 (162.7)	0.387

Bold: p-value<0.05.

Table S6. Spearman correlations between sleep variables.

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)
PSQI total score (1)	1.00										
PSQI Sleep quality (2)	**0.60**	1.00									
PSQI Daytime sleepiness (3)	**0.48**	**0.34**	1.00								
PSQI Sleep disturbances (4)	**0.48**	**0.39**	0.14	1.00							
PSQI Sleep duration (5)	**0.43**	**0.45**	**0.33**	0.13	1.00						
PSQI Total sleep efficiency (6)	**0.56**	-0.06	0.01	0.13	-0.01	1.00					
PSQI Sleep latency (7)	**0.52**	**0.45**	0.10	**0.37**	0.15	-0.03	1.00				
Total Sleep Time (8)	-0.13	-0.14	**-0.22**	-0.01	-0.05	0.04	-0.08	1.00			
Sleep efficiency (9)	-0.11	-0.01	-0.10	-0.15	0.05	-0.01	-0.03	**0.40**	1.00		
Sleep onset latency (10)	0.02	-0.06	-0.01	0.01	-0.11	0.13	-0.06	-0.08	**-0.35**	1.00	
Wake After Sleep Onset (11)	0.07	-0.03	0.07	0.15	-0.06	-0.01	0.03	**-0.20**	**-0.94**	**0.20**	1.00

Bold: p-value<0.05.

Table S7. Distribution of adolescents and family characteristics and their association with subjective sleep measures (n=226).

		Total score		**Sleep Quality**		
		Mean (SD) / ρ	**p-value**	**low**	**high**	**p-value**
Adolescents' characteristics and lifestyle						
Sex			0.098			0.582
	Female	5.8 (2.5)		53.7	50.0	
	Male	5.3 (2.2)		46.3	50.0	
Body mass index			0.299			
	Normal weight	5.7 (2.3)		84.3	84.8	0.567
	Overweight	5.2 (2.3)		10.5	12.7	
	Obese	4.7 (2.1)		5.2	2.5	
Physical activity			0.939			
	No	5.7 (2.8)		19.3	14.1	0.190
	< 4 hours/week	5.4 (2.4)		19.3	30.8	
	4-6 hours/week	5.6 (1.9)		24.1	17.9	
	>6 hours/week	5.6 (2.2)		37.3	37.2	
Caffeinated drinks intake			0.860			
	≤1 drink/week	5.7 (2.5)		44.8	50.6	0.683
	2-4 drinks/week	5.4 (2.2)		19.0	17.7	
	≥5 drinks/week	5.6 (2.2)		36.2	31.7	
Tobacco consumption			0.311			
	Never	5.7 (2.3)		71.1	70.5	0.253
	Not every day	5.1 (2.4)		18.5	12.8	
	Every day	5.5 (2.4)		10.4	16.7	
Chronotype			0.639			
	Morningness	5.3 (2.1)		20.3	29.5	0.280
	Intermediate	5.6 (2.0)		16.9	14.1	
	Eveningness	5.7 (2.5)		62.8	56.4	
Adolescents' current working situation						
	Only working	4.6 (2.3)	0.198	5.8	8.8	0.648
	Only studying	5.7 (2.2)		48.5	45.0	
	Studying and working	5.6 (2.4)		45.7	46.2	
Adolescents' self-perceived health-related quality of life						
Physical well-being		-0.2	**0.003**	36.9	43.9	**<0.001**
Psychological well-being		-0.1	0.254	35.7	35.7	0.968
Financial autonomy and parents relation		-0.3	**<0.001**	48.1	51.2	0.083
Social support and peers		-0.2	**0.001**	50.0	**53.2**	**0.070**
School environment		-0.2	**0.006**	46.7	49.7	0.099
Adolescents' bedroom environment						
Bedroom size			0.931			
	1 person	5.6 (2.3)		82.35	93.6	**0.018**
	≥2 persons	5.6 (2.1)		17.65	6.4	
Adolescents' family characteristics						
Household size			0.051			
	1-2 persons	5.6 (2.3)		43.4	45.0	0.512
	3 persons	5.9 (2.4)		41.7	41.2	
	≥4 persons	4.7 (1.9)		149	13.8	
Family structure			0.637			
	Living with mother and father	5.5 (2.2)		43.4	78.9	0.961
	mother or father	5.4 (2.6)		41.7	13.2	
	others	6.0 (2.4)		14.9	7.9	

Values are percentages and mean (SD) or rho coefficients (ρ) for continuous variables. P-values are based on chi-square, t-student, and spearman correlations. **Bold:** p-value<0.05

Table S7 continuation. Distribution of adolescents and family characteristics and their association with subjective sleep measures (n=226).

	Total score		Sleep Quality		
	Mean (SD)	**p-value**	**low**	**high**	**p-value**
Maternal educational level		0.973			0.922
University	5.6 (2.6)		16.1	17.5	
Secondary	5.5 (2.2)		32.3	30.0	
Primary or lower	5.6 (2.3)		51.5	52.5	
Paternal educational level		0.224			0.824
University	6.4 (3.3)		9.4	11.25	
Secondary	5.5 (1.9)		26.9	28.7	
Primary or lower	5.5 (2.3)		63.7	60.0	
Maternal social class		0.515			0.060
I/II managers/technicians	5.6 (2.6)		13.7	18.8	
IIIa/IIIb skilled non-manual	5.6 (2.4)		44.0	35.0	
IV/V semiskilled/unskilled	6.3 (2.2)		10.9	3.7	
Unemployed or housewife	5.4 (2.1)		31.4	42.5	
Paternal social class		0.778			0.407
I/II managers/technicians	5.9 (2.7)		20.1	17.5	
IIIa/IIIb skilled non-manual	5.5 (2.1)		61.0	68.7	
IV/V semiskilled/unskilled	5.8 (2.7)		12.6	6.3	
Unemployed	5.5 (2.6)		6.3	7.5	

Values are percentages and mean (SD) or rho coefficients (ρ) for continuous variables. P-values are based on chi-square, t-student, and spearman correlations. **Bold:** p-value<0.05.

Table S8. Distribution of adolescents and family characteristics and their association with objective sleep measures (n=110).

	Sleep duration (in hours)		**Sleep Efficiency (%)**		**Sleep onset Latency (in minutes)**		**Wake After Sleep Onset (in minutes)**	
	Mean (SD)	**p-value**	**Mean (SD)**	**p-value**	**Mean (SD)**	**p-value**	**Mean (SD)**	**p-value**
Adolescents' characteristics and lifestyle								
Sex (female vs. male)	6.9 (0.7)	0.149	83.0 (6.47)	0.406	9.2 (7.9)	0.673	78.4 (35.44)	0.604
Body mass index								
Normal weight	6.8 (0.7)	0.764	82.8 (6.1)	**0.033**	8.1 (6.2)	**0.004**	78.7 (33.02)	**0.008**
Overweight	6.8 (0.6)		81.6 (7.0)		14.0 (11.1)		79.7 (32.17)	
Obese	7.1 (0.6)		73.3 (7.1)		16.7 (7.5)		140.3 (40.71)	
Physical activity								
No	6.7 (0.9)	0.496	81.7 (8.7)	0.179	9.0 (8.5)	0.697	84.1 (41.04)	0.251
< 4 h/w	6.9 (0.7)		83.5 (5.1)		8.8 (5.6)		73.7 (26.67)	
4-6 h/w	6.7 (0.5)		80.7 (6.6)		9.4 (5.6)		89.1 (37.72)	
>6 h/w	6.9 (0.7)		84.0 (4.8)		7.5 (6.3)		73.7 (29.34)	
Caffeinated drinks intake								
1 drink/w or less	6.8 (0.7)	0.620	82.4 (6.3)	0.817	9.3 (7.5)	0.817	79.3 (33.72)	0.908
2-4 drinks/w	6.9 (0.6)		83.2 (7.3)		8.0 (5.8)		79.6 (41.94)	
5 drinks/w or more	6.7 (0.6)		82.0 (6.1)		8.8 (7.4)		82.5 (32.42)	
Tobacco consumption								
Never	6.7 (0.7)	0.074	82.3 (6.7)	0.827	9.4 (7.1)	0.298	79.8 (35.71)	0.998
Not every day	6.9 (0.6)		83.0 (5.4)		6.7 (6.5)		79.4 (29.24)	
Every day	7.1 (0.7)		83.2 (5.4)		9.7 (8.0)		79.4 (33.92)	
Chronotype								
Morningness	6.8 (0.6)	0.909	83.6 (5.1)	0.258	8.0 (5.0)	0.808	75.3 (25.32)	0.193
Intermediate	6.9 (0.8)		80.0 (8.2)		9.4 (5.9)		95.4 (47.93)	
Eveningness	6.8 (0.7)		82.6 (6.2)		9.1 (7.9)		78.8 (33.37)	
Adolescents' current working situation								
Working	6.8 (0.4)	0.842	75.5 (6.1)	**0.041**	10.8 (9.9)	0.850	128.4 (49.35)	**0.005**
Only studying	6.8 (0.7)		82.7 (6.0)		9.0 (8.1)		78.2 (31.92)	
Studying and working	6.8 (0.8)		82.8 (6.3)		8.9 (5.8)		78.2 (32.18)	

Values are means (SD) and rho coefficients (ρ). P-values are based on t-student and spearman correlation. **Bold:** p-value<0.05.

Table S8 continuation. Distribution of adolescents and family characteristics and their association with objective sleep measures (n=110).

		Sleep duration (in hours)		Sleep Efficiency (%)		Sleep onset Latency (in minutes)		Wake After Sleep Onset (in minutes)	
Adolescents' bedroom environment		**Mean (SD)**	**p-value**	**Mean (SD)**	**p-value**	**Mean (SD)**	**p-value**	**Mean (SD)**	**p-value**
Bedroom size	Sleep alone	6.8 (0.7)	0.765	82.0 (6.5)	0.253	8.9 (7.12)	0.512	82.5 (34.80)	0.148
	1-2 people same bedroom	6.8 (0.6)		84.2 (5.4)		10.3 (10.3)		67.7 (30.30)	
Adolescents' family characteristics									
Household size									
	Alone or with one more person	6.8 (0.7)	0.998	83.1 (6.5)	0.483	7.7 (5.7)	0.070	78.1 (37.0)	0.551
	3 people	6.8 (0.6)		82.2 (6.4)		10.8 (8.3)		79.4 (32.9)	
	4 people or more	6.8 (0.8)		80.8 (5.6)		7.4 (7.0)		89.7 (27.1)	
Family structure									
	mother and father	6.8 (0.7)	0.749	82.1 (6.1)	0.065	9.2 (7.2)	0.339	81.9 (33.6)	0.182
	mother or father	6.9 (0.7)		85.9 (6.1)		6.2 (6.1)		66.5 (37.9)	
	others	6.8 (0.8)		80.3 (7.9)		9.1 (7.7)		91.2 (37.5)	
Maternal educational level			0.298		0.910		0.138		0.668
	University	6.7(0.7)		82.6 (5.5)		6.5 (4.8)		80.7 (31.8)	
	Secondary	6.7 (0.7)		82.9 (7.9)		10.2 (8.6)		75.5 (40.0)	
	Primary or lower	6.9 (0.7)		82.3 (5.5)		9.4 (6.7)		82.3 (32.0)	
Paternal educational level			0.871		0.179		0.665		0.143
	University	6.7 (0.8)		85.0 (6.0)		7.3 (4.7)		65.9 (30.5)	
	Secondary	6.8 (0.6)		81.1 (6.8)		9.3 (5.9)		88.0 (36.8)	
	Primary or lower	6.8 (0.5)		82.6 (6.1)		9.1 (8.0)		79.2 (33.2)	
Maternal social class			0.103		0.648		0.674		0.758
	I/II managers/technicians	6.4 (0.6)		81.1 (5.7)		8.5 (5.5)		84.1 (33.8)	
	IIIa/IIIb skilled non-manual	6.8 (0.7)		82.7 (7.3)		8.6 (7.0)		75.7 (37.0)	
	IV/V semiskilled/unskilled	6.8 (0.7)		80.1 (7.6)		12.2 (9.6)		90.4 (34.2)	
	Unemployed or housewife	6.9 (0.7)		82.7 (5.8)		8.7 (6.0)		81.0 (35.5)	
Paternal social class			0.684		0.988		0.352		0.989
	I/II managers/technicians	6.6 (0.6)		82.3 (7.7)		9.2 (6.1)		79.2 (39.0)	
	IIIa/IIIb skilled non-manual	6.8 (0.6)		82.5 (4.3)		8.1 (7.6)		80.4 (32.9)	
	IV/V semiskilled/unskilled	6.8 (1.0)		83.0 (3.9)		6.0 (4.6)		78.2 (18.0)	
	Unemployed or housewife	7.0 (1.0)		83.1 (6.8)		6.6 (2.7)		75.1 (27.3)	

Values are means (SD) and rho coefficients (ρ). P-values are based on t-student and spearman correlation. **Bold:** p-value<0.05.

Table S8 continuation. Distribution of adolescents and family characteristics and their association with objective sleep measures (n=110).

	Sleep duration (in hours)		**Sleep Efficiency (%)**		**Sleep onset Latency (in minutes)**		**Wake After Sleep Onset (in minutes)**	
Adolescents' self-perceived health	**ρ**	**p-value**	**ρ**	**p-value**	**ρ**	**p-value**	**ρ**	**p-value**
Physical well-being	-0.16	0.097	-0.05	0.577	-0.05	0.625	0.03	0.761
Psychological well-being	0.13	0.170	0.18	0.063	0.02	0.834	-0.13	0.177
Financial autonomy and parents relation	0.05	0.602	0.06	0.547	0.01	0.924	-0.04	0.668
Social support and peers	0.18	0.068	0.02	0.794	0.01	0.877	-0.02	0.809
School environment	0.17	0.095	0.09	0.333	0.15	0.139	-0.08	0.416

Values are means (SD) and rho coefficients (ρ). P-values are based on t-student and spearman correlation. **Bold:** p-value<0.05.

Table S9. Adjusted association between telecommunication and other screen devices use and subjective sleep subscales in adolescents at 17-18 years old (n=226).

		Subjective sleep measures (n=226)				
		Daytime sleepiness (no/low vs. medium/high) PR (CI 95%)	**Sleep disturbances (No vs. low/medium/high) PR (CI 95%)**	**Sleep duration (≥7h vs. <7h) PR (CI 95%)**	**Sleep efficiency (≥85% vs. <85%) PR (CI 95%)**	**Sleep latency (No/low vs. medium/high) PR (CI 95%)**
Mobile phone calls						
Frequency	No calls	1	1	1	1	1
	< 1 call/week	0.73 (0.16; 3.36)	0.95 (0.79;1.13)	1.73 (0.58;5.18)	1.04 (0.81;1.34)	0.43 (0.13;1.46)
	≥1 call/week	1.16 (0.28; 4.78)	0.95 (0.81;1.12)	1.55 (0.52;4.57)	1.10 (0.86;1.40)	0.21 (0.06;0.70)
Duration (per Δ1 minute/day)		1.00 (0.98; 1.02)	1.00 (0.99;1.00)	0.99 (0.97;1.01)	1.00 (0.99;1.00)	0.99 (0.97;1.00)
Problematic mobile phone use						
	Occasional	1	1	1	1	1
	Habitual	1.46 (0.49; 4.34)	1.22 (0.99;1.51)	1.06 (0.40;2.79)	0.982 (0.79; 1.20)	1.62 (0.56;4.63)
	Frequent	0.68 (0.18; 2.57)	1.20 (0.96;1.51)	0.88 (0.28;2.73)	1.043 (0.80;1.35)	1.29 (0.38;4.32)
Cordless phone calls						
Frequency	No calls	1	1	1	1	1
	< 1 call/week	0.67 (0.30; 1.51)	1.09 (0.97;1.23)	1.32 (0.68;2.58)	1.11 (0.93;1.33)	1.27 (0.61;2.62)
	≥1 call/week	0.50 (0.19; 1.32)	1.01 (0.88;1.16)	1.34 (0.65;2.74)	1.05 (0.87;1.27)	0.84 (0.38;1.87)
Duration (per Δ1 minute/day)		0.95 (0.83; 1.09)	0.99 (0.98;1.00)	0.98 (0.90;1.07)	1.00 (0.98;1.01)	0.94 (0.88;1.01)

PR = prevalence ratio. IC 95% = 95% confidence interval. Models adjusted for maternal and paternal social class, maternal and paternal education level, maternal age, adolescents' characteristics and lifestyle variables (sex, age, body mass index, hours of physical activity per week, caffeinated drinks intake, tobacco consumption), adolescents' current working situation (working and/or studying), adolescents' bedroom size, household size, and family structure, adolescent's chronotype, adolescents' self-perceived health-related quality of life (physical well-being, autonomy and parents, peers and social support, psychological well-being, and school environment). **Bold:** p-value<0.05.

Table S9 continuation. Adjusted association between telecommunication and other screen devices use and subjective sleep subscales in adolescents at 17-18 years old (n=226).

	Subjective sleep measures (n=226)				
	Daytime sleepiness (no/low vs. medium/high) PR (CI 95%)	**Sleep disturbances (No vs. yes) PR (CI 95%)**	**Sleep duration (≥7h vs. <7h) PR (CI 95%)**	**Sleep efficiency (≥85% vs. <85%) PR (CI 95%)**	**Sleep onset latency (No/low vs. medium/high) PR (CI 95%)**
Screen time					
Mobile phone use excluding phone calls (per Δ10 minutes/day)	0.99 (0.95; 1.02)	0.99 (0.99;1.00)	0.97 (0.91;1.04)	1.00 (0.99;1.00)	0.95 (0.89;1.00)
Tablet (per Δ10 minutes/day)	0.99 (0.81; 1.20)	0.99 (0.94;1.04)	1.06 (0.90;1.26)	1.01 (0.97;1.05)	0.92 (0.71;1.20)
Laptop (per Δ10 minutes/day)	1.01 (0.99; 1.04)	0.99 (0.99;1.00)	1.00 (0.97;1.04)	1.00 (0.99;1.00)	1.01 (0.99;1.04)
Video game console (per Δ10 minutes/day)	0.97 (0.87; 1.09)	0.98 (0.95;1.01)	0.99 (0.91;1.08)	1.03 (1.01;1.06)	1.00 (0.91;1.10)
Television (per Δ30 minutes/day)	0.88 (0.73; 1.06)	1.00 (0.97;1.03)	1.08 (0.92;1.26)	1.00 (0.95;1.05)	0.98 (0.83;1.15)
Total screen time (per Δ30 minutes/day)	1.00 (0.95; 1.05)	0.99 (0.98;1.00)	1.01 (0.95;1.07)	1.00 (0.98;1.01)	1.01 (0.95;1.07)
Television in adolescents' bedroom					
Yes vs. no	0.72 (0.31; 1.67)	0.98 (0.89;1.09)	1.39 (0.76;2.56)	1.05 (0.89;1.25)	1.02 (0.54;1.93)
Use before going to sleep					
≥1 time/week vs. <1 time/week	1.04 (0.37; 2.89)	1.09 (0.92;1.30)	0.87 (0.35;2.17)	0.99 (0.76;1.29)	5.89 (0.76;45.23)

PR = prevalence ratio. IC 95% = 95% confidence interval. Models adjusted for maternal and paternal social class, maternal and paternal education level, maternal age, adolescents' characteristics and lifestyle variables (sex, age, body mass index, hours of physical activity per week, caffeinated drinks intake, tobacco consumption), adolescents' current working situation (working and/or studying), adolescents' bedroom size, household size, and family structure, adolescent's chronotype, adolescents' self-perceived health-related quality of life (physical well-being, autonomy and parents, peers and social support, psychological well-being, and school environment). **Bold:** p-value<0.05.

References

[1] M. Ohayon *et al.*, «National Sleep Foundation's sleep quality recommendations: first report», *Sleep Health*, vol. 3, n.º 1, pp. 6-19, feb. 2017, doi: 10.1016/j.sleh.2016.11.006.

[2] M. A. Carskadon, «Sleep in Adolescents: The Perfect Storm», *Pediatr. Clin. North Am.*, vol. 58, n.º 3, pp. 637-647, jun. 2011, doi: 10.1016/j.pcl.2011.03.003.

[3] N. Cain y M. Gradisar, «Electronic media use and sleep in school-aged children and adolescents: A review», *Sleep Med.*, vol. 11, n.º 8, pp. 735-742, sep. 2010, doi: 10.1016/j.sleep.2010.02.006.

[4] K. Roser *et al.*, «Personal radiofrequency electromagnetic field exposure measurements in Swiss adolescents», *Environ. Int.*, vol. 99, pp. 303-314, feb. 2017, doi: 10.1016/j.envint.2016.12.008.

[5] Y. W. Mak *et al.*, «Association between screen viewing duration and sleep duration, sleep quality, and excessive daytime sleepiness among adolescents in Hong Kong», *Int. J. Environ. Res. Public. Health*, vol. 11, n.º 11, pp. 11201-11219, oct. 2014, doi: 10.3390/ijerph111111201.

[6] O. Bruni, S. Sette, L. Fontanesi, R. Baiocco, F. Laghi, y E. Baumgartner, «Technology Use and Sleep Quality in Preadolescence and Adolescence», *J. Clin. Sleep Med.*, vol. 11, n.º 12, pp. 1433-1441, dic. 2015, doi: 10.5664/jcsm.5282.

[7] M. Hysing, S. Pallesen, K. M. Stormark, R. Jakobsen, A. J. Lundervold, y B. Sivertsen, «Sleep and use of electronic devices in adolescence: results from a large population-based study», *BMJ Open*, vol. 5, n.º 1, pp. e006748-e006748, feb. 2015, doi: 10.1136/bmjopen-2014-006748.

[8] A. D. Fobian, K. Avis, y D. C. Schwebel, «Impact of Media Use on Adolescent Sleep Efficiency», *J. Dev. Behav. Pediatr. JDBP*, vol. 37, n.º 1, pp. 9-14, ene. 2016, doi: 10.1097/DBP.0000000000000239.

[9] A. E. E. Johansson, M. A. Petrisko, y E. R. Chasens, «Adolescent Sleep and the Impact of Technology Use Before Sleep on Daytime Function», *J. Pediatr. Nurs.*, vol. 31, n.º 5, pp. 498-504, sep. 2016, doi: 10.1016/j.pedn.2016.04.004.

[10] E. L. Kenney y S. L. Gortmaker, «United States Adolescents' Television, Computer, Videogame, Smartphone, and Tablet Use: Associations with Sugary Drinks, Sleep, Physical Activity, and Obesity», *J. Pediatr.*, vol. 182, pp. 144-149, mar. 2017, doi: 10.1016/j.jpeds.2016.11.015.

[11] K. K. Murdock, M. Horissian, y C. Crichlow-Ball, «Emerging Adults' Text Message Use and Sleep Characteristics: A Multimethod, Naturalistic Study», *Behav. Sleep. Med.*, vol. 15, n.º 3, pp. 228-241, may 2017, doi: 10.1080/15402002.2015.1120203.

[12] R. B. Tremaine, J. Dorrian, y S. Blunden, «Subjective and objective sleep in children and adolescents: Measurement, age, and gender differences: Measurement of child & adolescent sleep», *Sleep Biol. Rhythms*, vol. 8, n.º 4, pp. 229-238, oct. 2010, doi: 10.1111/j.1479-8425.2010.00452.x.

[13] M. Guxens *et al.*, «Cohort Profile: The INMA—INfancia y Medio Ambiente—(Environment and Childhood) Project», *Int. J. Epidemiol.*, vol. 41, n.º 4, pp. 930-940, ago. 2012, doi: 10.1093/ije/dyr054.

[14] M. Gallastegi *et al.*, «Characterisation of exposure to non-ionising electromagnetic fields in the Spanish INMA birth cohort: study protocol», *BMC Public Health*, vol. 16, n.º 1, dic. 2016, doi: 10.1186/s12889-016-2825-3.

[15] M. Foerster, K. Roser, A. Schoeni, y M. Röösli, «Problematic mobile phone use in adolescents: derivation of a short scale MPPUS-10», *Int. J. Public Health*, vol. 60, n.º 2, pp. 277-286, feb. 2015, doi: 10.1007/s00038-015-0660-4.

[16] J. de-Sola, H. Talledo, F. Rodríguez de Fonseca, y G. Rubio, «Prevalence of problematic cell phone use in an adult population in Spain as assessed by the Mobile Phone Problem Use Scale (MPPUS)», *PLOS ONE*, vol. 12, n.º 8, p. e0181184, ago. 2017, doi: 10.1371/journal.pone.0181184.

[17] D. J. Buysse, C. F. Reynolds, T. H. Monk, S. R. Berman, y D. J. Kupfer, «The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research», *Psychiatry Res.*, vol. 28, n.º 2, pp. 193-213, may 1989.

[18] A. Sadeh, «The role and validity of actigraphy in sleep medicine: An update», *Sleep Med. Rev.*, vol. 15, n.º 4, pp. 259-267, ago. 2011, doi: 10.1016/j.smrv.2010.10.001.

[19] A. Zavada, M. C. M. Gordijn, D. G. M. Beersma, S. Daan, y T. Roenneberg, «Comparison of the Munich Chronotype Questionnaire with the Horne-Ostberg's Morningness-Eveningness Score», *Chronobiol. Int.*, vol. 22, n.º 2, pp. 267-278, 2005.

[20] U. Ravens-Sieberer *et al.*, «The European KIDSCREEN approach to measure quality of life and well-being in children: development, current application, and future advances», *Qual. Life Res.*, vol. 23, n.º 3, pp. 791-803, abr. 2014, doi: 10.1007/s11136-013-0428-3.

[21] A. Espelt, M. Marí-Dell'Olmo, E. Penelo, y M. Bosque-Prous, «Applied Prevalence Ratio estimation with different Regression models: An example from a cross-national study on substance use research», *Adicciones*, vol. 29, n.º 2, p. 105, jun. 2016, doi: 10.20882/adicciones.823.

[22] L. Exelmans y J. Van den Bulck, «Bedtime, shuteye time and electronic media: sleep displacement is a two-step process», *J. Sleep Res.*, vol. 26, n.º 3, pp. 364-370, jun. 2017, doi: 10.1111/jsr.12510.

[23] B. Carter, P. Rees, L. Hale, D. Bhattacharjee, y M. S. Paradkar, «Association Between Portable Screen-Based Media Device Access or Use and Sleep Outcomes: A Systematic Review and Meta-analysis», *JAMA Pediatr.*, vol. 170, n.º 12, p. 1202, dic. 2016, doi: 10.1001/jamapediatrics.2016.2341.

[24] O. Lauer, P. Frei, M.-C. Gosselin, W. Joseph, M. Röösli, y J. Fröhlich, «Combining near- and far-field exposure for an organ-specific and whole-body RF-EMF proxy for epidemiological research: A reference case», *Bioelectromagnetics*, vol. 34, n.º 5, pp. 366-374, jul. 2013, doi: 10.1002/bem.21782.

[25] M. Redmayne, E. Smith, y M. J. Abramson, «The relationship between adolescents' well-being and their wireless phone use: a cross-sectional study», *Environ. Health Glob. Access Sci. Source*, vol. 12, p. 90, oct. 2013, doi: 10.1186/1476-069X-12-90.

[26] N. Nathan y J. Zeitzer, «A survey study of the association between mobile phone use and daytime sleepiness in California high school students», *BMC Public Health*, vol. 13, p. 840, sep. 2013, doi: 10.1186/1471-2458-13-840.

[27] N. Küçer y T. Pamukçu, «Self-reported symptoms associated with exposure to electromagnetic fields: a questionnaire study», *Electromagn. Biol. Med.*, vol. 33, n.º 1, pp. 15-17, ene. 2014, doi: 10.3109/15368378.2013.783847.

[28] A. Huss *et al.*, «Environmental Radiofrequency Electromagnetic Fields Exposure at Home, Mobile and Cordless Phone Use, and Sleep Problems in 7-

Year-Old Children», *PLOS ONE*, vol. 10, n.º 10, p. e0139869, oct. 2015, doi: 10.1371/journal.pone.0139869.

[29] R. Durusoy, H. Hassoy, A. Özkurt, y A. O. Karababa, «Mobile phone use, school electromagnetic field levels and related symptoms: a cross-sectional survey among 2150 high school students in Izmir», *Environ. Health*, vol. 16, n.º 1, dic. 2017, doi: 10.1186/s12940-017-0257-x.

[30] S. Heinrich, S. Thomas, C. Heumann, R. von Kries, y K. Radon, «The impact of exposure to radio frequency electromagnetic fields on chronic well-being in young people--a cross-sectional study based on personal dosimetry», *Environ. Int.*, vol. 37, n.º 1, pp. 26-30, ene. 2011, doi: 10.1016/j.envint.2010.06.008.

[31] SCENIHR, «Potential health effects of exposure to electromagnetic fields», 2015.

[32] B. Wood, M. S. Rea, B. Plitnick, y M. G. Figueiro, «Light level and duration of exposure determine the impact of self-luminous tablets on melatonin suppression», *Appl. Ergon.*, vol. 44, n.º 2, pp. 237-240, mar. 2013, doi: 10.1016/j.apergo.2012.07.008.

[33] G. Tosini, I. Ferguson, y K. Tsubota, «Effects of blue light on the circadian system and eye physiology», *Mol. Vis.*, vol. 22, pp. 61-72, 2016.

[34] L. Hale y S. Guan, «Screen time and sleep among school-aged children and adolescents: A systematic literature review», *Sleep Med. Rev.*, vol. 21, pp. 50-58, jun. 2015, doi: 10.1016/j.smrv.2014.07.007.

[35] Y.-S. Yang, J.-Y. Yen, C.-H. Ko, C.-P. Cheng, y C.-F. Yen, «The association between problematic cellular phone use and risky behaviors and low self-esteem among Taiwanese adolescents», *BMC Public Health*, vol. 10, n.º 1, dic. 2010, doi: 10.1186/1471-2458-10-217.

[36] S. Sahin, K. Ozdemir, A. Unsal, y N. Temiz, «Evaluation of mobile phone addiction level and sleep quality in university students», *Pak. J. Med. Sci.*, vol. 29, n.º 4, pp. 913-918, jul. 2013.

[37] L. Gallimberti *et al.*, «Problematic cell phone use for text messaging and substance abuse in early adolescence (11- to 13-year-olds)», *Eur. J. Pediatr.*, vol. 175, n.º 3, pp. 355-364, mar. 2016, doi: 10.1007/s00431-015-2645-y.

[38] D. Freeman *et al.*, «The effects of improving sleep on mental health (OASIS): a randomised controlled trial with mediation analysis», *Lancet Psychiatry*, vol. 4, n.º 10, pp. 749-758, oct. 2017, doi: 10.1016/S2215-0366(17)30328-0.

[39] INE, «Survey on Equipment and Use of Information and Communication Technologies in Households», 2017.

[40] Bitkom Research, «Pressekonferenz – Studie „Kinder und Jugend 3.0“», Bitkom Research, Berlin, 28., abr. 2014. [En línea]. Disponible en: https://www.bitkom.org/Presse/Anhaenge-an-PIs/2014/April/BITKOM-PK-Kinder-und-Jugend-3-0.pdf.

Study II: Estimated all-day and evening whole-brain radiofrequency electromagnetic fields doses and sleep in preadolescents

Alba Cabré-Riera, Luuk van Wel, Ilaria Liorni, M. Elisabeth Koopman-Verhoeff, Liher Imaz, Jesús Ibarluzea, Anke Huss, Joe Wiart, Roel Vermeulen, Wout Joseph, Martine Vrijheid, Elisabeth Cardis, Martin Röösli, Arno Thielens, Marloes Eeftens, Myles Capstick, Henning Tiemeier, Mònica Guxens

To be submitted to Environment International

Abstract

Objective: To investigate the association of estimated all-day and evening whole-brain radiofrequency electromagnetic field (RF-EMF) doses with sleep disturbances and objective sleep measures in preadolescents.

Methods: We included preadolescents aged 9-12 years from two population-based birth cohorts, the Dutch Generation R Study (n=974) and the Spanish INfancia y Medio Ambiente Project (n=868). All-day and evening overall whole-brain RF-EMF doses (mJ/kg/day) were estimated for several RF-EMF sources including mobile and Digital Enhanced Cordless Telecommunications (DECT) phone calls (named phone calls), other mobile phone uses, tablet use, laptop use (named screen activities), and far-field sources. We also estimated all-day and evening whole-brain RF-EMF doses in these three groups separately (i.e. phone calls, screen activities, and far-field). The Sleep Disturbance Scale for Children was completed by mothers to assess sleep disturbances. Wrist accelerometers together with sleep diaries were used to measure sleep characteristics objectively for 7 consecutive days.

Results: Overall all-day whole-brain RF-EMF dose and all-day whole-brain RF-EMF dose from phone calls were not associated with sleep parameters. However, all-day whole-brain RF-EMF dose from screen activities was associated with excessive somnolence [2.19 score symptoms (95%CI 0.10; 4.27)] and all-day whole-brain RF-EMF dose from far-field sources was associated with longer sleep onset latency [0.28 minutes (95%CI 0.07; 0.49)]. When we focused on evening doses, preadolescents with high evening whole-brain RF-EMF dose from phone calls had shorter total sleep time and longer sleep onset latency [-11.86 minutes (95%CI -21.22; -2.51) and 0.34 minutes (95%CI 0.04; 0.65), respectively].

Conclusions: Our findings suggest the evening as a potentially relevant window of RF-EMF exposure for sleep. However, we cannot exclude that observed associations are due to the activities producing RF-EMF exposure (e.g. exciting phone calls) rather than the RF-EMF exposure itself or due to chance finding.

Introduction

Sleep is crucial for the health and development of adolescents. Inadequate sleep duration or quality is known to lead to adverse physical and mental health consequences. Despite its importance to health, insufficient sleep duration and resultant daytime sleepiness are prevalent among adolescents [1]. Several biological, social, and environmental factors play a role in determining sleep patterns and have been related to insufficient sleep duration [2]. The use of mobile communication devices such as mobile phones and tablets has been described as a potential factor impairing adolescents' sleep [3]–[5]. The social and mental stress of use, the screen blue light, and the exposure to radiofrequency electromagnetic fields (RF-EMF) emitted by these devices against the background of the rapid increase of mobile communication device use in the last years, especially in adolescents, raised concern.

The association between RF-EMF exposure emitted by mobile communication devices and sleep has scarcely been studied in adolescents. One study that estimated whole-brain RF-EMF dose and assessed its association with reported health symptoms did not find any relationship with tiredness, lack of energy, and exhaustibility in adolescents at 12-17 years old [6]. However, studies that assessed the use of mobile communication devices for activities that lead to RF-EMF exposure using reported questionnaires found an association between higher use with daytime sleepiness and higher symptoms of sleep disturbances in 14-24 years olds [7]–[13]. Moreover, studies that assessed environmental RF-EMF exposure at home or school find associations with tiredness and exhaustibility [14] but did not find any association with sleep disturbances [11] at 12-18 years old. None of these studies assessed the overall RF-EMF exposure, which combines exposures from different sources in different microenvironments, and assessed its association with sleep characteristics. Moreover, it is unclear whether the all-day RF-EMF exposure (i.e. RF-EMF exposure received during a day) or the evening RF-EMF exposure is more relevant. Only three cross-sectional studies have assessed the use of mobile communication devices in the evening for activities that lead to RF-EMF exposure to the brain, including phone calls, in relation to sleep, and only one of them assessed sleep disturbances and sleep measures objectively with actigraphy [15]. The authors reported that higher evening use was related to more symptoms of sleep disturbances [16], [17] and lower objective sleep efficiency [15] at 12-18 years of age. There are no studies assessing RF-EMF exposure to the brain, including a differentiation between all-day and evening exposure, and its relationship with objective sleep measures in adolescents.

Therefore, the aim of this study was to investigate the association between i) estimated overall and source-specific all-day whole-brain RF-EMF doses with sleep disturbances and objective sleep measures, and ii) estimated overall and source-specific evening whole-brain RF-EMF doses with sleep disturbances and objective sleep measures across seven days in preadolescents at 9-12 years.

Methods

Study design and population

This analysis used data from two population-based birth cohorts: the Dutch Generation R Study [18] and the Spanish INfancia y Medio Ambiente (INMA) Project [19] for which we included two INMA sub-cohorts (Sabadell and Gipuzkoa). Pregnant women were invited to participate between 2002 and 2006. A total number of 9,901 pregnant women for Generation R and 1,415 for INMA enrolled and their children have been followed through childhood. Whole-brain RF-EMF doses, sleep disturbances, and objective sleep measures were assessed at 9-12 years in all cohorts. We included a total of 1,842 preadolescents with information on mobile communication devices use to estimate all-day and evening whole-brain RF-EMF doses and sleep disturbances or objective sleep measures (Supplementary Figure S1). In 1,599 of them, we collected information on all-day mobile communication devices use, and sleep disturbances with a general questionnaire completed by the mother. We additionally collected information on objective sleep measures using a wrist accelerometer (GENEActiv; Activinsights, UK) for 7 consecutive days in 1,080 preadolescents. We estimated whole-brain RF-EMF doses during a day, the "all-day whole-brain RF-EMF dose". In a sub-study sample of the INMA cohort (n=335), we collected information on the use of mobile communication devices after 7 p.m. and before falling asleep with sleep diaries reported by preadolescents for 7 consecutive days and we estimated daily evening whole-brain RF-EMF doses in a subsample.

Estimated whole-brain RF-EMF doses

We applied an integrative RF-EMF exposure model to estimate all-day and evening whole-brain RF-EMF doses from several RF-EMF exposure sources [20]–[22]. The integrated exposure model is applied using information on the personal use of mobile communication devices (i.e. near-field RF-EMF sources) and estimations of exposure to other sources than personal mobile communication devices use (i.e. environmental or far-field RF-EMF sources).

Near-field RF-EMF sources

To estimate near-field RF-EMF exposure, information of the use of RF-EMF sources was collected using a questionnaire completed by the mother when participants were 9-12 years in Generation R and INMA. Duration of use of i) mobile phone for calling, ii) DECT phone calls, iii) other mobile phone uses, iv) tablet while wirelessly connected to internet, and v) laptop while wirelessly connected to internet was assessed in minutes/day (Supplementary Table S1-S2). To estimate evening whole-brain RF-EMF doses, this information for use after 7 p.m. until falling asleep was collected for 7 consecutive days with sleep diaries completed by preadolescents at 9-12 years in INMA.

Far-field RF-EMF sources

We estimated all-day RF-EMF exposure to environmental RF-EMF sources (mobile phone base stations, FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) in Generation R and INMA. We based our estimations on different microenvironments where preadolescents spend most of their time during a day such as home, school, commuting, and outdoors. Moreover, we assessed evening RF-EMF exposure in our sub-study sample using the estimations for the home.

To estimate RF-EMF exposure from mobile phone base stations at home, a validated 3D geospatial radio wave propagation model NISMap was used [23]–[26]. In brief, NISMap computes the field strengths of mobile phone base stations for any location in 3D-space using detailed characteristics of the antennas and the 3D geometry of the urban environment. The model has been validated with outside, inside, and personal measurements showing reliable rank-order predictions [24], [25], [27]. We assessed the emission of the three mobile phone communication systems in use at the time of the study (GSM900, GSM1800, and UMTS) using a country-wide mobile phone base stations data set from 2015. These systems operated in the following downlink frequency bands: 925-960 MHz, 1805-1880 MHz, and 2110-2170 MHz, respectively. Using the geo-coded address of each participant and the floor level of his/her bedroom at the time of the sleep assessment, we computed the RF-EMF exposure from mobile phone base stations at each participant's bedroom.

RF-EMF exposure from the other far-field RF-EMF sources (FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) and from mobile phone base stations outside the preadolescent's home was assessed in a previous study using personal RF-EMF measurements of up to 72 hours between 2014 and 2015 [28]. We used the average of the personal RF-EMF measurements done by 56 adolescents with an average age of 12 years in Amsterdam, as data was not available for the participants of the Generation R Study. In the INMA sub-cohorts, 148 preadolescents participated in the RF-EMF measurements.

Integrated RF-EMF exposure model

We applied the integrated RF-EMF exposure model to estimate all-day and evening whole-brain RF-EMF doses [20]–[22]. In summary, the model combines three types of information: i) the estimated ratio of the absorbed power in the brain over the mass of the brain for each specific RF-EMF source, which takes into account individual characteristics (e.g. sex, age, height, and weight), known as specific absorption rate (SAR, in Watts (W) / kilogram (kg)), normalized to 1 W output power, ii) the output power of each RF-EMF source and activity (in W), and iii) the duration of use or exposure to each RF-EMF source and activity (in minutes (min)/day).

First, the model estimated all-day and evening whole-brain RF-EMF doses (millijoules (mJ)/kg/day) induced by each RF-EMF source as follows:

Equation 1: Source-specific all-day whole-brain RF-EMF dose $(\mathrm{mJ/kg/day})_{\mathrm{source}}$=

$$\Big(\frac{\mathbf{SAR}\left(\frac{\mathrm{W}}{\mathrm{kg}}\right)\mathrm{source}}{\mathrm{normalized\ output\ power\ 1\ W}}\ \mathrm{x}\ \mathbf{Output\ power}(\mathrm{W})\mathrm{source}\ \mathrm{x}\ \mathbf{Duration}\left(\frac{\mathrm{min}}{\mathrm{day}}\right)\mathrm{source}\Big)$$

Equation 2: Source-specific evening whole-brain RF-EMF dose $(\mathrm{mJ/kg/day})_{\mathrm{source,day}}$=

$$\Big(\frac{\mathbf{SAR}\left(\frac{\mathrm{W}}{\mathrm{kg}}\right)\mathrm{source}}{\mathrm{normalized\ output\ power\ 1\ W}}\ \mathrm{x}\ \mathbf{Output\ power}(\mathrm{W})\mathrm{source}\ \mathrm{x}\ \mathbf{Duration}\left(\frac{\mathrm{min}}{\mathrm{evening}}\right)\mathrm{source,\ day}\Big)$$

The integrated exposure model required some input information that we did not collect, such as network used for phone calls, characteristics of the network when using screen activities, and the distance to the device. We assumed a proportion of 35% 2G calls, 65% 3G calls, and no hands-free devices use. We based our assumptions on mobile phone use data in preadolescents, adolescents, and young adults in Europe collected in the same time period than in our study using a specifically designed software application installed on participants' mobile phone to collect data on the their use [29]. The output power depends on the characteristics of the network. We assumed that screen activities with mobile communication devices occur using WiFi at 2.4 GHz [22], [30] and that WiFi data transfer rates were 54 Megabits per second. Moreover, the brain SAR depends on the relative distance to the device. SAR values were simulated in a previous study [20] and we used averaged SAR values from different available positions to obtain one averaged SAR value per device and activity that could be inserted in Equations 1 to 2. Finally, we assigned output powers to each mobile communication device and activity based on expert opinion (Supplementary Tables S1 and S2).

Second, we summed source-specific all-day whole-brain RF-EMF doses and source-specific evening whole-brain RF-EMF doses for each day of measurement:

Equation 3: Overall all-day whole-brain RF-EMF dose (mJ/kg/day) =

$$\sum\nolimits_{\text{source}} \left(\frac{\mathbf{SAR}\left(\frac{\text{W}}{\text{Kg}}\right)\text{source}}{\text{normalized output power 1 W}} \text{ x } \mathbf{Output\ power}(\text{W})\text{source x } \mathbf{Duration}\left(\frac{\text{min}}{\text{day}}\right)\text{source}\right)$$

Equation 4: Overall daily evening whole-brain RF-EMF dose (mJ/kg/evening)$_{\text{day}}$ =

$$\sum\nolimits_{\text{source,day}} \left(\frac{\mathbf{SAR}\left(\frac{\text{W}}{\text{Kg}}\right)\text{source}}{\text{normalized output power 1 W}} \text{ x } \mathbf{Output\ power}\ (\text{W})\text{source x } \mathbf{Duration}\left(\frac{\text{min}}{\text{evening}}\right)\text{source, day}\right)$$

Third, RF-EMF sources were combined in three groups each that lead to different all-day and evening whole-brain RF-EMF exposure patterns: i) high RF-EMF doses from peak exposures very close to the head but for short periods of time (i.e. mobile and DECT phone calls), ii) low RF-EMF doses that might mainly represent non-RF-EMF factors related to the use of mobile communication devices (i.e. use of other mobile phone uses than calling, tablet, and laptop while wirelessly connected to the internet), and iii) low RF-EMF doses received continuously throughout the day (i.e. far-field sources such as mobile phone base stations, FM radio and TV broadcast antennas, and WiFi). This resulted in 8 exposure variables: i) overall all-day whole-brain RF-EMF dose, ii) all-day whole-brain RF-EMF dose from mobile and DECT phone calls (named phone calls), iii) all-day whole-brain RF-EMF dose from use of other mobile phone uses, tablet, and laptop while wirelessly connected to the internet (named screen activities), iv) all-day whole-brain RF-EMF dose from far-field sources, v) overall evening whole-brain RF-EMF dose, vi) evening whole-brain RF-EMF dose from phone calls, vii) evening whole-brain RF-EMF dose from screen activities, and viii) evening whole-brain RF-EMF dose from far-field sources. Since only 15-20% of the preadolescents reported phone calls in the evening, we categorized the evening whole-brain RF-EMF dose from phone calls as zero, low dose (preadolescents with evening phone calls dose of or below the median of the mobile phone calls users (2.3 mJ/kg/evening), and high dose (preadolescents with evening phone calls dose above the median of the mobile phone calls users). Overall and source-specific all-day whole-brain RF-RMF doses, overall evening whole-brain RF-EMF dose, and evening whole-brain RF-EMF dose from screen activities were analysed as continuous variables.

Sleep disturbances

Sleep disturbances were assessed using the Sleep Disturbance Scale for Children (SDSC) [31] in Generation R and INMA. SDSC is a validated questionnaire completed by the mother. The SDSC consists of 26 items that quantify sleep problems in a 5-Likert scale over the past 6 months. The items are grouped into 6 subscales evaluating different sleep disturbances. For this study, we included the SDSC subscales of: i) problems with initiating and maintaining sleep, ii) excessive somnolence, and iii) sleep arousal problems (i.e. a shift from deep sleep to light sleep or from sleep to wakefulness). Problems with initiating and maintaining sleep (range = 0 – 28), and excessive somnolence (range = 0 - 20) were treated as continuous variables. We categorized sleep arousal problems based on its distribution in our study population (presence of symptoms (yes) vs. no symptoms (no)).

Moreover, we collected information on sleep quality (“How did you sleep last night?”), categorized as very good, good, or regular/bad/very bad, and restfulness (“How rested do you feel this morning?”), categorized as very well rested, rested, or moderately/poorly/very poorly rested, for 7 consecutive days using a sleep diary completed by preadolescents.

Objective sleep measures

Preadolescents wore a tri-axial wrist accelerometer (GENEActiv; Activinsights, UK) on their non-dominant wrist and completed a sleep diary for 7 consecutive days in Generation R and INMA [32], [33]. Measurements were processed using the R-package GGIR [34]. We obtained objective sleep measures for each day which included total sleep time (time between falling asleep and final awakening from which the time spent awake in between is subtracted, in hours), sleep efficiency (total sleep time divided by total time in bed, in %), sleep onset latency (time between lying down in bed and falling asleep, in minutes), and wake after sleep onset (time awake between falling asleep and final awakening, in minutes). We also calculated the mean of each objective sleep measure across 7 days.

Potential confounding variables

The potential confounding variables were *a priori* defined with a Directed Acyclic Graph (DAG) [35] (Supplementary Figure S2). Maternal characteristics included maternal age, maternal country of birth collected in pregnancy, and maternal educational level (low, medium, or high) collected at 5-12 years of the child. Child characteristics included sex, age, body mass index (kg/m^2), minutes of television watching, and self-perceived general health (very bad, bad, good, very good, or excellent) assessed at 9-12 years of the child. Moreover, a sleep diary was used to collect information on preadolescents habits' after 7 p.m. for 7 days. Preadolescents habits included minutes of console/computer gaming, minutes of television watching, caffeinated drinks intake (yes, or no), and sleeping alone in preadolescents' bedroom (yes, or no).

Statistical analysis

Preadolescents included in at least one of the analyses (n = 1,842) were more likely to be female, have a very good self-perceived general health, and have mothers with a higher level of education and from the country of the cohort, compared with those non-included (n= 9,474). We used inverse probability weighting to correct for loss to follow-up and account for potential selection bias that results from including only the preadolescents with available data. Multiple imputation of missing confounding variables was performed using chained equations where 25 completed datasets were generated and analyzed for the overall sample and sub-study sample [36]. The percentage of missing values was low (<15 % in the overall sample and <20% in the sub-study sample). Distributions in imputed datasets were very similar to those in the observed dataset (data not shown). Problems with initiating and maintaining sleep, excessive somnolence, and sleep onset latency were square root transformed to approach normality of the residuals. We fitted generalized additive models for each association and we removed those observations identified as outliers (<0.5%) to achieve linearity.

To address our first research objective (i.e. association between all-day RF-EMF doses with sleep disturbances and objective sleep measures), we applied linear regression models to assess the association of overall and source-specific all-day whole-brain RF-EMF doses with problems of initiating and maintaining sleep, excessive somnolence and total sleep time, sleep efficiency, wake after sleep onset, and sleep onset latency. We applied Poisson regression models with robust variance to assess the relationship of overall and source-specific all-day whole-brain RF-EMF doses with sleep arousal problems. Prevalence ratios (PR) were calculated instead of odds ratios due to the potential overestimation of the odds ratios when the prevalence of the outcome is high (> 10%) in cross-sectional studies [37]. All models were adjusted for cohort, maternal country of birth, age, educational level, and preadolescents' age, sex, body mass index, television watching, and self-perceived general health. As an ad-hoc analysis, we tested the associations between all-day whole-brain RF-EMF doses with sleep disturbances and objective sleep measures in the sub-study sample.

To address our second objective (i.e. association between evening RF-EMF doses with sleep disturbances and objective sleep measures), we use the repeated measures of evening whole-brain RF-EMF doses and objective sleep parameters using the sub-study sample and we fitted mixed effects models with random intercepts to capitalize on the repeated measures and gain precision in our effect estimates. We used linear mixed effects models with repeated overall and specific evening whole-brain RF-EMF doses from phone calls and screen activities in relation to repeated measures of total sleep time, sleep efficiency, sleep onset latency, and wake after sleep onset across 7 days. We used ordered logistic mixed effects models using repeated overall and source-specific evening whole-brain RF-EMF doses in relation to repeated measures of sleep quality and restfulness. Far-field exposure was assessed only at one time point. Thus, the overall evening whole-brain RF-EMF dose included evening whole-brain RF-EMF dose from far-field sources (constant for each day), but evening whole-brain RF-EMF dose from far-field sources could not be analysed independently. We analysed the correlations of overall, phone calls, and screen activities doses between days of the week to explore the variation in exposures (overall evening dose, r = 0.41 – 0.69; evening dose from phone calls, r= 0.13 – 0.45, and evening dose from screen activities, r = 0.40 – 0.65). This variation was sufficient to allow estimations of the overall effect of evening RF-EMF doses to objective sleep measures, and sleep quality and restfulness. We did not include an interaction term between exposure and time (i.e. day of the week) because we expected the associations to be similar between days of the week. Mixed effect models were adjusted for cohort, maternal country of birth, age, educational level, and preadolescents’ age, sex, body mass index, television watching, self-perceived general health, and preadolescents’ habits after 7 p.m.

All analyses were performed using Stata version 15 (StataCorp, College Station, TX) and R version 3.6.1.

Results

Descriptive analysis

About 52% of preadolescents of our population were female, 56%of preadolescents in the sample and 42% in the sub-study sample had mothers with a high level of education, and 44% of preadolescents in the sample and 53% in the sub-study sample had very good self-perceived general health (Table 1). Preadolescents spend 48.9 minutes/day using mobile communication devices for screen activities and 2.5 minutes/day making phone calls (Supplementary Table S3). The overall estimated all-day whole-brain RF-EMF dose was 199.4 mJ/kg/day and the main contributor to the all-day whole-brain RF-EMF dose were phone calls (64.6%) (Table 2). Preadolescents of the sub-study sample reported fewer phone calls during a day than in the evening (mean (standard deviation (SD)) of the all-day calls dose = 116.6 (535.8) mJ/kg/day vs. mean (SD) of the evening calls dose = 208.6 (1000.7) mJ/kg/evening in the sub-study sample) (Supplementary Table S4). Specific doses from phone calls were low to moderately and positively correlated with dose from screen activities (r= between 0.07 and 0.25) and specific doses from far-field sources were low to moderately and negatively correlated with dose from phone calls and screen activities (r = between -0.01 and -0.24) (Supplementary Table S5-S6). Average overall all-day whole-brain RF-EMF doses were different between cohorts (197.6 mJ/kg/day in Generation R, 375.1 mJ/kg/day in INMA-Sabadell, and 104.4 mJ/kg/day in INMA-Gipuzkoa) (Supplementary Table S7). Preadolescents who spent more time with console/computer gaming or television watching were more likely to have higher evening whole-brain RF-EMF dose from screen activities (Supplementary Table S8).

Objective total sleep time was on average 7.5 hours, sleep efficiency was 84%, and wake after sleep onset was 71.4 minutes in the study sample (Table 2). Objective sleep onset latency and wake after sleep onset were moderately and positively correlated with problems of initiating and maintaining sleep (r = 0.25 and 0.35, respectively), and weakly and positively correlated with excessive somnolence (r = 0.08 and 0.11, respectively) (Supplementary Table S9). Preadolescents with sleep arousal problems had less favourable objective sleep measures such as total sleep time, sleep efficiency, and sleep latency onset (Supplementary Table S10).

All-day whole-brain RF-EMF doses, sleep disturbances, and objective sleep measures

Overall all-day whole-brain RF-EMF dose and all-day whole-brain RF-EMF dose from phone calls were not associated with sleep disturbances or objective sleep measures (Table 3-4). However, higher all-day whole-brain RF-EMF dose from screen activities was associated with higher symptoms of excessive somnolence [2.19 symptom score (95%CI 0.10; 4.27) per increase in 100 mJ/kg/day]. Finally, higher all-day whole-brain RF-EMF dose from far-field sources was associated with longer sleep onset latency [0.28 minutes (95%CI 0.07; 0.49) per increase in 100 mJ/kg/day]. In the sub-study sample, overall all-day whole-brain RF-EMF dose, and all-day whole-brain RF-EMF dose from screen activities was not association with sleep disturbances or objective sleep measures (data not shown), but higher all-day whole-brain RF-EMF dose from far-field sources was associated with longer sleep onset latency [0.27 minutes (95%CI 0.05; 0.48) per increase in 100 mJ/kg/day].

Evening whole-brain RF-EMF doses, sleep disturbances, and objective sleep measures

Preadolescents with high evening whole-brain RF-EMF dose from phone calls had a shorter total sleep time and longer sleep latency compared to preadolescents with zero evening whole-brain RF-EMF dose from phone calls [-11.86 minutes (95%CI -21.22; -2.51) and) 0.34 minutes (95%CI 0.04; 0.65), respectively]. Overall evening whole-brain RF-EMF dose, and evening dose from screen activities were not associated with objective sleep measures and none of the evening whole-brain RF-EMF doses were associated with sleep quality and restfulness.

Table 1. Preadolescents' characteristics and habits after 7 p.m.

	Study sample[a] (n = 1,599)	Sub-study sample[b] (n = 335)
Preadolescents' characteristics		
Cohort		
Generation R	60.4	0.0
INMA-Sabadell	15.8	58.8
INMA-Gipuzkoa	23.8	41.1
Maternal educational level at child's birth		
High	56.8	42.8
Medium	35.8	35.9
Low	7.4	21.2
Sex (female vs. male)	52.0	52.2
Maternal country of birth (country of the cohort vs. others)	88.1	96.8
Age, in years	10.2 (0.7)	10.9 (0.5)
Self-perceived general health		
Excellent	33.6	21.0
Very Good	44.3	53.7
Good/bad/very bad	22.1	25.2
Body mass index, in kg/m2	17.9 (3.0)	19.5 (3.8)
Television viewing per day, in min	90.5 (68.3)	84.0 (68.2)
Preadolescents habits after 7 p.m[c]		
How many minutes do you play console/computer games?	--	20.7 (30.3)
How many minutes do you watch television? ,	--	65.7 (57.2)
Do you intake caffeinated drinks? (yes vs. no)		23.3
Do you sleep alone in your bedroom? (yes vs. no)	--	63.2

Values are percentages for categorical variables and mean (SD) for continuous variables.

[a] Preadolescents included in the study sample are those with information on total day whole-brain RF-EMF doses and at least one subscale of the Sleep Disturbances Scale for Children, or one objective sleep measure.

[b] Preadolescents included in the sub-study sample are those with information on evening whole-brain RF-EMF doses and at least one objective sleep measure.

[c] Average preadolescents' habits after 7 p.m across 7 days.

Table 2. Estimated overall and source-specific all-day and evening whole-brain RF-EMF doses, sleep disturbances, and objective sleep measures in preadolescents.

	Study sample (n = 1,599)	**Sub-study sample (n = 335)**
Whole-brain RF-EMF doses (mJ/kg/day)[a]		
Overall dose		
Mean (SD)	166.24.4 (699.6)	274.2 (1000.5)
Median (p25; p75)	59.6 (19.7; 118.2)	64.0 (11.9; 180.0)
Phone calls[b]		
Median (p25; p75)	21.0 (2.0; 72.3)	2.3 (0.0; 60.8)
Contribution to the overall dose (mean phone calls dose/overall dose, in %)	77.4	76.1
Screen activities[c]		
Median (p25; p75)	1.9(1.1; 2.7)	0.3 (0.1; 1.0)
Contribution to the overall dose (mean screen activities dose/overall dose, in %)	1.3	0.9
Far-field sources[d]		
Median (p25; p75)	11.0 (7.3; 24.9)	12.9 (4.6; 65.7)
Contribution to the overall dose (mean far-field dose/overall dose, in %)	21.1	23.0
Sleep disturbances		
Problems with initiating and maintaining sleep[e]	4.3 (3.4)	--
Excessive somnolence[f]	2.7 (2.3)	--
Arousal problems (yes vs. no)	26.5	--
Sleep quality		
Very good	--	64.0
Good	--	27.2
Regular/bad/very bad	--	8.8
Restfulness		
Very well rested	--	45.4
Rested	--	41.3
Moderately/ poorly/very poorly rested	--	13.3
Objective sleep measures		
Total sleep time (hours)	7.6 (0.7)	7.4 (0.8)
Sleep efficiency (%)	84.2 (4.4)	84.9 (4.3)
Sleep latency onset (min)	39.2 (39.1)	13.1 (13.3)
Wake After Sleep Onset (min)	71.4 (30.2)	55.2 (30.1)

Values are percentages for categorical variables and mean (standard deviation) or median (p25; p75) for continuous variables. RF-EMF, Radiofrequency Electromagnetic Fields; mJ, millijoules; kg, kilograms.

[a] Whole-brain RF-EMF doses in the sample represent all-day whole-brain RF-EMF doses and inthe sub-study sample represent evening whole-brain RF-EMF doses across 7 days.

[b] Phone calls refer to mobile and DECT phone calls.

[c] Screen activities refer to screen activities with mobile communication devices including mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop while wirelessly connected to the internet.

[d] RF-EMF exposure from different environmental RF-EMF sources (mobile phone base stations, FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) from different microenvironments (home, school, commuting, and outdoors).

[e] Higher scores indicate more sleep disturbances. Range = 0 – 20.

[f] Higher scores indicate more sleep disturbances. Range = 0 – 28.

Table 3. Association between estimated overall and source-specific all-day whole-brain RF-EMF doses and sleep disturbances in preadolescents (n=1,599).

	Problems with initiating and maintaining sleep[d]	**Excessive somnolence**[d]	**Arousal problems** (yes vs. no)
All-day doses (Δ100 mJ/kg/day)	**B (95% CI)**	**B (95% CI)**	**B (95% CI)**
Overall dose			
B (95% CI)	0.00 (-0.00; 0.01)	0.00 (-0.00; 0.01)	1.00 (0.98; 1.01)
Source-specific doses			
Phone calls[a]	0.00 (-0.00; 0.01)	0.00 (-0.00; 0.01)	0.99 (0.98; 1.01)
Screen activities[b]	1.64 (-0.36; 3.64)	**2.19 (0.10; 4.27)**	2.20 (0.07; 68.83)
Far-field sources[c]	0.01 (-0.04; 0.06)	-0.00 (-0.05; 0.05)	1.04 (0.95; 1.13)

B, Beta Coefficient ; CI, confidence interval; kg, kilograms; mJ, millijoules; PR, prevalence ratio; RF-EMF, Radiofrequency Electromagnetic Fields.

[a] Phone calls refer to mobile and DECT phone calls.

[b] Screen activities refer to screen activities with mobile communication devices including mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop while wirelessly connected to the internet.

[c] RF-EMF exposure from different environmental RF-EMF sources (mobile phone base stations, FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) from different microenvironments (home, school, commuting, and outdoors).

[d] Square root transformed.

Linear or Poisson with robust variance regression models adjusted for cohort, sex, age at sleep assessment, body mass index at sleep assessment (kg/m2), maternal age, maternal education at child's birth, maternal country of birth, minutes of television watching, and self-perceived general health.

Table 4. Association between estimated overall and source-specific all-day whole-brain RF-EMF doses and objective sleep measures in preadolescents (n=1,080).

	Total sleep time (min)	**Sleep efficiency (%)**	**Wake After Sleep Onset (min)**	**Sleep onset latency[c] (min)**
All-day doses (Δ100 mJ/kg/day)	**B (95% CI)**	**B (95% CI)**	**B (95% CI)**	**B (95% CI)**
Overall dose	0.01(-0.43; 0.45)	-0.00(-0.05; 0.04)	-0.03 (-0.30; 0.23)	0.01 (-0.02; 0.03)
Source-specific doses				
Phone calls[a]	0.01 (-0.44; 0.44)	-0.00 (-0.05; 0.04)	-0.02 (-0.30; 0.24)	0.00 (-0.02; 0.03)
Screen activities[b]	-30.70 (-162.33; 100.92)	10.31(-3.52; 24.15)	-69.86(-149.69; 9.96)	-0.48 (-8.07; 7.09)
Far-field sources[c]	0.07 (-3.56; 3.70)	0.154(-0.23; 0.53)	-0.34 (-2.53; 1.84)	**0.28 (0.07; 0.49)**

B, Beta Coefficient ; CI, confidence interval;kg, kilograms; mJ, millijoules; RF-EMF, Radiofrequency Electromagnetic Fields.

[a] Phone calls refer to mobile and DECT phone calls

[b] Screen activities refer to screen activities with mobile communication devices including mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop while wirelessly connected to the internet.

[c] RF-EMF exposure from different environmental RF-EMF sources (mobile phone base stations, FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) from different microenvironments (home, school, commuting, and outdoors).

[c] Square root transformed.

Linear regression models adjusted for cohort, sex, age at sleep assessment, body mass index at sleep assessment (kg/m2), maternal age, maternal education at child’s birth, maternal country of birth, minutes of television watching, and self-perceived general health.

Table 5. Overall effects [B(95% CI)] of the associations between estimated overall and source-specific evening whole-brain RF-EMF doses, and objective sleep measures, sleep quality, and restfulness across seven days (n = 335).

Evening doses	**Total sleep time (min)**	**Sleep efficiency (%)**	**Wake After Sleep Onset (min)**	**Sleep onset latency[c] (min)**	**Sleep quality**	**Restfulness**
Overall dose (Δ100 mJ/kg/evening)	**B (95% CI)**	**B (95% CI)**	**B (95% CI)**	**B (95% CI)**	**B (95% CI)**	**B (95% CI)**
B	-0.08	0.01	-0.16	-0.00	0.00	0.00
(95% CI)	(-0.24; 0.08)	(-0.01; 0.03)	(-0.44; 0.10)	(0.00; 0.00)	(-0.00; 0.01)	(-0.00; 0.01)
Source-specific doses						
Phone calls[a] (Low vs. 0)						
B	-6.20	0.16	0.36	0.00	-0.04	-0.01
(95% CI)	(-14.81; 2.40)	(-0.78; 1.11)	(-6.53; 7.25)	(-0.28; 0.29)	(-0.40; 0.32)	(-0.35; 0.33)
Phone calls[a] (High vs. 0)						
B	**-11.86**	-0.30	-0.25	**0.34**	0.08	-0.10
(95% CI)	**(-21.22; -2.51)**	(-1.31; 0.71)	(-7.35; 6.84)	**(0.04; 0.65)**	(-0.28; 0.45)	(-0.46; 0.25)
Screen activities[b] (Δ100 mJ/kg/evening)						
B	-11.76	-0.51	8.37	0.10	0.20	-0.23
(95% CI)	(-32.50; 8.97)	(-1.83; 0.81)	(-2.09; 18.84)	(-0.35; 0.56)	(-0.35; 0.76)	(-0.73; 0.28)

[a] Phone calls refer to mobile and DECT phone calls

[b] Screen activities refer to screen activities with mobile communication devices including mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop while wirelessly connected to the internet.

[c] Square root transformed.

Categories for the phone calls dose variable are 0 which included preadolescents with null evening whole-brain RF-EMF dose from phone calls; low which included preadolescents with an evening whole-brain RF-EMF dose from evening phone calls of or below 2.3 mJ/Kg/day; and high which included preadolescents with an evening whole-brain RF-EMF dose from evening phone calls above 2.3 mJ/Kg/day.

Linear or ordered logistic regression mixed models with individuals as random intercept adjusted for cohort, sex, age at baseline, body mass index at baseline (kg/m2), maternal education at child's birth, maternal country of birth, self-perceived general health at baseline, and time-varying preadolescents evening habits (minutes of console/computer gaming, minutes of television watching, caffeinated drinks intake, and sleeping alone in preadolescents' bedroom).

Discussion

Summary of main results

This study investigated the association of overall and source-specific all-day and evening whole-brain RF-EMF doses with sleep parameters in preadolescents. We found that the overall all-day whole-brain RF-EMF dose and the all-day whole-brain RF-EMF dose from phone calls were not associated with sleep disturbances and objective sleep measures. However, we found associations between all-day whole-brain RF-EMF dose from screen activities and excessive somnolence, and all-day whole-brain RF-EMF dose from far-field sources and longer sleep onset latency. Regarding evening doses, preadolescents with a high evening whole-brain RF-EMF dose from phone calls had shorter total sleep time and longer sleep onset latency.

Whole-brain RF-EMF dose from phone calls and sleep

To the best of our knowledge, there are no prior studies estimating overall whole-brain RF-EMF doses or assessing RF-EMF exposure from different sources and their relationship with preadolescents' sleep. Previous studies have used questionnaires or operator data (e.g. phone call records) to approximate all-day RF-EMF exposure from phone calls, the primary contributor to the overall whole-brain RF-EMF dose [22], [28]. Higher duration of phone calls has been related to higher daytime sleepiness and more sleep disturbances (e.g. difficulties initiating or maintaining sleep) in children and adolescents between 5 and 17 years old [7], [10], [11], [26], [38], [39]. However, we did not find any association of all-day RF-EMF dose from phone calls with sleep disturbances or objective sleep measures. One longitudinal study in adults also suggested little or no effect of all-day mobile phone calls estimated from operator-recorded data on sleep disturbances [40]. The all-day RF-EMF exposure may underestimate peak RF-EMF exposures at certain time of the day such as the evening window that is most relevant to assess the impact on sleep characteristics. Although less than 20% of our study population reported phone calls in the evening, those who made phone calls did so more in the evening.

The awareness about the importance of reducing the use of mobile communication devices before going to sleep increased in the last years [41], [42]. Previous studies have related the use of mobile communication devices in the evening (i.e. after 6-9 p.m.), including mobile phone use for calling, with shorter sleep duration, higher daytime sleepiness, and higher symptoms of sleep disturbances in preadolescents and adolescents at 12-18 years old [16], [15], [17]. Unfortunately, none of these studies differentiated between the use of a mobile phone for calling and other uses with mobile communication devices that lead to lower levels of RF-EMF exposure to the brain (e.g. texting or browsing the internet). In our study we observed that evening dose of RF-EMF was associated with shorter total sleep time and longer sleep onset latency. Experimental studies in humans showed encephalogram (EEG) alterations induced by RF-EMF emitted by mobile phone for all common frequency bands of the EEG [43], [44] and impairment of sleep-depending learning processes in those individuals exposed to RF-EMF during sleep [45]. However, it is not known whether these EEG changes translate to symptoms of sleep disturbances or altered objective sleep measures in humans. Moreover, in our study the estimated evening RF-EMF dose from phone calls and the reported duration of phone calls during the evening were highly correlated (r = 0.80) and we could not disentangle between them. Consequently, our results should be interpreted with caution, we cannot discard that other non-RF-EMF factors related to the use of phone calls are behind the observed associations (e.g. arousal or sleep displacement).

Whole-brain RF-EMF dose from screen activities and sleep

Higher all-day whole-brain RF-EMF dose from screen activities were associated with higher symptoms of excessive somnolence but evening dose from screen activities was not. Previous studies used reported questionnaires to assess use of mobile communication devices for screen activities such as other mobile phone uses than calling, tablet use, or laptop use. They found that higher all-day device use was related to excessive daytime sleepiness [9], [10], [12] and higher symptoms of sleep disturbances [8], [12], [46], [47] in adolescents and young adults at 10-24 years old. Moreover, the use of screen devices in the evening has been related to more symptoms of sleep disturbances and less objective sleep efficiency at ages between 3 and 21 years old [15], [16], [48]–[57]. If the observed associations were driven by the cumulative RF-EMF exposure to the brain during a day, we would expect to find an association with the all-day dose from phone calls in our study since phone calls represent higher RF-EMF doses to the brain. This can indicate that the association between the use of mobile communication devices for screen activities and impaired sleep is more likely to be explained by individual or social factors related to the use of these devices for screen activities than by the RF-EMF exposure. However, preadolescents are reducing the use of phones for calling and those who make phone calls use hands-free devices or mobile phone applications that allow voice or video calls (e.g. WhatsApp) [58]. This changing pattern might decrease the overall RF-EMF dose the brain receives but increase the amount of RF-EMF dose from screen activities with mobile communication devices.

Whole-brain RF-EMF dose from far-field sources and sleep

The levels of RF-EMF exposure from far-field sources are low and do not produce peak and high intensity exposures to the brain such as those from personal use of mobile communication devices for phone calls or screen activities [59]. In our study, higher dose from far-field sources was related to longer sleep onset latencies. Previous studies assessing the association between RF-EMF exposure from far-field sources and sleep showed mixed results. Two studies reported no association between indoor and outdoor school RF-EMF levels [11], or daytime RF-EMF levels at preadolescents' bedroom [60] and sleep disturbances in adolescents at 15-18 years old. Another study found that higher RF-EMF exposure was related to shorter sleep duration and less sleep arousal problems in children at 5-7 years old [26]. RF-EMF exposure has a large spatial variability [28]. Studies assessing the association between RF-EMF exposure from far-field sources and sleep should focus at RF-EMF exposure at home, where adolescents spent most of the time in the evening or at night while sleeping.

Strengths and limitations

Several methodological aspects should be discussed. One strength of this study is the availability of data in a large sample of almost 1,600 preadolescents from two population birth-based cohort studies from two different countries which used the same questionnaire to assess the mobile communication devices use, and equivalent methods to estimate RF-EMF exposure from far-field sources. Moreover, this is the first study using repetitive measures on evening use of mobile communication devices, and sleep, combining both reported sleep disturbances and objective sleep measures, across 7 consecutive days. Our study also had some limitations. All-day and evening mobile communication devices use was assessed with different instruments (i.e. general questionnaire or sleep diary). Mothers reported all-day use retrospectively which might have introduced recall bias, thus underestimating adolescents' use during a day. Moreover, we used an innovative and comprehensive tool to estimate all-day and evening whole-brain RF-EMF doses but it builds on some assumptions which could lead to non-differential misclassification of the exposure leading to a potential underestimation of the effect estimates. Objective measures such as applications installed in preadolescents' mobile communication devices would improve the accuracy of RF-EMF dose estimations. Unfortunately, we did not estimate RF-EMF doses during the night and we could not differentiate it from evening RF-EMF doses. Less than 10% of our population, however, reported using a mobile communication device in bed. Of those who used a device, none of them reported making phone calls, and only very few were involved in screen activities with mobile communication devices that lead to potential RF-EMF exposure to the brain. Finally, our results might also be due to chance finding since we performed a large number of analysis and the results should be interpreted as hypothesis generating.

Conclusion

Overall all-day whole-brain RF-EMF dose and all-day dose from phone calls were not associated with sleep, though evening whole-brain RF-EMF dose from phone calls were associated with less favourable sleep characteristics as objectively measured by actigraphy. These findings suggest the evening as a potentially relevant window of exposure. Since this is the first study investigating the association between RF-EMF dose and sleep and there is not known biological mechanism explaining the observed associations, our results should be interpreted with caution. Studies exploring the relationship of RF-EMF exposure to the brain and sleep should assess the amount of RF-EMF dose absorbed by the brain in the evening or at night which might be more relevant for preadolescents' sleep.

Acknowledgements

We acknowledge support from the Spanish Ministry of Science, Innovation and Universities through the "Centro de Excelencia Severo Ochoa 2019-2023" Program (CEX2018-000806-S), and support from the Generalitat de Catalunya through the CERCA Program".

Source of financial support

This work was supported by the European Union Seventh Framework Program (FP7/2007–2013 No. 603794 GERoNiMO project).

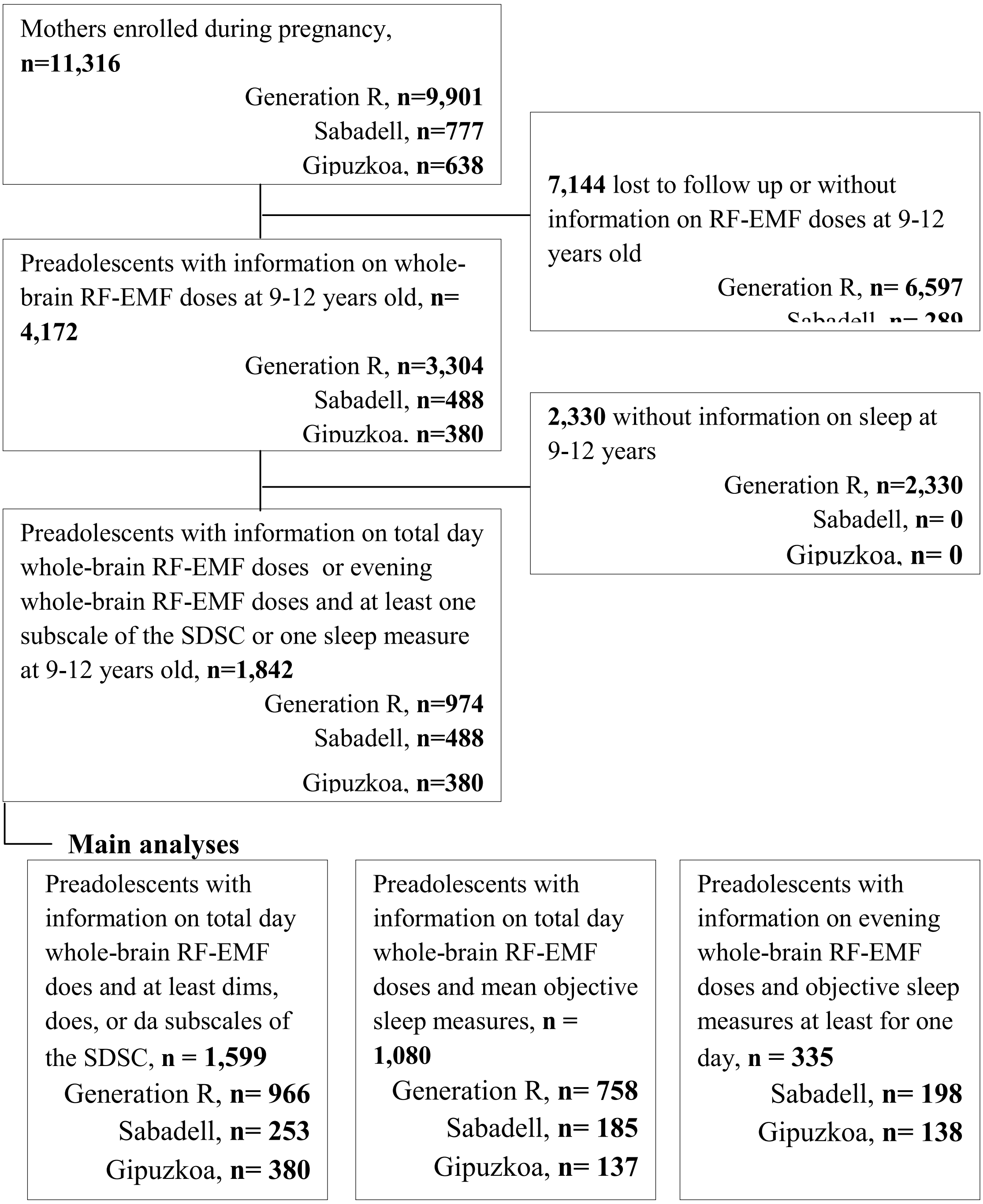
INMA-Sabadell: This study was funded by grants from Instituto de Salud Carlos III (Red INMA G03/176; CB06/02/0041; PI041436; PI081151 incl. FEDER funds; PI12/01890incl. FEDER funds; CP13/00054 incl. FEDER funds, MS13/00054, CPII18/00018; PI17/01340 incl. FEDER funds), CIBERESP, Generalitat de Catalunya-CIRIT 1999SGR 00241, Generalitat de Catalunya-AGAUR (2009 SGR 501, 2014 SGR 822), Fundació La Marató de TV3 (090430), Spanish Ministry of Economy and Competitiveness (SAF2012-32991 incl. FEDER funds), French Agency for Food, Environmental and Occupational Health & Safety (EST-2016 RF-21), EU Commission (261357, 308333, 603794 and 634453).

INMA-Gipuzkoa: This study was funded by grants from Instituto de Salud Carlos III (FIS-PI13/02187), CIBERESP, Department of Health of the Basque Government (2015111065), and the Provincial Government of Gipuzkoa (DFG15/221) and annual agreements with the municipalities of the study area (Zumarraga, Urretxu, Legazpi, Azkoitia y Azpeitia y Beasain).

The Generation R Study: The general design of the Generation R Study is supported by the Erasmus Medical Center-Rotterdam, the Erasmus University Rotterdam, the Netherlands Organization for Health Research and Development, the Netherlands Organization for Scientific Research, and the Ministry of Health, Welfare and Sport, and the Stichting Trombosedienst and Artsenlaboratorium Rijnmond. This study was funded by a grant from the Netherlands organization for Health Research and Development (85500036). Henning Tiemeier was supported by a grant of the Netherlands Organization for Scientific Research (NWO/ZonMW grant016.VICI.170.200).

Supplementary material

Figure S1. Flowchart of the study.



da, disorders of arousal; dims, disorders of initiating and maintaining sleep; does, disorders of excessive somnolence; SDSC, Sleep Disturbance Scale for Children

Table S1. Output powers to estimate overall and source-specific all-day whole-brain RF-EMF doses.

General questionnaire	Variable (min/day)	device	proportion	Output power (mW)		Cohort
How much time does your child spend making or receiving mobile phone calls?	Mobile phone calls	phone_nearhead_2G	35%	87.9 (50%) 44 (50%)	*GSM call (800-1800MHz)*	Gen R, INMA-Sab, and INMA-Gip
		phone_nearhead_3G	65%	0.45	*UTMS call (2100Mhz)*	
How much time does your child spend making or receiving cordless phone calls?	DECT phone calls	dect_nearhead	100%	7	*DECT phone near head, Call*	Gen R, INMA-Sab, and INMA-Gip
How much time does your child spend using a mobile phone for text messaging?	Mobile phone use for text messaging	phone_data	100%	0.25	*surfing web(news), 2.4 Ghz WIFI 54 MBPS*	Gen R, INMA-Sab, and INMA-Gip
How much time does your child spend using a mobile phone for sending videos, files, or e-mails?	Mobile phone use for e-mailing	phone_data	100%	0.25	*surfing web(news), 2.4 Ghz WIFI 54 MBPS*	Gen R, INMA-Sab, and INMA-Gip
How much time does your child spend using a mobile phone for other use of data?	Mobile phone use for internet browsing or checking social networks	phone_data	100%	0.25	*surfing web(news), 2.4 Ghz WIFI 54 MBPS*	Gen R, INMA-Sab, and INMA-Gip
How much time does your child spend using a tablet while wirelessly connected to the internet?	Tablet use while wirelessly connected to internet	tablet	33.33%	0.25	*surfing web (news), 2.4 Ghz WIFI 54 MBPS*	Gen R, INMA-Sab, and INMA-Gip
			33.33%	1.069	*streaming video (high res), 2.4 Ghz WIFI 54 MBPS*	
			33.33%	0.13	*gaming on-line, 2.4 Ghz WIFI 54 MBPS*	
How much time does your child spend using a laptop while wirelessly connected to the internet?	Laptop use while wirelessly connected to internet	laptop	33.33%	0.25	*surfing web (news), 2.4 Ghz WIFI 54 MBPS*	Gen R, INMA-Sab, and INMA-Gip
			33.33%	1.069	*streaming video (low/high res), 2.4 Ghz WIFI 54 MBPS*	
			33.33%	0.13	*gaming on-line, 2.4 Ghz WIFI 54 MBPS*	

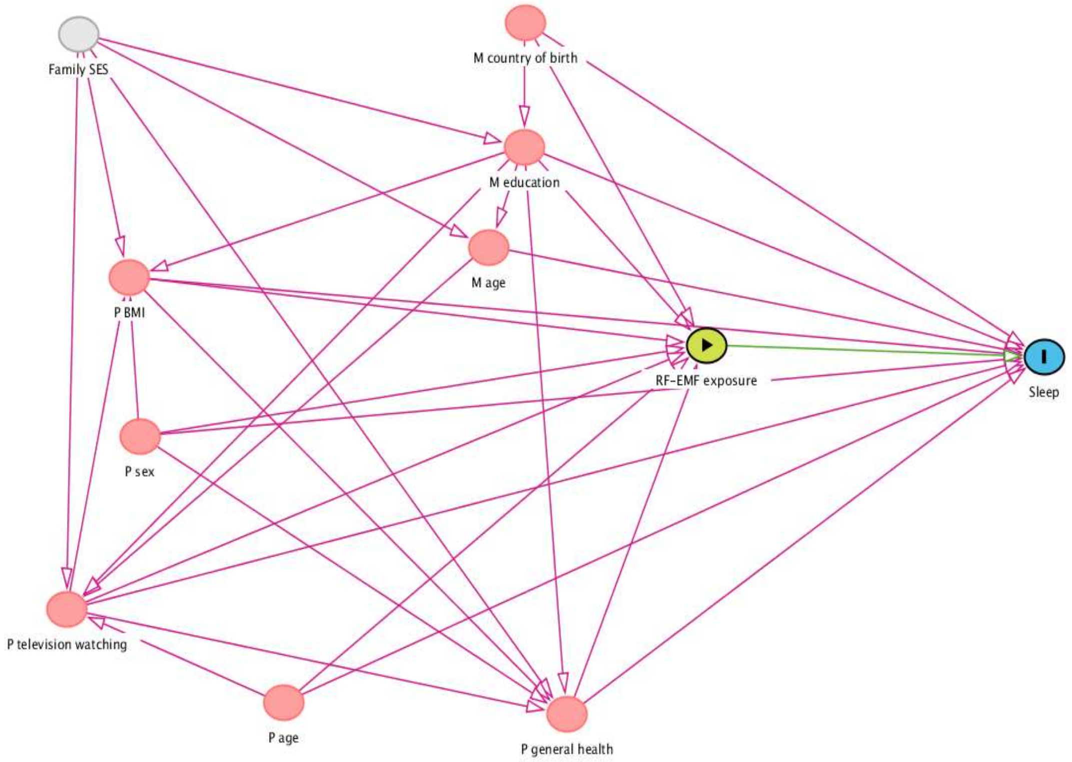
Table S2. Output powers to estimate overall and source-specific evening whole-brain RF-EMF doses.

Sleep diary	Variable (min/day)	Device	Proportion	Output power (mW)		Cohort
How much time do you spend making or receiving mobile phone calls after 7p.m.?	Mobile phone calls after 7p.m.	phone_nearhead_2G	35%	87.9 (50%) 44 (50%)	*GSM call (800-1800MHz)*	INMA-Sab, and INMA-Gip
		phone_nearhead_3G	65%	0.45	*UTMS call (2100Mhz)*	
How much time do you spend making or receiving mobile phone text messages after 7p.m.?	Mobile phone use for texting after 7p.m.	phone_data	100%	0.25	*mobile phone near head, GSM call (900 MHz)*	INMA-Sab, and INMA-Gip
How much time do you spend making or receiving cordless phone calls after 7p.m.?	DECT phone calls after 7p.m.	dect_nearhead	100%	7	*DECT phone near head, Call*	INMA-Sab, and INMA-Gip
How much time do you check facebook, instagram, twitter, or the news with your la tablet or mobile phone after 7p.m.?	Mobile phone use for checking social media networks or the news after 7p.m.	phone_data	50%	0.25	*surfing web(news), 2.4 Ghz WIFI 54 MBPS*	INMA-Sab, and INMA-Gip
	Tablet use for checking social media networks or the news after 7p.m.	tablet	50%	0.25	*surfing web(news), 2.4 Ghz WIFI 54 MBPS*	
How much time do you make video calls with a mobile phone app after 7p.m.?	Mobile phone use for video calls after 7p.m.	phone_data	100%	1.08	*skype video, 2.4 Ghz WIFI 54 MBPS*	INMA-Gip
How much time do you use your mobile phone, tablet, or laptop for sending, sharing, or posting photos or videos after 7p.m.?	Mobile phone use far sending, sharing, or posting photos or videos after 7p.m.	phone_data	33.33%	46.18	*file transfer, 2.4 Ghz WIFI 54 MBPS*	INMA-Gip
	Tablet use for sending, sharing, or posting photos or videos after 7p.m.	tablet	33.33%	46.18	*file transfer, 2.4 Ghz WIFI 54 MBPS*	
	Laptop use far sending, sharing, or posting photos or videos after 7p.m.	laptop	33.33%	46.18	*file transfer, 2.4 Ghz WIFI 54 MBPS*	

Table S2 continuation. Output powers to estimate overall and source-specific evening whole-brain RF-EMF doses.

Sleep diary	Variable (min/day)	Device	Proportion	Output power (mW)		Cohort
How much time do you use your mobile phone or tablet for browsing the internet, or playing on-line after 7p.m.?	Tablet use for browsing the internet after 7p.m.	tablet	25%	0.25	*surfing web(news), 2.4 Ghz WIFI 54 MBPS*	INMA-Gip
	Tablet use for playing on-line after 7p.m.	tablet	25%	0.13	*gaming on-line, 2.4 Ghz WIFI 54 MBPS*	
	Mobile phone use for browsing the internet after 7p.m.	phone_data	25%	0.25	*surfing web(news), 2.4 Ghz WIFI 54 MBPS*	
	Mobile phone use for playing on-line after 7p.m.	phone_data	25%	0.13	*gaming on-line, 2.4 Ghz WIFI 54 MBPS*	
How much time do you spend using a mobile phone for sending, sharing, or posting photos or video?	Mobile phone use for sending, sharing, or posting photos or videos after 7p.m.	phone_data	100%	46.18	*file transfer, 2.4 Ghz WIFI 54 MBPS*	INMA-Sab
How much time do you spend using a mobile phone for other use of data?	Mobile phone use for browsing the internet, streaming videos, or gaming on-line after 7p.m.	phone_data	33.33%	0.25	*surfing web (news), 2.4 Ghz WIFI 54 MBPS*	INMA-Sab
		phone_data	33.33%	1.069	*streaming video (low/high res), 2.4 Ghz WIFI 54 MBPS*	
		phone_data	33.33%	0.13	*gaming on-line, 2.4 Ghz WIFI 54 MBPS*	

Figure S2. Directed Acyclic Graph (DAG) of the association between RF-EMF exposure to the brain and preadolescents' sleep.



The exposure is radiofrequency electromagnetic fields exposure to the brain (**RF-EMF exposure**); the outcomes are sleep disturbances and objective sleep measures (**Sleep**); and potential confounding variables are maternal country of birth (**M country of birth**), education (**M education**), age (**M age**), and preadolescent body mass index (**P BMI**), sex (**P sex**), television watching (**P television watching**), age (**P age**), and self-perceived general health (**P general health**). Family socioeconomic status (**Family SES**) is an unobserved variable.

Table S3. Minutes of the use of mobile communication devices (n = 1,599).

Overall	
Mean (SD)	51.42 (68.23)
Median (p25; p75)	35.71 (17.28; 67.14)
Phone calls[a]	
Mean (SD)	2.51 (10.43)
Median (p25; p75)	0.71 (0.00; 2.14)
Screen activities[b]	
Mean (SD)	48.91 (65.55)
Median (p25; p75)	34.28 (15.71; 64.28)

[a] Phone calls refer to mobile and DECT phone calls.

[b] Screen activities refer to screen activities with mobile communication devices including mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop while wirelessly connected to the internet.

Table S4. Estimated overall and source-specific all-day whole-brain RF-EMF doses in the sub-study sample (n = 335).

Overall dose	
Mean (SD)	198.7 (556.7)
Median (p25; p75)	78.3 (37.5; 172.6)
Phone calls[a]	
Mean (SD)	116.1 (535.8)
Median (p25; p75)	6.1 (0.0; 55.6)
Contribution to the overall dose (%)	58.4
Screen activities[b]	
Mean (SD)	13.1 (12.5)
Median (p25; p75)	10.9 (4.7; 17.9)
Contribution to the overall dose (%)	6.5
Far-field sources[c]	
Mean (SD)	69.5 (119.4)
Median (p25; p75)	20.2 (11.3; 70.3)
Contribution to the overall dose (%)	34.9

Values are percentages for categorical variables and mean (standard deviation) or median (p25; p75) for continuous variables. RF-EMF, Radiofrequency Electromagnetic Fields; mJ, millijoules; Kg, kilograms.

[a] Phone calls refer to mobile and DECT phone calls.

[b] Screen activities refer to screen activities with mobile communication devices including mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop while wirelessly connected to the internet.

[c] RF-EMF exposure from different environmental RF-EMF sources (mobile phone base stations, FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) from different microenvironments (home, school, commuting, and outdoors).

[d] Higher scores indicate more sleep disturbances.

Table S5. Correlation between total day whole-brain RF-EMF doses (mJ/Kg/day) (n = 1,599).

	(1)	**(2)**	**(3)**	**(4)**
Overall dose **(1)**	1.00			
Phone calls **(2)**	**0.67**	1.00		
Screen activities **(3)**	**0.35**	0.07	1.00	
Far-field sources **(4)**	**0.25**	-0.07	**-0.24**	1.00

Values are rho coefficients from spearman correlations. **Bold:** p-value<0.05

Table S6. Correlation between evening whole-brain RF-EMF doses (mJ/Kg/day) (n = 355).

	(1)	**(2)**	**(3)**	**(4)**
Overall dose **(1)**	1.00			
Phone calls **(2)**	**0.62**	1.00		
Screen activities **(3)**	**0.25**	**0.25**	1.00	
Far-field sources **(4)**	**0.50**	-0.07	-0.01	1.00

Values are rho coefficients from spearman correlations. **Bold:** p-value<0.05.

Table S7. Association between preadolescents' characteristics, and estimated overall and source-specific all-day whole-brain RF-EMF doses (mJ/kg/day) in preadolescents (n = 1,599).

	Overall dose		Phone calls[a]		Screen activities[b]		Far-field sources[c]	
Preadolescents' characteristics	**Mean (SD)/ ρ**	**p-value**	**Mean (SD)/ ρ**	**p-value**	**Mean (SD)/ ρ**	**p-value**	**Mean (SD)/ ρ**	**p-value**
Cohort		<0.001		<0.001		<0.001		<0.001
Generation R	197.60 (571.28)		113.00 (564.41)		49.26 (54.29)		21.24 (50.22)	
INMA-Sabadell	375.19 (1251.22)		268.08 (1242.20)		11.63 (14.98)		95.47 (156.96)	
INMA-Gipuzkoa	104.44 (167.73)		58.48 (163.70)		16.49 (15.67)		29.47 (43.90)	
Maternal educational level		0.736		0.830		0.002		<0.001
High	195.72 (726.48)		118.89 (722.08)		35.35 (34.15)		31.27 (66.27)	
Medium	221.49 (633.61)		140.47 (625.10)		36.62 (61.70)		37.67 (87.37)	
Low	229.16 (770.33)		137.84 (733.73)		21.00 (35.23)		68.26 (151.30)	
Sex		0.112		0.054		<0.001		0.975
Female	213.33 (668.57)		137.60 (655.87)		31.45 (31.77)		35.44 (89.42)	
Male	168.25 (427.64)		84.03 (417.52)		40.41 (58.24)		35.32 (74.25)	
Maternal country of birth		0.234		0.243		0.009		0.102
Country of the cohort	185.52 (549.31)		105.86 (537.84)		34.71 (46.86)		36.65 (84.73)	
Others	237.82 (677.41)		156.13 (667.20)		44.07 (45.06)		26.19 (63.13)	
Age, in years	-0.12	<0.001	-0.07	0.003	-0.49	<0.001	0.33	<0.001
Self-perceived general health		0.343		0.400		0.008		0.007
Excellent	156.39 (419.53)		82.18 (409.19)		35.65 (40.01)		28.06 (64.23)	
Very Good	209.15 (765.28)		129.79 (756.16)		29.15 (30.17)		44.11 (98.29)	
Good/bad/very bad	189.96 (369.11)		103.15 (347.90)		38.09 (74.86)		41.73 (92.05)	
Body mass index, in kg/m2	-0.05	0.041	-0.00	0.910	-0.28	<0.001	0.10	<0.001
Television viewing, in min	0.17	<0.001	0.09	<0.001	0.21	<0.001	-0.06	0.010

Values are means (SD) or rho coefficients (ρ). P-values are based on one-way anova or spearman correlations.

[a] Phone calls refer to mobile and DECT phone calls

[b] Screen activities refer to screen activities with mobile communication devices including mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop while wirelessly connected to the internet.

[c] RF-EMF exposure from different environmental RF-EMF sources (mobile phone base stations, FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) from different microenvironments (home, school, commuting, and outdoors).

Table S8. Association between preadolescents' characteristics, preadolescents' habits after 7 p.m, and estimated overall and source-specific evening whole-brain RF-EMF doses (mJ/kg/day) in preadolescents (n = 335).

	Overall dose		Phone calls[a]				Screen activities[b]		Far-field sources[c]	
Preadolescents' characteristics	**Mean (SD)/ ρ**	**p-value**	**No % / Mean (SD)**	**Low % / Mean (SD)**	**High % / Mean (SD)**	**p-value**	**Mean (SD)/ ρ**	**p-value**	**Mean (SD)/ ρ**	**p-value**
Cohort		0.882				0.397		<0.001		<0.001
INMA-Sabadell	294.7 (646.9)		84.46	9.84	5.70		0.6 (0.7)		97.5 (144.3)	
INMA-Gipuzkoa	277.4 (1431.4)		84.78	12.32	2.90		5.8 (17.0)		31.2 (50.6)	
Maternal educational level		0.567				0.443		0.541		0.916
Low	331.0 (861.3)		80.00	11.43	8.57		1.6 (4.1)		71.8 (107.7)	
Medium	205.5 (370.3)		84.75	11.02	4.24		2.7 (7.9)		72.0 (138.3)	
High	335.4 (1440.5)		86.62	10.56	2.82		3.4 (15.3)		66.4 (108.1)	
Sex		0.405				0.017		0.085		0.455
Female	330.7 (968.8)		78.53	14.72	6.75		1.8 (6.3)		65.3 (120.6)	
Male	230.8 (1148.7)		89.93	8.05	2.01		4.1 (15.4)		75.7 (124.2)	
Maternal country of birth		0.892				0.464		0.008		0.398
Country of the cohort	286.9 (1079.6)		84.28	11.37	4.35		2.6 (9.8)		71.7 (124.3)	
Others	240.7 (255.6)		70.00	20.00	10.00		12.5 (37.0)		38.3 (50.1)	
Age, in years	0.19	<0.001	10.9 (0.5)	10.8 (0.4)	11.1 (0.6)	0.234	0.10	0.018	0.25	<0.001
Self-perceived general health		0.629				0.873		0.864		0.150
Excellent	296.6 (89.4)		88.57	8.57	2.86		2.4 (7.0)		51.9 (71.3)	
Very Good	329.1 (1300.7)		83.52	11.36	5.11		3.1 (13.7		67.3 (104.0)	
Good/bad/very bad	194.8 (327.7)		83.13	12.05	4.82		2.4 (8.1)		89.0 (170.5)	
Body mass index, in kg/m2	0.02	0.589	19.44 (4.00)	19.64 (3.25)	21.12 (3.17)	0.263	0.01	0.751	-0.04	0.397

Values are means (SD), rho coefficients (ρ), or percentages (%). P-values are based on one-way anova or spearman correlations.

[a] Phone calls refer to mobile and DECT phone calls.

[b] Screen activities refer to screen activities with mobile communication devices including mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop while wirelessly connected to the internet.

[c] RF-EMF exposure from different environmental RF-EMF sources (mobile phone base stations, FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) from different microenvironments (home, school, commuting, and outdoors).

Table S8 continuation. Association between preadolescents' characteristics, preadolescents' habits after 7 p.m, and estimated overall and source-specific evening whole-brain RF-EMF doses (mJ/kg/day) in preadolescents (n = 335).

	Overall dose		**Phone calls**[a]				**Screen activities**[b]		**Far-field sources**[c]	
Preadolescents habits after 7 p.m	**Mean (SD)/ ρ**	**p-value**	**No % / Mean (SD)**	**Low % / Mean (SD)**	**High % / Mean (SD)**	**p-value**	**Mean (SD)/ ρ**	**p-value**	**Mean (SD)/ ρ**	**p-value**
Console/computer gaming, in minutes	0.09	0.080	20.0 (30.3)	24.8 (33.1)	24.3 (23.5)	0.597	0.20	<0.001	0.06	0.220
Television watching, in minutes	0.05	0.367	62.5 (51.5)	81.5 (90.2)	89.0 (51.0)	0.051	0.14	0.008	-0.03	0.582
Do you intake caffeinated drinks?		0.659				0.380		0.218		0.284
No	299.4 (1135.6)		84.19	11.76	4.04		3.1 (12.3)		66.6 (118.7)	
Yes	233.0 (443.5)		86.44	6.78	6.78		1.1 (3.0)		85.0 (122.0)	
Do you sleep alone in your bedroom?		0.316				0.998		0.078		0.230
No	369.8 (1606.8)		84.40	11.01	4.59		4.3 (14.2)		58.6 (84.5)	
Yes	247.1 (605.9)		84.68	10.81	4.50		2.0 (9.4)		75.41 (133.0)	

Values are means (SD), rho coefficients (ρ), or percentages (%). P-values are based on one-way anova or spearman correlations.

[a] Phone calls refer to mobile and DECT phone calls.

[b] Screen activities refer to screen activities with mobile communication devices including mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop while wirelessly connected to the internet.

[c] RF-EMF exposure from different environmental RF-EMF sources (mobile phone base stations, FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) from different microenvironments (home, school, commuting, and outdoors).

[d] Average preadolescents' evening habits across seven days.

Table S9. Correlations between sleep disturbances and objective sleep measures (n = 1,599).

	(1)	(2)	(3)	(4)	(5)
Problems with initiating and maintaining sleep (1)	1.00				
Excessive somnolence (2)	**0.35**	1.00			
Total sleep time (3)	-0.01	-0.01	1.00		
Sleep efficiency (4)	-0.06	-0.05	**0.46**	1.00	
Sleep onset latency (5)	**0.35**	**0.11**	**-0.22**	**-0.14**	1.00
Wake After Sleep Onset (6)	**0.25**	0.08	**-0.13**	**-0.76**	**0.36**

Values are rho coefficients from spearman correlations. **Bold:** p-value<0.05.

Table S10. Association between arousal problems and objective sleep measures (n = 1,599).

	Arousal problems		
	Mean (SD)		**p-value**
	No	**Yes**	
Problems with initiating and maintaining sleep	4.09 (3.30)	5.00 (3.58)	<0.001
Excessive somnolence	2.62 (2.29)	2.96 (2.64)	0.012
Total sleep time (hours)	7.64 (0.69)	7.63 (0.68)	0.770
Sleep efficiency (%)	84.44 (0.04)	83.84 (0.04)	0.056
Sleep onset latency (min)	42.63 (40.61)	32.92 (34.21)	<0.001
Wake After Sleep Onset (min)	72.30 (28.07)	71.43 (34.05)	0.677

Values are means (SD). P-values are based on one-way anova.

References

[1] J. Owens, «Insufficient Sleep in Adolescents and Young Adults: An Update on Causes and Consequences», *PEDIATRICS*, vol. 134, n.º 3, pp. e921-e932, sep. 2014, doi: 10.1542/peds.2014-1696.

[2] S. J. Crowley, A. R. Wolfson, L. Tarokh, y M. A. Carskadon, «An update on adolescent sleep: New evidence informing the perfect storm model», *J. Adolesc.*, vol. 67, pp. 55-65, ago. 2018, doi: 10.1016/j.adolescence.2018.06.001.

[3] S. Adams, D. Williford, y J. Daly, «Adolescent Sleep and Cellular Phone Use: Recent Trends and Implications for Research», *Health Serv. Insights*, p. 99, oct. 2013, doi: 10.4137/HSI.S11083.

[4] N. Cain y M. Gradisar, «Electronic media use and sleep in school-aged children and adolescents: A review», *Sleep Med.*, vol. 11, n.º 8, pp. 735-742, sep. 2010, doi: 10.1016/j.sleep.2010.02.006.

[5] M. Gradisar, A. R. Wolfson, A. G. Harvey, L. Hale, R. Rosenberg, y C. A. Czeisler, «The Sleep and Technology Use of Americans: Findings from the National Sleep Foundation's 2011 Sleep in America Poll», *J. Clin. Sleep Med.*, dic. 2013, doi: 10.5664/jcsm.3272.

[6] A. Schoeni, K. Roser, y M. Röösli, «Symptoms and the use of wireless communication devices: A prospective cohort study in Swiss adolescents», *Environ. Res.*, vol. 154, pp. 275-283, ene. 2017, doi: 10.1016/j.envres.2017.01.004.

[7] M. Redmayne *et al.*, «Use of mobile and cordless phones and cognition in Australian primary school children: a prospective cohort study», *Environ. Health Glob. Access Sci. Source*, vol. 15, p. 26, feb. 2016, doi: 10.1186/s12940-016-0116-1.

[8] X. Jiang, L. L. Hardy, L. A. Baur, D. Ding, L. Wang, y H. Shi, «Sleep duration, schedule and quality among urban Chinese children and adolescents: associations with routine after-school activities», *PloS One*, vol. 10, n.º 1, p. e0115326, 2015, doi: 10.1371/journal.pone.0115326.

[9] V. C. Brunetti, E. K. O'Loughlin, J. O'Loughlin, E. Constantin, y É. Pigeon, «Screen and nonscreen sedentary behavior and sleep in adolescents», *Sleep Health*, vol. 2, n.º 4, pp. 335-340, dic. 2016, doi: 10.1016/j.sleh.2016.09.004.

[10] Y. W. Mak *et al.*, «Association between screen viewing duration and sleep duration, sleep quality, and excessive daytime sleepiness among adolescents in Hong Kong», *Int. J. Environ. Res. Public. Health*, vol. 11, n.º 11, pp. 11201-11219, oct. 2014, doi: 10.3390/ijerph111111201.

[11] R. Durusoy, H. Hassoy, A. Özkurt, y A. O. Karababa, «Mobile phone use, school electromagnetic field levels and related symptoms: a cross-sectional survey among 2150 high school students in Izmir», *Environ. Health*, vol. 16, n.º 1, dic. 2017, doi: 10.1186/s12940-017-0257-x.

[12] S. Liu, Y. K. Wing, Y. Hao, W. Li, J. Zhang, y B. Zhang, «The associations of long-time mobile phone use with sleep disturbances and mental distress in technical college students: a prospective cohort study», *Sleep*, vol. 42, n.º 2, feb. 2019, doi: 10.1093/sleep/zsy213.

[13] A. Cabré-Riera, M. Torrent, D. Donaire-Gonzalez, M. Vrijheid, E. Cardis, y M. Guxens, «Telecommunication devices use, screen time and sleep in adolescents», *Environ. Res.*, vol. 171, pp. 341-347, abr. 2019, doi: 10.1016/j.envres.2018.10.036.

[14] A. Schoeni, K. Roser, A. Bürgi, y M. Röösli, «Symptoms in Swiss adolescents in relation to exposure from fixed site transmitters: a prospective cohort study», *Environ. Health*, vol. 15, n.º 1, p. 77, dic. 2016, doi: 10.1186/s12940-016-0158-4.

[15] A. D. Fobian, K. Avis, y D. C. Schwebel, «Impact of Media Use on Adolescent Sleep Efficiency», *J. Dev. Behav. Pediatr. JDBP*, vol. 37, n.º 1, pp. 9-14, ene. 2016, doi: 10.1097/DBP.0000000000000239.

[16] S. Lemola, N. Perkinson-Gloor, S. Brand, J. F. Dewald-Kaufmann, y A. Grob, «Adolescents' Electronic Media Use at Night, Sleep Disturbance, and Depressive Symptoms in the Smartphone Age», *J. Youth Adolesc.*, vol. 44, n.º 2, pp. 405-418, feb. 2015, doi: 10.1007/s10964-014-0176-x.

[17] C. J. Calamaro, T. B. A. Mason, y S. J. Ratcliffe, «Adolescents Living the 24/7 Lifestyle: Effects of Caffeine and Technology on Sleep Duration and Daytime Functioning», *PEDIATRICS*, vol. 123, n.º 6, pp. e1005-e1010, jun. 2009, doi: 10.1542/peds.2008-3641.

[18] M. N. Kooijman *et al.*, «The Generation R Study: design and cohort update 2017», *Eur. J. Epidemiol.*, vol. 31, n.º 12, pp. 1243-1264, dic. 2016, doi: 10.1007/s10654-016-0224-9.

[19] M. Guxens *et al.*, «Cohort Profile: The INMA—INfancia y Medio Ambiente—(Environment and Childhood) Project», *Int. J. Epidemiol.*, vol. 41, n.º 4, pp. 930-940, ago. 2012, doi: 10.1093/ije/dyr054.

[20] Ilaria Liorni, «Approximation Formulas for Evaluation of Specific Absorption Rate in the Far-Field, Near-to-Far Field and Near-Field Regions for Integrative Radiofrequency Exposure Assessment in Epidemiological Studies (under review)».

[21] Luuk van Wel, «Organ-specific integrative exposure assessment: Radio-frequency electromagnetic field exposure and contribution of sources in the general population (under review)».

[22] L. E. Birks *et al.*, «Radiofrequency Electromagnetic Fields from Mobile Communication: Description of Modeled Dose in Brain Regions and the Body in European Children and Adolescents (under review)».

[23] A. Bürgi *et al.*, «A model for radiofrequency electromagnetic field predictions at outdoor and indoor locations in the context of epidemiological research», *Bioelectromagnetics*, p. n/a-n/a, 2009, doi: 10.1002/bem.20552.

[24] J. Beekhuizen, R. Vermeulen, H. Kromhout, A. Bürgi, y A. Huss, «Geospatial modelling of electromagnetic fields from mobile phone base stations», *Sci. Total Environ.*, vol. 445-446, pp. 202-209, feb. 2013, doi: 10.1016/j.scitotenv.2012.12.020.

[25] J. Beekhuizen *et al.*, «Modelling indoor electromagnetic fields (EMF) from mobile phone base stations for epidemiological studies», *Environ. Int.*, vol. 67, pp. 22-26, jun. 2014, doi: 10.1016/j.envint.2014.02.008.

[26] A. Huss *et al.*, «Environmental Radiofrequency Electromagnetic Fields Exposure at Home, Mobile and Cordless Phone Use, and Sleep Problems in 7-Year-Old Children», *PLOS ONE*, vol. 10, n.º 10, p. e0139869, oct. 2015, doi: 10.1371/journal.pone.0139869.

[27] A. L. Martens, J. F. B. Bolte, J. Beekhuizen, H. Kromhout, T. Smid, y R. C. H. Vermeulen, «Validity of at home model predictions as a proxy for personal exposure to radiofrequency electromagnetic fields from mobile phone base stations», *Environ. Res.*, vol. 142, pp. 221-226, oct. 2015, doi: 10.1016/j.envres.2015.06.029.

[28] L. E. Birks *et al.*, «Spatial and temporal variability of personal environmental exposure to radio frequency electromagnetic fields in children in Europe», *Environ. Int.*, vol. 117, pp. 204-214, ago. 2018, doi: 10.1016/j.envint.2018.04.026.

[29] C. E. Langer *et al.*, «Patterns of cellular phone use among young people in 12 countries: Implications for RF exposure», *Environ. Int.*, vol. 107, pp. 65-74, oct. 2017, doi: 10.1016/j.envint.2017.06.002.

[30] W. Joseph *et al.*, «Determination of the duty cycle of WLAN for realistic radio frequency electromagnetic field exposure assessment», *Prog. Biophys. Mol. Biol.*, vol. 111, n.º 1, pp. 30-36, ene. 2013, doi: 10.1016/j.pbiomolbio.2012.10.002.

[31] O. Bruni *et al.*, «The Sleep Disturbance Scale for Children (SDSC). Construction and validation of an instrument to evaluate sleep disturbances in childhood and adolescence», *J. Sleep Res.*, vol. 5, n.º 4, pp. 251-261, dic. 1996.

[32] M. E. Koopman-Verhoeff *et al.*, «During day and night: Childhood psychotic experiences and objective and subjective sleep problems», *Schizophr. Res.*, vol. 206, pp. 127-134, abr. 2019, doi: 10.1016/j.schres.2018.12.002.

[33] M. E. Koopman-Verhoeff *et al.*, «Preschool family irregularity and the development of sleep problems in childhood: a longitudinal study», *J. Child Psychol. Psychiatry*, p. jcpp.13060, abr. 2019, doi: 10.1111/jcpp.13060.

[34] V. T. van Hees *et al.*, «A Novel, Open Access Method to Assess Sleep Duration Using a Wrist-Worn Accelerometer», *PLOS ONE*, vol. 10, n.º 11, p. e0142533, nov. 2015, doi: 10.1371/journal.pone.0142533.

[35] M. A. Hernán, S. Hernández-Díaz, M. M. Werler, y A. A. Mitchell, «Causal knowledge as a prerequisite for confounding evaluation: an application to birth defects epidemiology», *Am. J. Epidemiol.*, vol. 155, n.º 2, pp. 176-184, ene. 2002.

[36] C. D. Nguyen, J. B. Carlin, y K. J. Lee, «Model checking in multiple imputation: an overview and case study», *Emerg. Themes Epidemiol.*, vol. 14, n.º 1, dic. 2017, doi: 10.1186/s12982-017-0062-6.

[37] A. Espelt, M. Marí-Dell'Olmo, E. Penelo, y M. Bosque-Prous, «Applied Prevalence Ratio estimation with different Regression models: An example from a cross-national study on substance use research», *Adicciones*, vol. 29, n.º 2, p. 105, jun. 2016, doi: 10.20882/adicciones.823.

[38] N. Küçer y T. Pamukçu, «Self-reported symptoms associated with exposure to electromagnetic fields: a questionnaire study», *Electromagn. Biol. Med.*, vol. 33, n.º 1, pp. 15-17, ene. 2014, doi: 10.3109/15368378.2013.783847.

[39] N. Nathan y J. Zeitzer, «A survey study of the association between mobile phone use and daytime sleepiness in California high school students», *BMC Public Health*, vol. 13, p. 840, sep. 2013, doi: 10.1186/1471-2458-13-840.

[40] G. Tettamanti *et al.*, «Long-term effect of mobile phone use on sleep quality: Results from the cohort study of mobile phone use and health (COSMOS)», *Environ. Int.*, p. 105687, abr. 2020, doi: 10.1016/j.envint.2020.105687.

[41] C. A. Czeisler y T. L. Shanahan, «Problems Associated With Use of Mobile Devices in the Sleep Environment—Streaming Instead of Dreaming», *JAMA Pediatr.*, vol. 170, n.º 12, p. 1146, dic. 2016, doi: 10.1001/jamapediatrics.2016.2986.

[42] J. He, Z. Tu, L. Xiao, T. Su, y Y. Tang, «Effect of restricting bedtime mobile phone use on sleep, arousal, mood, and working memory: A randomized pilot

trial», *PLOS ONE*, vol. 15, n.º 2, p. e0228756, feb. 2020, doi: 10.1371/journal.pone.0228756.

[43] H. Danker-Hopfe, T. Eggert, H. Dorn, y C. Sauter, «Effects of RF-EMF on the Human Resting-State EEG—the Inconsistencies in the Consistency. Part 1: Non-Exposure-Related Limitations of Comparability Between Studies», *Bioelectromagnetics*, vol. 40, n.º 5, pp. 291-318, jul. 2019, doi: 10.1002/bem.22194.

[44] J. Wallace y B. Selmaoui, «Effect of mobile phone radiofrequency signal on the alpha rhythm of human waking EEG: A review», *Environ. Res.*, vol. 175, pp. 274-286, ago. 2019, doi: 10.1016/j.envres.2019.05.016.

[45] C. Lustenberger *et al.*, «Stimulation of the Brain With Radiofrequency Electromagnetic Field Pulses Affects Sleep-Dependent Performance Improvement», *Brain Stimulat.*, vol. 6, n.º 5, pp. 805-811, sep. 2013, doi: 10.1016/j.brs.2013.01.017.

[46] F. Söderqvist, M. Carlberg, y L. Hardell, «Use of wireless telephones and self-reported health symptoms: a population-based study among Swedish adolescents aged 15–19 years», *Environ. Health*, vol. 7, n.º 1, dic. 2008, doi: 10.1186/1476-069X-7-18.

[47] E. L. Kenney y S. L. Gortmaker, «United States Adolescents' Television, Computer, Videogame, Smartphone, and Tablet Use: Associations with Sugary Drinks, Sleep, Physical Activity, and Obesity», *J. Pediatr.*, vol. 182, pp. 144-149, mar. 2017, doi: 10.1016/j.jpeds.2016.11.015.

[48] N. Dube, K. Khan, S. Loehr, Y. Chu, y P. Veugelers, «The use of entertainment and communication technologies before sleep could affect sleep and weight status: a population-based study among children», *Int. J. Behav. Nutr. Phys. Act.*, vol. 14, n.º 1, dic. 2017, doi: 10.1186/s12966-017-0547-2.

[49] A. I. Nathanson y I. Beyens, «The Relation Between Use of Mobile Electronic Devices and Bedtime Resistance, Sleep Duration, and Daytime Sleepiness Among Preschoolers», *Behav. Sleep. Med.*, vol. 16, n.º 2, pp. 202-219, mar. 2018, doi: 10.1080/15402002.2016.1188389.

[50] D. Akçay y B. D. Akçay, «The influence of media on the sleep quality in adolescents», *Turk. J. Pediatr.*, vol. 60, n.º 3, p. 255, 2018, doi: 10.24953/turkjped.2018.03.004.

[51] B. Amra *et al.*, «The association of sleep and late-night cell phone use among adolescents», *J. Pediatr. (Rio J.)*, vol. 93, n.º 6, pp. 560-567, nov. 2017, doi: 10.1016/j.jped.2016.12.004.

[52] O. Bruni, S. Sette, L. Fontanesi, R. Baiocco, F. Laghi, y E. Baumgartner, «Technology Use and Sleep Quality in Preadolescence and Adolescence», *J. Clin. Sleep Med.*, vol. 11, n.º 12, pp. 1433-1441, dic. 2015, doi: 10.5664/jcsm.5282.

[53] O. E. Olorunmoteni, A. O. Fatusi, M. A. Komolafe, y A. Omisore, «Sleep pattern, socioenvironmental factors, and use of electronic devices among Nigerian school-attending adolescents», *Sleep Health*, vol. 4, n.º 6, pp. 551-557, dic. 2018, doi: 10.1016/j.sleh.2018.09.002.

[54] G. Murugesan, L. Karthigeyan, P. Selvagandhi, y V. Gopichandran, «Sleep patterns, hygiene and daytime sleepiness among adolescent school-goers in three districts of Tamil Nadu: A descriptive study», *Natl. Med. J. India*, vol. 31, n.º 4, p. 196, 2018, doi: 10.4103/0970-258X.258216.

[55] K. Bartel *et al.*, «Protective and risk factors associated with adolescent sleep: findings from Australia, Canada, and The Netherlands», *Sleep Med.*, vol. 26, pp. 97-103, oct. 2016, doi: 10.1016/j.sleep.2016.07.007.

[56] M. O. Mireku *et al.*, «Total recall in the SCAMP cohort: Validation of self-reported mobile phone use in the smartphone era», *Environ. Res.*, vol. 161, pp. 1-8, feb. 2018, doi: 10.1016/j.envres.2017.10.034.

[57] A. E. E. Johansson, M. A. Petrisko, y E. R. Chasens, «Adolescent Sleep and the Impact of Technology Use Before Sleep on Daytime Function», *J. Pediatr. Nurs.*, vol. 31, n.º 5, pp. 498-504, sep. 2016, doi: 10.1016/j.pedn.2016.04.004.

[58] M. Sudan, J. Olsen, T. Sigsgaard, y L. Kheifets, «Trends in cell phone use among children in the Danish national birth cohort at ages 7 and 11 years», *J. Expo. Sci. Environ. Epidemiol.*, vol. 26, n.º 6, pp. 606-612, nov. 2016, doi: 10.1038/jes.2016.17.

[59] M. Eeftens *et al.*, «Personal exposure to radio-frequency electromagnetic fields in Europe: Is there a generation gap?», *Environ. Int.*, vol. 121, pp. 216-226, dic. 2018, doi: 10.1016/j.envint.2018.09.002.

[60] G. Berg-Beckhoff *et al.*, «Mobile phone base stations and adverse health effects: phase 2 of a cross-sectional study with measured radio frequency electromagnetic fields», *Occup. Environ. Med.*, vol. 66, n.º 2, pp. 124-130, feb. 2009, doi: 10.1136/oem.2008.039834.

Study III: Estimated whole-brain and lobe-specific RF-EMF doses and brain volumes in preadolescents

Cabré-Riera, A., Marroun, H.E., Muetzel, R., van Wel, L., Liorni, I., Thielens, A., Birks, L.E., Pierotti, L., Huss, A., Joseph, W., Wiart, J., Capstick, M., Hillegers, M., Vermeulen, R., Cardis, E., Vrijheid, M., White, T., Röösli, M., Tiemeier, H., Guxens, M., 2020. Estimated whole-brain and lobe-specific radiofrequency electromagnetic fields doses and brain volumes in preadolescents. Environment International 142, 105808. https://doi.org/10.1016/j.envint.2020.105808

Abstract

Objective: To assess the association between estimated whole-brain and lobe-specific RF-EMF doses, using an improved integrated RF-EMF exposure model, and brain volumes in preadolescents at 9-12 years old.

Methods: Cross-sectional analysis in preadolescents aged 9-12 years from the Generation R Study, a population-based birth cohort set up in Rotterdam, The Netherlands (n=2,592). An integrated exposure model was used to estimate whole-brain and lobe-specific RF-EMF doses (mJ/kg/day) from different RF-EMF sources including mobile and Digital Enhanced Cordless Telecommunications (DECT) phone calls, other mobile phone uses than calling, tablet use, laptop use, and far-field sources. Whole-brain and lobe-specific RF-EMF doses were estimated for all RF-EMF sources together (i.e. overall) and for three groups of RF-EMF sources that lead to a different pattern of RF-EMF exposure. Information on brain volumes was extracted from magnetic resonance imaging scans.

Results: Estimated overall whole-brain RF-EMF dose was 84.3 mJ/kg/day. The highest overall lobe-specific dose was estimated in the temporal lobe (307.1 mJ/kg/day). Whole-brain and lobe-specific RF-EMF doses from all RF-EMF sources together, from mobile and DECT phone calls, and from far-field sources were not associated with global, cortical, or subcortical brain volumes. However, a higher whole-brain RF-EMF dose from mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop use while wirelessly connected to the internet was associated with a smaller caudate volume.

Conclusions: Our results suggest that estimated whole-brain and lobe-specific RF-EMF doses were not related to brain volumes in preadolescents at 9-12 years old. Screen activities with mobile communication devices while wirelessly connected to the internet lead to low RF-EMF dose to the brain and our observed association may thus rather reflect effects of social or individual factors related these specific uses of mobile communication devices. However, we cannot discard residual confounding, chance finding, or reverse causality. Further studies on mobile communication devices and their potential negative associations with brain development are warranted, regardless whether associations are due to RF-EMF exposure or to other factors related to their use.

Introduction

Children have dramatically increased their use of mobile communication devices such as mobile phones or tablets in the last decade [1], [2]. The use of these devices has raised concerns among paediatricians, parents, teachers, and public health practitioners due to their possible negative health consequences [3], [4]. One of the concerns is related to the exposure to radiofrequency electromagnetic fields (RF-EMF) emitted by these devices [5]–[7]. Children are the most vulnerable part of the population to the potential RF-EMF effects as their brain is still rapidly developing [8]. Moreover, children will experience long periods of exposure to RF-EMF because they start using mobile communication devices at an early age and are likely to continue using them through their life.

Brain development is a multistep process beginning early in gestation and continuing into the postnatal period [9]. Brain magnetic resonance imaging (MRI) has been used to examine typical and atypical morphological brain development and some associations have been described between brain volume alterations and cognitive function and behavioural problems [10]–[13]. However, epidemiological studies examining the association between RF-EMF exposure and brain development in children have only used neuropsychological tests or questionnaires measuring cognitive function and behavioural problems [14]–[21]. The study of brain volumes using MRI might give insight to the potential structural brain alterations behind some of the observed associations between RF-EMF exposure and cognitive function and behavioural problems.

Another important issue in this type of research is the assessment of the exposure to RF-EMF. Most epidemiological studies have used parental or self-reported information on use of different mobile communication devices (e.g. mobile phone, digital enhanced cordless telecommunications (DECT) phone, tablet) [14]–[16], [18], [20], [22], [23], estimated residential exposure to RF-EMF from mobile phone base stations [18], or measured personal exposure of different RF-EMF sources using portable devices for a short period of time [24]. All these approaches only assessed a portion of the overall RF-EMF exposure. Thus an estimation that would integrate the exposure of all RF-EMF sources, and more specifically that would also estimate the dose of RF-EMF received in the brain, is needed to better investigate the potential associations between RF-EMF exposure and brain development. So far, only one study developed an RF-EMF exposure model which included several RF-EMF exposure sources and estimated the RF-EMF dose of all these sources received in the whole brain [25]. They found that higher estimated whole-brain RF-EMF dose was not associated with behavioural problems and concentration capacity but was related to lower figural memory in children and adolescents at 12-17 years old [6], [16], [19]. In the present study, we use a recently developed integrated RF-EMF exposure model including a larger number of RF-EMF exposure sources and the assessment of lobe-specific RF-EMF doses, which allows for a more comprehensive study of the potential association between RF-EMF exposure and brain development. Moreover, we estimated whole-brain and lobe-specific RF-EMF doses from three groups of RF-EMF sources that lead to a different pattern of RF-EMF exposure: i) brain RF-EMF doses from mobile and DECT phone calls which are the primary contributors of RF-EMF exposure to the brain leading to peak exposures very close to the head but for short periods of time; ii) brain RF-EMF doses from mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop use while wirelessly connected to the internet which lead to low doses and might mainly represent a variety of social or individual factors related to these type of uses; and iii) brain RF-EMF doses from far-field sources (e.g. mobile phone base stations, FM radio and TV broadcast antennas, WiFi) which lead to low doses but are received continuously along the day [2], [26].

Therefore, the aim of the current study was to assess the association between estimated whole-brain and lobe-specific RF-EMF doses using an improved integrated RF-EMF exposure model and brain volumes in preadolescents at 9-12 years old.

Methods

Study design and population

This is a cross-sectional analysis embedded in the Generation R Study, a population-based birth cohort study from fetal life onwards in Rotterdam, the Netherlands. A total of 9,901 pregnant women were enrolled and children were born between April 2002 and January 2006. Between 2013 and 2015, a total of 3,992 preadolescents at 9-12 years old underwent a MRI assessment, and 3,303 of them had information on mobile communication devices use. After excluding preadolescents with incidental findings or poor neuroimaging quality, we included 2,592 preadolescents (26.2% of the original cohort) in our analyses (Supplementary Figure S1). The Medical Ethics Committee of the Erasmus Medical Centre approved the study and written informed consent was obtained from parents.

Estimated whole-brain and lobe-specific RF-EMF dose

We applied an integrative RF-EMF exposure model to estimate whole-brain and lobe-specific (i.e. frontal, parietal, temporal, occipital) RF-EMF doses due to several RF-EMF exposure sources [26]–[28]. This model is built using information on the use of mobile communication devices (i.e. near-field RF-EMF sources) and estimations of exposure to environmental RF-EMF sources (i.e. far-field RF-EMF sources).

Near-field RF-EMF sources

Information of the use of mobile communication devices close to the body was reported by one of the parents using questionnaires when participants were 9-12 years. Duration of use of i) mobile phone for calling, ii) DECT phone for calling, iii) mobile phone for internet browsing, e-mailing, and text messaging (named other mobile phone uses), iv) tablet while wirelessly connected to the internet, and v) laptop while wirelessly connected to the internet were collected in minutes/day.

Far-field RF-EMF sources

We estimated RF-EMF exposure to different environmental RF-EMF sources (mobile phone base stations, FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) based on the microenvironments where preadolescents spend most of their time such as home, school, commuting, and outdoors.

To estimate RF-EMF exposure from mobile phone base stations at home, a validated 3D geospatial radio wave propagation model called NISMap was used [29]–[32]. In brief, NISMap computes the field strengths induced by emissions from mobile phone base stations for any location in 3D-space using detailed characteristics of the antennas and the 3D geometry of the urban environment. The model has been validated with outside, inside, and personal measurements showing reliable rank-order predictions [30], [31], [33]. We assessed the emission in three mobile phone communication bands that were in use at the time of the study (GSM900, GSM1800, and UMTS) using a country-wide mobile phone base stations data set from 2014. Using the geo-coded address of each child and the floor level of his/her bedroom at the time of the brain imaging, we computed the RF-EMF exposure from mobile phone base stations at each child's bedroom.

RF-EMF exposure from mobile phone base stations in the other microenvironments besides home and from the other far-field RF-EMF sources (FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) in all microenvironments was approximated using the average of personal RF-EMF measurements done over up to 72 hours by 56 preadolescents of around 12 years of age in Amsterdam in a previous study [2], as data was not available for the participants of the Generation R Study.

Integrated RF-EMF exposure model

We applied the integrated RF-EMF exposure model to estimate whole-brain and lobe-specific (i.e. frontal, parietal, temporal, occipital) RF-EMF doses [26]–[28]. Briefly, the model combines three types of information: i) the estimated ratio of the absorbed power to the mass in which it is absorbed of each specific RF-EMF source for each brain region which already takes into account the protection role of the head, known as specific absorption rate (SAR, in Watts (W)/kilogram (kg)), normalized to 1 W output power, ii) the output power of each RF-EMF source (in W), and iii) the daily duration of use of each RF-EMF source (in minutes (min)/day). First, for each brain region the model estimated a specific RF-EMF dose (millijoules (mJ)/kg/day) to each RF-EMF source (mobile phone calls, DECT phone calls, other mobile phone uses, tablet use, laptop use, and far-field RF-EMF sources) as follows:

Equation 1: $\text{Specific RF-EMF dose (mJ/kg/day)}_{brain\ region,\ source}$

$$= (\mathbf{SAR}\ brain\ region, source \text{ x } \mathbf{Output\ power}\ source \text{ x } \mathbf{Duration}\ source)$$

Then, overall whole-brain RF-EMF doses and overall frontal, parietal, temporal, and occipital RF-EMF doses were calculated combining the specific RF-EMF doses of all RF-EMF sources by brain region:

Equation 2: Overall RF-EMF dose $(\mathrm{mJ/kg/day})_{brain\ region}$

$= \sum_{\text{source}} (\mathbf{SAR}\ brain\ region, source \text{ x } \mathbf{Output\ power}\ source \text{ x } \mathbf{Duration} source)$

Moreover, whole-brain and lobe-specific RF-EMF doses for three groups of RF-EMF exposure sources (i) mobile and DECT phone calls, ii) other mobile phone uses, tablet use, and laptop use while wirelessly connected to the internet (named screen activities with mobile communication devices while wirelessly connected to the internet), and iii) far-field sources) were calculated following the same procedure.

To apply the integrated RF-EMF exposure model, we had to make some assumptions [27]. Based on the mobile phone use in preadolescents, adolescents, and young adults in Europe collected in the same period of time than in our study, we assumed a proportion of 35% 2G calls, 65% 3G calls, and no hands-free devices use [34], and that each preadolescent held the phone on the right side for 63% of the time versus 37% on the left side [35]. Other mobile phone uses, laptop use, and tablet use were assumed to occur using WiFi at 2.4 GHz and WiFi data transfer rates were estimated to be 54 Megabits per second. During the timeslots where children were using other mobile phone uses, we assumed that preadolescents were 40% of that time playing video games, 40% of that time streaming video, and 20% of that time browsing the internet or checking social media. For each device and activity, we averaged the SAR values from the different possible positions of use available to obtain one SAR value per activity that could be inserted in Equation 1 and Equation 2.

Brain volumes

To familiarize the participating preadolescents with magnetic resonance environment, each child underwent a mock scanning session prior to the actual MRI session [36]. The scans were performed on a 3 Tesla General Electric scanner (GE, MR750W, Milwaukee, USA) using an 8-channel receive-only head coil. The structural T1 images were obtained using the following sequence parameters: TR = 8.77 ms; TE = 3.4 ms; TI = 600 ms; Flip Angle = 10°; FOV = 220 mm x 220 mm; acquisition matrix = 220 x 220; slice thickness = 1mm; number of slices = 230; voxel size = 1 mm x 1 mm x 1 mm; and ARC Acceleration = 2. The obtained T1 imageswere then processed through the FreeSurfer analysis suite, version 6.0 [37]. Global metrics of cortical and subcortical volumes were extracted. For our analysis we included the volumes of the total brain, cortical gray matter, cortical white matter, cerebellar gray matter, and cerebellar white matter as global brain volumes. The volumes of frontal, parietal, temporal, and occipital lobes were included as cortical lobar volumes. The volumes of the hippocampus, amygdala, thalamus, putamen, caudate, nucleus accumbens, and pallidum were considered as subcortical volumes (Supplementary Table S1). The pre-processing, correction, and assessment of the quality of the images are described in detail elsewhere [38].

Potential confounding variables

The potential confounding variables were *a priori* defined with a Directed Acyclic Graph [39]. Maternal and family characteristics included maternal ethnicity (Dutch, Asian, African, or European and others) collected during pregnancy, maternal educational level (primary or lower (low), secondary (medium), or university or higher (high)) collected when the child was 5 years old, as well as maternal smoking (yes vs. no), employment status (paid vs. non-paid), household income (<2,000€/month (low), 2,000-3,999€ (medium), or >3,999€ (high)) and anxiety and depressive symptoms assessed using the Brief Symptom Inventory [40], [41] collected when the child was 9-12 years. Child characteristics included age at the brain imaging assessment, sex collected at birth, intelligence quotient assessed using the Snijders-Oomen Nonverbal Intelligence test [42] at 5 years, and body mass index (kg/m^2) measured at 9-12 years.

Other covariates

We also collected information on child's handedness due to the previously reported differences in brain volumes between right and left-handers [43].

Statistical Analysis

After checking that all assumptions of the models were fulfilled, we used linear regression models to assess the association between overall and source-specific whole-brain RF-EMF doses and global and subcortical brain volumes, and between overall and source-specific RF-EMF doses to each specific lobe and cortical lobar volumes. We also adjusted our models for the potential confounding variables described above and child's handedness. All models were corrected for multiple testing using false discovery rate [44]. We applied false discovery rating at once to a total of 64 tests and we obtained corrected critical p-values for each association. Additionally, we adjusted cortical lobar volumes, subcortical volumes, and cortical gray matter, cortical white matter, cerebellar cortex, and cerebellar white matter volumes for intracranial volume to ascertain relativity to the head size. Total brain volume was not adjusted for intracranial volume because they were highly correlated (r=0.93).

Multiple imputation of missing confounding variables was performed using chained equations where 25 completed datasets were generated and analyzed [45]. The percentage of missing values was <18% and distributions in imputed datasets were very similar to those in the observed dataset (data not shown). Preadolescents included in the analysis (n=2,592) were more likely to have parents with a higher level of education, with a higher household income, and older compared with those non-included (n=7,309) (Supplementary Table S2). We used inverse probability weighting to correct for loss to follow-up and account for potential selection bias when including only preadolescents with available data (n=2,592) compared to the full cohort recruited at pregnancy (n=9,901).

All analyses were performed using Stata version 15 (StataCorp, College Station, TX).

Results

Most of the children had Dutch and highly educated mothers and were from middle or high income families (Table 1). Estimated overall whole-brain RF-EMF dose was 84.3 mJ/kg/day and the highest dose was estimated in the temporal lobe (307.1 mJ/kg/day). The major contributor to the overall whole-brain RF-EMF dose was the dose from mobile and DECT phone calls (61.5%) while the dose from screen activities with mobile communication devices while wirelessly connected to the internet and from far-field sources contributed 17.4% and 21.1%, respectively (Supplementary Table S3). These percentages varied between each lobe-specific RF-EMF dose. Overall whole-brain RF-EMF dose was highly correlated with overall lobe-specific doses (r>0.79) and source-specific whole-brain doses were not correlated between each other (between -0.02 and -0.12) (data not shown). The associations between maternal, family, preadolescents' characteristics and overall and source-specific estimated whole-brain RF-EMF doses are shown in Table S4.

None of the estimated whole-brain RF-EMF doses was associated with global brain volumes (Table 2). Regarding cortical lobar volumes, only higher estimated frontal RF-EMF dose from screen activities with mobile communication devices while wirelessly connected to the internet was related to a smaller frontal lobe volume [B -39.72 mm^3 (95% CI -78.23; -1.21)] (Table 3). However, this association did not remain after correcting for multiple testing. Overall estimated whole-brain RF-EMF dose and whole-brain RF-EMF dose from mobile and DECT phone calls and from far-field sources were not related to subcortical volumes (Table 4). However, higher estimated whole-brain RF-EMF dose from screen activities with mobile communication devices while wirelessly connected to the internet was associated with smaller caudate volume [B -5.02 mm^3 (95% CI -7.78; -2.25)] and this association remained after correcting for multiple testing. Associations did not materially change after adjusting for intracranial volume (data not shown).

Table 1. Distribution of maternal, family, and preadolescent characteristics, and overall whole-brain and lobe-specific RF-EMF doses (n=2,592).

Maternal characteristics	**Distribution**
Ethnicity, %	
Dutch	60.9
Asian	19.6
African	10.1
European and others	9.4
Educational level, %	
High	54.9
Medium	39.2
Low	5.9
Smoking (yes vs. no), %	13.5
Depressive symptoms[a], median (IQR)	0.0 (0.0; 0.2)
Anxiety symptoms[a], median (IQR)	0.2 (0.0; 0.3)
Employment status (paid vs. non-paid), %	79.4
Family characteristics	
Household income, %	
High	42.3
Medium	39.2
Low	18.5
Preadolescent characteristics	
Sex (female vs. male), %	50.7
Age(in years), median (IQR)	9.9 (9.8; 10.3)
IQ score at 5 years old[b], median (IQR)	103.0 (93.0; 113.0)
BMI at 9-12 years old (kg/m^2), median (IQR)	16.9 (15.7; 18.6)
Overall RF-EMF doses	
Whole-brain (mJ/kg/day), median (IQR)	84.3 (43.4; 155.5)
Frontal lobe (mJ/kg/day), median (IQR)	111.8 (66.5; 202.0)
Parietal lobe (mJ/kg/day), median (IQR)	81.6 (57.6; 147.0)
Temporal lobe (mJ/kg/day), median (IQR)	307.1 (70.8;612.8)
Occipital lobe (mJ/kg/day), median (IQR)	100.6 (62.3; 179.9)

BMI, body mass index; IQ, intelligence quotient; IQR, interquartile range; mJ, milijoules; kg, Kilograms; RF-EMF, Radiofrequency Electromagnetic Fields.

If there are two categories: the listed percentage indicates the fraction in the first category.

[a], higher score indicates more symptoms.

[b], higher score indicates higher IQ

Table 2. Association between estimated overall and source-specific whole-brain RF-EMF doses and global brain volumes (mm^3) in preadolescents at 9-12 years of age.

	Total brain volume	Cortical gray matter volume	Cortical white matter volume	Cerebellar cortex volume	Cerebellar white matter volume
Whole-brain RF-EMF doses (Δ1 mJ/kg/day)	**B (95% CI)**	**B (95% CI)**	**B (95% CI)**	**B (95% CI)**	**B (95% CI)**
Overall dose	-1.29 (-9.91; 7.32)	-0.97 (-5.24; 3.31)	-0.79 (-4.74; 3.16)	0.26 (-0.66; 1.18)	0.20 (-0.05; 0.44)
Source-specific doses					
Phone calls	-0.69 (-9.41; 8.03)	-0.68 (-5.01; 3.64)	-0.54 (-4.53; 3.46)	0.30 (-0.63; 1.23)	0.22 (-0.03; 0.47)
Screen activities[a]	-173.66 (-443.86; 96.53)	-60.22 (-194.31; 73.86)	-91.49 (-215.31; 32.33)	-12.20 (-41.07; 16.67)	-2.13 (-9.82; 5.57)
Far-field sources[b]	-20.74 (-79.40; 37.92)	-11.05 (-40.18; 18.08)	-8.04 (-34.91; 18.83)	-0.78 (-7.04; 5.49)	-0.64 (-2.31; 1.02)

B, Beta coefficient; CI, confidence interval; kg, kilograms; mJ, millijoules; RF-EMF, Radiofrequency Electromagnetic Fields.

[a] Screen activities includes mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop use while wirelessly connected to the internet.

[b] RF-EMF exposure from different environmental RF-EMF sources (mobile phone base stations, FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) from different microenvironments (home, school, commuting, and outdoors).

Linear regression models adjusted for maternal educational level; maternal ethnicity; maternal employment status, maternal smoking; maternal depressive and anxiety symptoms; household income, and child IQ, sex, age, body mass index, and handedness.

Table 3. Association between estimated overall and source-specific RF-EMF doses to each brain lobe and cortical lobar volumes (mm^3) in preadolescents at 9-12 years of age.

	Frontal lobe	**Parietal lobe**	**Temporal lobe**	**Occipital lobe**
Lobe-specific RF-EMF doses (Δ1 mJ/kg/day)	**B (95% CI)**	**B (95% CI)**	**B (95% CI)**	**B (95% CI)**
Overall dose	-0.19 (-1.89; 1.51)	-1.43 (-3.84; 0.98)	0.01 (-0.18; 0.20)	-0.36 (-1.13; 0.42)
Source-specific doses				
Phone calls	-0.04 (-1.84; 1.77)	-2.16 (-6.18; 1.87)	0.01 (-0.18; 0.21)	0.01 (-0.91; 0.93)
Screen activities[a]	**-39.72** **(-78.23; -1.21)**	-17.89 (-61.11; 25.32)	-29.37 (-94.41; 35.67)	-2.68 (-26.11; 20.75)
Far-field sources[b]	-0.80 (-5.96; 4.37)	-0.97 (-3.99; 2.05)	-0.83 (-4.36; 2.71)	-1.29 (-2.74; 0.16)

B, Beta coefficient; CI, confidence interval; kg, kilograms; mJ, millijoules; RF-EMF, Radiofrequency Electromagnetic Fields.

[a] Screen activities includes mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop use while wirelessly connected to the internet.

[b] RF-EMF exposure from different environmental RF-EMF sources (mobile phone base stations, FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) from different microenvironments (home, school, commuting, and outdoors).

Linear regression models adjusted for maternal educational level; maternal ethnicity; maternal employment status, maternal smoking; maternal depressive and anxiety symptoms; household income, and child IQ, sex, age, body mass index, and handedness. In bold, p-value < 0.05.

Table 4. Association between estimated overall and source-specific whole-brain RF-EMF doses and subcortical volumes (mm^3) in preadolescents at 9-12 years of age.

	Hippocampus	**Amygdala**	**Thalamus**	**Putamen**	**Caudate**	**Nucleus accumbens**	**Pallidum**
Whole-brain RF-EMF doses (Δ1 mJ/kg/day)	**B (95% CI)**	**B (95% CI)**	**B (95% CI)**	**B (95% CI)**	**B (95% CI)**	**B (95% CI)**	**B (95% CI)**
Overall dose	-0.02	0.00	0.01	0.03	-0.02	0.01	0.00
	(-0.08; 0.05)	(-0.04; 0.03)	(-0.10; 0.12)	(-0.06; 0.13)	(-0.11; 0.07)	(-0.01; 0.03)	(-0.03; 0.04)
Source-specific doses							
Phone calls	-0.02	0.00	0.02	0.03	-0.01	0.01	0.00
	(-0.08; 0.05)	(-0.03; 0.03)	(-0.10; 0.13)	(-0.07; 0.13)	(-0.10; 0.08)	(-0.01; 0.03)	(-0.03; 0.04)
Screen activities	0.86	0.13	-1.34	-0.38	**-5.02**	-0.48	-0.93
	(-1.13; 2.85)	(-0.89; 1.15)	(-4.91; 2.22)	(-3.46; 2.70)	**(-7.78; -2.25)***	(-1.02; 0.06)	(-2.07; 0.22)
Far-field sources[b]	-0.05	-0.12	-0.19	0.30	-0.29	0.05	0.05
	(-0.49; 0.38)	(-0.34; 0.10)	(-0.96; 0.58)	(-0.36; 0.97)	(-0.89; 0.31)	(-0.07; 0.17)	(-0.20; 0.30)

B, Beta coefficient; CI, confidence interval; kg, kilograms; mJ, millijoules; RF-EMF, Radiofrequency Electromagnetic Fields.

[a] Screen activities with mobile communication devices includes mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop use while wirelessly connected to the internet.

[b] RF-EMF exposure from different environmental RF-EMF sources (mobile phone base stations, FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) from different microenvironments (home, school, commuting, and outdoors).

Linear regression models adjusted for maternal educational level; maternal ethnicity; maternal employment status, maternal smoking; maternal depressive and anxiety symptoms; household income, and child IQ, sex, age, body mass index, and handedness. In bold and *, associations that remained after correction for multiple testing (p-value < corrected critical p-value (0.0008)).

Discussion

In the present study, we applied an improved integrated RF-EMF exposure model to estimate whole-brain and lobe-specific RF-EMF doses including several RF-EMF exposure sources and we investigated their association with brain volumes in preadolescents at 9-12 years of age. We did not find a relationship of estimated whole-brain or lobe-specific RF-EMF doses from overall RF-EMF sources, from mobile and DECT phone calls, or from far-field sources with global, cortical, or subcortical brain volumes. However, we found an association between higher estimated whole-brain dose from mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop use while wirelessly connected to the internet, a group of RF-EMF sources that lead to low RF-EMF exposure to the brain, and smaller caudate volume.

We conducted the first epidemiological study exploring the relationship of RF-EMF brain doses with brain volumes in children. Most of the previous studies have assessed the association between the different RF-EMF sources separately and the development of the brain, but our integrative approach allows a more comprehensive assessment of the overall brain dose from several RF-EMF sources, as well as the brain dose from three groups of RF-EMF sources that lead to a different pattern of RF-EMF exposure. We did not find an association between estimated whole-brain or lobe-specific RF-EMF doses from overall RF-EMF sources or from mobile and DECT phone calls and brain volumes. However, higher estimated whole-brain dose from other mobile phone uses, tablet use, and laptop use while wirelessly connected to the internet was associated with a smaller caudate volume. If this observed association was driven by the RF-EMF dose that the brain absorbs from the use of the mobile communication devices, we would expect to also find an association with the brain dose received from mobile and DECT phone calls. These are the primary contributors of RF-EMF exposure to the brain leading to peak exposures very close to the head, while mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop use while wirelessly connected to the internet lead to low RF-EMF exposure to the brain including the subcortical brain structures such as the caudate [26]. Thus there is concern whether the possible health effects of these specific uses of mobile phone, tablet, and laptop are due to social or individual factors related to the time preadolescents spend with these devices or the specific activities that they undertake with these devices instead of their emitted RF-EMF exposure. In our study, almost all participants reported to use these mobile communication devices always wirelessly connected to the internet, thus the estimated RF-EMF brain dose from each device and the reported time spent with each device were highly correlated (between 0.75 and 0.99). Hence, we were unable to disentangle them. Moreover, we might miss relevant information related to the use of these mobile communication devices which is essential for properly studying its relationship with brain development (e.g. type of screen activity performed with these devices, family structure, psychological well-being, or relationship with friends). Therefore, we cannot entirely discard that our results are due to residual confounding or to chance finding. Moreover, reverse causality could also explain our results. Children and young adults with some psychiatric disorders such as Attention-Deficit/Hyperactivity Disorder have been shown to have a smaller caudate brain volume [46]–[48], and it could be hypothesized that individuals with these disorders have a higher use of mobile communication devices. Given that the potential relationship of RF-EMF exposure and brain volumes was not investigated to date, our analysis was exploratory and needs to be replicated in other population-based studies. Moreover, further studies are warranted due to the expected increase in the use of mobile communication devices and changes in RF-EMF exposure (e.g. introduction of new devices to the market, changes in the patterns of use such as more texting and less calling, or changes in network and devices characteristics such as the introduction of the 5G technology).

Experimental studies in animals have previously showed that exposure to RF-EMF is related to brain morphology alterations. In particular, higher RF-EMF exposure induced denditric remodelling and decreased viable cells in the hippocampus and the amygdala in rats [49]–[53]. In our study, we did not find an association between the brain RF-EMF doses and the volume of the hippocampus or the amygdala. Unfortunately, we could not estimate RF-EMF doses in these subcortical structures. Among other functions, the hippocampus plays an important role in the formation of new memories [54] and the amygdala is involved in memory consolidation [55]. Interestingly, a longitudinal epidemiological study found that a higher estimated whole-brain RF-EMF dose in preadolescents and adolescents with right-side preference for the phone calls was related to a decreased figural memory performance, which involves mainly the right hemisphere [56], and not to verbal memory performance, which involves mainly the left hemisphere, after one year of follow-up [6]. The authors suggested that the association between RF-EMF brain dose and memory might be driven by disturbed sleep [6], as previous studies found alterations in the electroencephalogram (EEG) during sleep in participants exposed to RF-EMF [57]–[60] and disturbed sleep have been related to poorer memory consolidation [61] and disturbed subcortical structures such as hippocampus [62], [63]. The brain is dynamic and responds to many external inputs, including environmental exposures. This dynamism might not always translate to detectable structural brain alterations but to small brain activity changes that could explain the observed associations between RF-EMF exposure and impaired cognitive function in previous studies [6], [15]–[17], [19], [20], [22]–[24], [64], [18], [65], as well as the observed brain effects in animal studies [49]–[53]. Studies investigating the relationship between brain exposure to RF-EMF and functional magnetic resonance imaging measures would be of interest.

The strengths of this study are the collection of detailed information on the use of mobile communication devices in a large cohort of preadolescents, the estimation of whole-brain and lobe-specific RF-EMF doses including a large number of RF-EMF exposure sources, and the availability of brain structural imaging data for about 2,500 participants. The main limitation of this study is its cross-sectional design. If an association between RF-EMF exposure to the brain and brain volumes exists, effects might appear after a longer cumulative exposure. Thus studies with longitudinal data on both the use of mobile communication devices and brain volumes are needed. Moreover, we used an innovative and comprehensive tool to estimate brain RF-EMF doses but it builds on several assumptions which could lead to non-differential misclassification of the exposure leading to a potential underestimation of the effect estimates [27], [28]. In addition, the use of mobile communication devices was reported by the parents and did not include its use at school which might underestimate the actual use. Objective measures such as applications installed in children’s devices tracking their actual use, previously validated, could be used in new studies to improve accuracy of the measurement of the use of mobile communication devices. Finally, although we adjusted our models for several potential confounding variables we cannot discard residual confounding for unavailable variables such as paternal socioeconomic status.

Conclusion

Our results suggest that estimated whole-brain and lobe-specific RF-EMF doses were not related to brain volumes in preadolescents aged 9-12 years. Our findings might also indicate that social or individual factors related to certain uses of mobile communication devices such as mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop use while wirelessly connected to the internet, instead of the RF-EMF exposure to the brain by these uses, could be related to a smaller caudate volume, although we cannot discard residual confounding, chance finding, or reverse causality. Further studies on mobile communication devices and their potential negative associations with brain development are warranted, regardless whether associations are due to RF-EMF exposure or to other factors related to their use.

Acknowledgements

The Generation R Study is conducted by the Erasmus Medical Centre in close collaboration with the Municipal Health Service Rotterdam area, the Rotterdam Homecare Foundation and the Stichting Trombosedienst & Artsenlaboratorium Rijnmond (STAR), Rotterdam. We gratefully acknowledge the contribution of general practitioners, hospitals, midwives and pharmacies in Rotterdam.

We also acknowledge support from the Spanish Ministry of Science and Innovation, and State Research Agency through the “Centrode Excelencia Severo Ochoa 2019–2023” Program (CEX2018-000806-S), and support from the Generalitat de Catalunya through the CERCA Program.

Source of financial support

This work was supported by Stichting Volksbond Rotterdam, the Dutch Brain Foundation (De Hersenstichting, project number GH2016.2.01), the NARSAD Young Investigator Grant from the Brain & Behavior Research Foundation (grant number 27853), the Netherlands Organization for Health Research and Development (ZonMwVici project grant number 016.VICI.170.200, and TOP project grant number91211021), the European Union Seventh Framework Program (FP7/2007–2013No.603794 GERoNiMO), ACTION: Aggressionin Children: Unravelling gene-environment interplay to inform Treatment and InterventiON strategies (grant number 602768), the European Union’s Horizon 2020 research and innovation programme (grant agreement No.633595 DynaHEALTH, No.733206 LifeCycle), the Spanish Institute of Health Carlos III (CP13/00054, MS13/00053, CPII18/00018), and the French Agency for Food, Environmental and Occupational Health & Safety (EST-2016RF-21, and EST/2013/2/22 CREST-Characterization of exposure to RF induced by new uses and technologies of mobile communication systems).

Supplementary material

Figure S1. Flowchart of the study

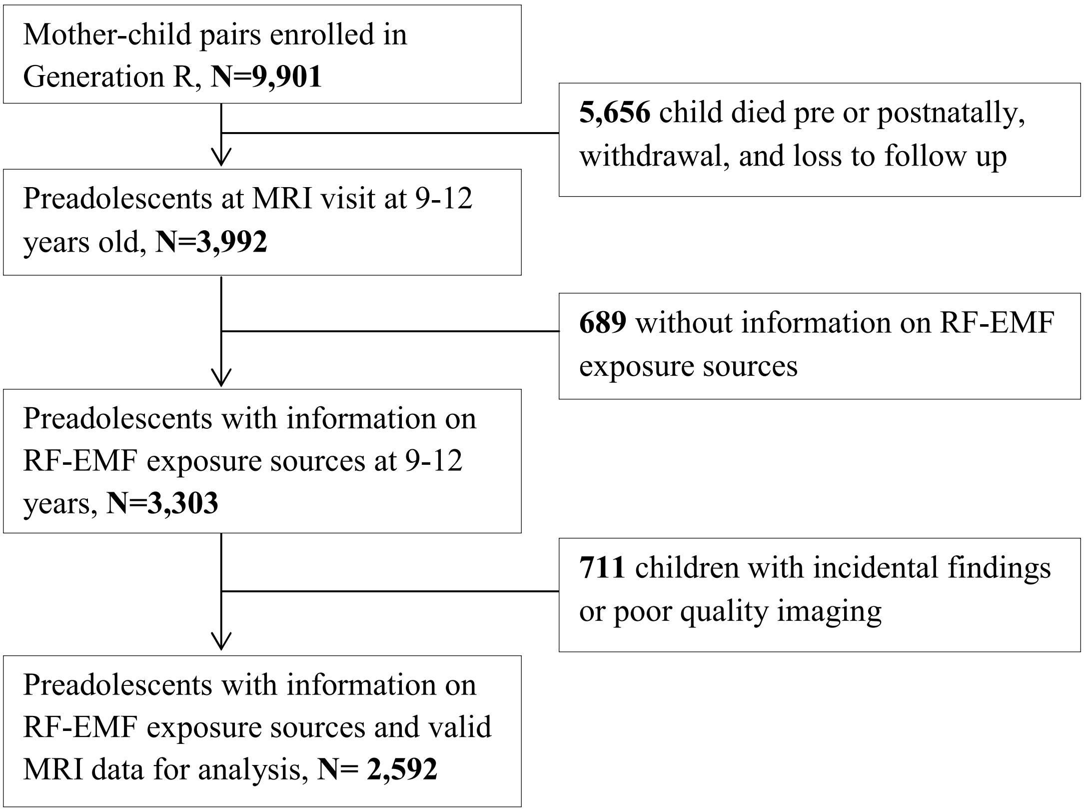


Table S1. Means and standard deviations of the global brain volumes, cortical lobar volumes, and subcortical volumes (mm^3) in preadolescents.

Global brain volumes	
Total brain	1,214,919 (110507)
Cortical gray matter	582,473 (53,615)
Cortical white matter	425,503 (49138)
Cerebellar cortex	118,258 (11,202)
Cerebellar white matter	26,066 (2,785)
Cortical lobar volumes	
Frontal lobe	218,232 (218,100)
Parietal lobe	146,883 (15,359)
Temporal lobe	123,865 (12,386)
Occipital lobe	55,553 (7,007)
Subcortical volumes	
Hippocampus	8048 (736)
Amygdala	3543 (382)
Thalamus	14887 (1346)
Putamen	10764 (1124)
Caudate	8143 (984)
Accumbens	1360 (189)
Pallidum	3910 (412)

Table S2. Comparison of maternal, family, and individual characteristics of included (n=2,592) vs. non-included (n=7,309) preadolescents.

	Included (n=2,592)	Not-included (n=7,309)	P-value
Preadolescent characteristics			
Sex (female vs. male)	50.7	48.9	0.115
Weight at birth, in grams	3430.8 (572.0)	3366.0 (594.5)	<0.001
Maternal characteristics			
Ethnicity			<0.001
Dutch	60.9	50.4	
Asian	19.6	25.6	
African	10.1	13.9	
European and others	9.4	10.1	
Educational level			<0.001
High	54.9	37.7	
Medium	39.2	48.8	
Low	5.9	13.5	
Age at recruitment, in years	31.1 (4.8)	29.3 (5.5)	<0.001
Body mass index before pregnancy, in kg/m2	23.5 (4.1)	23.8 (4.5)	0.022
Gestational age at birth, in weeks	39.8 (1.8)	39.6 (2.1)	<0.001
Parity at child's birth	0.6 (0.8)	0.7 (0.9)	<0.001
Alcohol use during pregnancy (yes vs. no)	44.0	33.0	<0.001
Smoking use during pregnancy (yes vs. no)	12.4	19.4	<0.001
Paternal characteristics			
Ethnicity			<0.001
Dutch	64.9	53.8	
Asian	18.7	24.4	
African	10.2	14.0	
European and others	6.2	7.8	
Educational level			<0.001
High	56.1	47.7	
Medium	39.0	42.0	
Low	4.9	10.3	
Age at recruitment, in years	33.6 (5.5)	32.6 (6.2)	<0.001
Body mass index at child's birth, in kg/m2	25.2 (3.4)	25.3 (3.6)	0.470
Family characteristics			
Household income at 9-12 years (>2000 vs.<2000 €)	71.8	55.5	<0.001

Values are percentages for categorical variables and mean (SD) for continuous variables. P-values are based on chi-square and t-student.

Table S3. Distribution of source-specific RF-EMF doses to the whole brain and to each lobe (n = 2,592).

Source-specific doses to the whole brain	**mJ/kg/day (median (IQR))**	**Contribution to the overall dose (%)**
From mobile and DECT phone calls	41.7 (2.6; 105.3)	61.5
From screen activities with mobile communication devices[a]	11.7 (5.5; 19.2)	17.4
From far-field sources[b]	14.3 (10.8; 28.6)	21.1
Source-specific doses to the the frontal lobe		
From mobile and DECT phone calls	39.5 (2.0; 100.8)	45.7
From screen activities with mobile communication devices[a]	15.8 (6.5; 26.8)	18.3
From far-field sources[b]	31.1 (23.0; 62.9)	36.0
Source-specific doses to the the parietal lobe		
From mobile and DECT phone calls	16.0 (1.8; 33.9)	25.0
From screen activities with mobile communication devices[a]	10.0 (4.3; 17.1)	15.6
From far-field sources[b]	38.1 (27.9; 78.0)	59.4
Source-specific doses to the the temporal lobe		
From mobile and DECT phone calls	227.6 (13.8; 569.5)	88.3
From screen activities with mobile communication devices[a]	2.4 (0.7; 5.4)	0.9
From far-field sources[b]	27.7 (20.6; 55.3)	10.8
Source-specific doses to the the occipital lobe		
From mobile and DECT phone calls	27.6 (1.7; 69.5)	36.9
From screen activities with mobile communication devices[a]	8.7 (3.9; 15.2)	11.7
From far-field sources[b]	38.4 (28.3; 77.3)	51.4

DECT, Digital Enhanced Cordless Telecommuncations; IQR, interquartile range; RF-EMF, Radiofrequency Electromagnetic Fields; mJ, millijoules; kg, kilograms.

[a] Screen activities with mobile communication devicesincludes mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop use while wirelessly connected to the internet.

[b] RF-EMF exposure from different environmental RF-EMF sources (mobile phone base stations, FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) from different microenvironments (home, school, commuting, and outdoors).

Table S4. Association between maternal, family, and preadolescent characteristics and overall and source-specific whole-brain RF-EMF doses (mJ/kg/day).

	Overall dose		Phone calls		Screen activities		Far-field sources[b]	
Maternal characteristics	**Mean (SD)/ ρ**	**p-value**	**Mean (SD)/ ρ**	**p-value**	**Mean (SD)/ ρ**	**p-value**	**Mean (SD)/ ρ**	**p-value**
Ethnicity		<0.001		<0.001		0.005		0.148
Dutch	136.9 (244.0)		86.1 (220.5)		14.61 (11.9)		30.3 (55.0)	
Asian	257.8 (528.1)		205.8 (524.2)		15.04 (15.8)		35.8 (63.6)	
African	270.6 (693.5)		219.0 (690.3)		11.82 (15.3)		36.3 (87.3)	
European and others	189.1 (599.3)		140.6 (595.8)		15.57 (13.81)		28.5 (35.5)	
Educational level		0.004		<0.001		0.038		0.106
High	157.7 (386.0)		92.4 (262.07)		14.3 (11.7)		29.4 (47.4)	
Medium	210.4 (451.9)		145.5 (351.8)		15.0 (14.9)		34.9 (72.5)	
Low	285.8 (494.7)		167.0 (414.6)		10.5 (15.3)		43.5 (92.8)	
Smoking		<0.001		<0.001		0.001		0.098
Yes	264.3 (518.4)		212.9 (501.8)		16.6 (15.9)		37.0 (82.2)	
No	165.0 (397.5)		100.9 (283.7)		14.1 (12.3)		30.9 (55.5)	
Depressive symptoms	0.0	0.206	0.0	0.156	-0.0	0.910	0.0	0.901
Anxiety symptoms	0.0	0.263	0.0	0.057	0.0	0.394	-0.0	0.183
Employment status		0.330		0.719		0.338		0.880
Paid	177.6 (420.1)		112.1 (311.3)		14.6 (13.0)		31.5 (60.5)	
Non-paid	181.5 (406.4)		118.1 (304.3)		13.9 (13.3)		31.1 (49.0)	
Family characteristics								
Household income		<0.001		<0.001		0.004		0.010
High	152.4 (353.7)		91.4 (252.3)		15.0 (11.3)		27.2 (41.3)	
Medium	184.1 (436.9)		121.1 (350.2)		14.6 (12.7)		34.3 (67.9)	
Low	224.5 (495.2)		165.9 (419.0)		12.5 (15.8)		36.8 (78.7)	
Preadolescent characteristics								
Sex		<0.001		<0.001		<0.001		0.201
Female	210.8 (528.7)		162.5 (526.6)		13.2 (12.2)		33.6 (64.1)	
Male	146.4 (262.0)		97.6 (256.5)		15.8 (14.3)		30.6 (55.6)	
Age, in years	0.1	<0.001	0.1	<0.001	0.0	0.523	0.0	0.114
IQ score at 5 years old	-0.1	<0.001	-0.1	0.001	0.1	0.012	0.0	0.954
BMI at 9-12 years old, in kg/m2	0.0	0.001	0.1	<0.001	-0.1	<0.001	0.0	0.662

BMI, body mass index; IQ, intelligence quotient. Values are means (SD) or rho coefficients (ρ). P-values are based on one-way anova or spearman correlations. [a]Screen activities includes mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop use while wirelessly connected to the internet. [b]RF-EMF exposure from different environmental RF-EMF sources (mobile phone base stations, FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) from different microenvironments (home, school, commuting, and outdoors).

References

[1] ICT, «ICT Facts and Figures (Internet). International Telecommunication Union (2017).», 2017.

[2] L. E. Birks *et al.*, «Spatial and temporal variability of personal environmental exposure to radio frequency electromagnetic fields in children in Europe», *Environ. Int.*, vol. 117, pp. 204-214, ago. 2018, doi: 10.1016/j.envint.2018.04.026.

[3] Vijayalaxmi y M. Scarfi, «International and National Expert Group Evaluations: Biological/Health Effects of Radiofrequency Fields», *Int. J. Environ. Res. Public. Health*, vol. 11, n.º 9, pp. 9376-9408, sep. 2014, doi: 10.3390/ijerph110909376.

[4] SSM's scientific council, «Recent research on EMF and health risk : eleventh report from SSM's scientific council on electromagnetic fields : including thirteen years of electromagnetic field research monitored by SSM's Scientific Council on EMF and health : how has the evidence changed over time?» 2016.

[5] K. Roser *et al.*, «Personal radiofrequency electromagnetic field exposure measurements in Swiss adolescents», *Environ. Int.*, vol. 99, pp. 303-314, feb. 2017, doi: 10.1016/j.envint.2016.12.008.

[6] M. Foerster, A. Thielens, W. Joseph, M. Eeftens, y M. Röösli, «A Prospective Cohort Study of Adolescents' Memory Performance and Individual Brain Dose of Microwave Radiation from Wireless Communication», *Environ. Health Perspect.*, vol. 126, n.º 7, p. 077007, jul. 2018, doi: 10.1289/EHP2427.

[7] World Health Organization, «Electromagnetic fields and public health: mobile phones», *Key features - World Health Organization*, oct. 2014. https://www.who.int/en/news-room/fact-sheets/detail/electromagnetic-fields-and-public-health-mobile-phones.

[8] L. Kheifets, «The Sensitivity of Children to Electromagnetic Fields», *PEDIATRICS*, vol. 116, n.º 2, pp. e303-e313, ago. 2005, doi: 10.1542/peds.2004-2541.

[9] D. Rice y S. Barone, «Critical periods of vulnerability for the developing nervous system: evidence from humans and animal models», *Environ. Health Perspect.*, vol. 108 Suppl 3, pp. 511-533, jun. 2000.

[10] E. Arhan *et al.*, «Regional brain volume reduction and cognitive outcomes in preterm children at low risk at 9 years of age», *Childs Nerv. Syst.*, vol. 33, n.º 8, pp. 1317-1326, ago. 2017, doi: 10.1007/s00381-017-3421-2.

[11] L. E. Libero, T. P. DeRamus, H. D. Deshpande, y R. K. Kana, «Surface-based morphometry of the cortical architecture of autism spectrum disorders: volume, thickness, area, and gyrification», *Neuropsychologia*, vol. 62, pp. 1-10, sep. 2014, doi: 10.1016/j.neuropsychologia.2014.07.001.

[12] L. M. E. Blanken *et al.*, «Cortical Morphology in 6- to 10-Year Old Children With Autistic Traits: A Population-Based Neuroimaging Study», *Am. J. Psychiatry*, vol. 172, n.º 5, pp. 479-486, may 2015, doi: 10.1176/appi.ajp.2014.14040482.

[13] M. M. Pangelinan, G. Zhang, J. W. VanMeter, J. E. Clark, B. D. Hatfield, y A. J. Haufler, «Beyond age and gender: Relationships between cortical and subcortical brain volume and cognitive-motor abilities in school-age children», *NeuroImage*, vol. 54, n.º 4, pp. 3093-3100, feb. 2011, doi: 10.1016/j.neuroimage.2010.11.021.

[14] S. Thomas, S. Heinrich, R. von Kries, y K. Radon, «Exposure to radiofrequency electromagnetic fields and behavioural problems in Bavarian children and adolescents», *Eur. J. Epidemiol.*, vol. 25, n.º 2, pp. 135-141, feb. 2010, doi: 10.1007/s10654-009-9408-x.

[15] F. Zheng *et al.*, «Association between mobile phone use and inattention in 7102 Chinese adolescents: a population-based cross-sectional study», *BMC Public Health*, vol. 14, p. 1022, oct. 2014, doi: 10.1186/1471-2458-14-1022.

[16] A. Schoeni, K. Roser, y M. Röösli, «Memory performance, wireless communication and exposure to radiofrequency electromagnetic fields: A prospective cohort study in adolescents», *Environ. Int.*, vol. 85, pp. 343-351, dic. 2015, doi: 10.1016/j.envint.2015.09.025.

[17] A. Schoeni, K. Roser, y M. Röösli, «Symptoms and Cognitive Functions in Adolescents in Relation to Mobile Phone Use during Night», *PloS One*, vol. 10, n.º 7, p. e0133528, 2015, doi: 10.1371/journal.pone.0133528.

[18] M. Guxens *et al.*, «Outdoor and indoor sources of residential radiofrequency electromagnetic fields, personal cell phone and cordless phone use, and cognitive function in 5–6 years old children», *Environ. Res.*, vol. 150, pp. 364-374, oct. 2016, doi: 10.1016/j.envres.2016.06.021.

[19] K. Roser, A. Schoeni, y M. Röösli, «Mobile phone use, behavioural problems and concentration capacity in adolescents: A prospective study», *Int. J. Hyg. Environ. Health*, vol. 219, n.º 8, pp. 759-769, nov. 2016, doi: 10.1016/j.ijheh.2016.08.007.

[20] M. Redmayne *et al.*, «Use of mobile and cordless phones and cognition in Australian primary school children: a prospective cohort study», *Environ. Health Glob. Access Sci. Source*, vol. 15, p. 26, feb. 2016, doi: 10.1186/s12940-016-0116-1.

[21] M. Guxens *et al.*, «Radiofrequency electromagnetic fields, screen time, and emotional and behavioural problems in 5-year-old children», *Int. J. Hyg. Environ. Health*, oct. 2018, doi: 10.1016/j.ijheh.2018.09.006.

[22] M. J. Abramson *et al.*, «Mobile telephone use is associated with changes in cognitive function in young adolescents», *Bioelectromagnetics*, vol. 30, n.º 8, pp. 678-686, dic. 2009, doi: 10.1002/bem.20534.

[23] C. R. Bhatt *et al.*, «Use of mobile and cordless phones and change in cognitive function: a prospective cohort analysis of Australian primary school children», *Environ. Health*, vol. 16, n.º 1, dic. 2017, doi: 10.1186/s12940-017-0250-4.

[24] S. Heinrich, S. Thomas, C. Heumann, R. von Kries, y K. Radon, «Association between exposure to radiofrequency electromagnetic fields assessed by dosimetry and acute symptoms in children and adolescents: a population based cross-sectional study», *Environ. Health*, vol. 9, n.º 1, dic. 2010, doi: 10.1186/1476-069X-9-75.

[25] K. Roser, A. Schoeni, A. Bürgi, y M. Röösli, «Development of an RF-EMF Exposure Surrogate for Epidemiologic Research», *Int. J. Environ. Res. Public. Health*, vol. 12, n.º 5, pp. 5634-5656, may 2015, doi: 10.3390/ijerph120505634.

[26] L. E. Birks *et al.*, «Radiofrequency Electromagnetic Fields from Mobile Communication: Description of Modeled Dose in Brain Regions and the Body in European Children and Adolescents (under review)».

[27] Luuk van Wel, «Organ-specific integrative exposure assessment: Radiofrequency electromagnetic field exposure and contribution of sources in the general population (under review)».

[28] Ilaria Liorni, «Approximation Formulas for Evaluation of Specific Absorption Rate in the Far-Field, Near-to-Far Field and Near-Field Regions for Integrative Radiofrequency Exposure Assessment in Epidemiological Studies (under review)».

[29] A. Bürgi *et al.*, «A model for radiofrequency electromagnetic field predictions at outdoor and indoor locations in the context of epidemiological research», *Bioelectromagnetics*, p. n/a-n/a, 2009, doi: 10.1002/bem.20552.

[30] J. Beekhuizen, R. Vermeulen, H. Kromhout, A. Bürgi, y A. Huss, «Geospatial modelling of electromagnetic fields from mobile phone base stations», *Sci. Total Environ.*, vol. 445-446, pp. 202-209, feb. 2013, doi: 10.1016/j.scitotenv.2012.12.020.

[31] J. Beekhuizen *et al.*, «Modelling indoor electromagnetic fields (EMF) from mobile phone base stations for epidemiological studies», *Environ. Int.*, vol. 67, pp. 22-26, jun. 2014, doi: 10.1016/j.envint.2014.02.008.

[32] A. Huss *et al.*, «Environmental Radiofrequency Electromagnetic Fields Exposure at Home, Mobile and Cordless Phone Use, and Sleep Problems in 7-Year-Old Children», *PLOS ONE*, vol. 10, n.º 10, p. e0139869, oct. 2015, doi: 10.1371/journal.pone.0139869.

[33] A. L. Martens, J. F. B. Bolte, J. Beekhuizen, H. Kromhout, T. Smid, y R. C. H. Vermeulen, «Validity of at home model predictions as a proxy for personal exposure to radiofrequency electromagnetic fields from mobile phone base stations», *Environ. Res.*, vol. 142, pp. 221-226, oct. 2015, doi: 10.1016/j.envres.2015.06.029.

[34] C. E. Langer *et al.*, «Patterns of cellular phone use among young people in 12 countries: Implications for RF exposure», *Environ. Int.*, vol. 107, pp. 65-74, oct. 2017, doi: 10.1016/j.envint.2017.06.002.

[35] W. Joseph *et al.*, «Determination of the duty cycle of WLAN for realistic radio frequency electromagnetic field exposure assessment», *Prog. Biophys. Mol. Biol.*, vol. 111, n.º 1, pp. 30-36, ene. 2013, doi: 10.1016/j.pbiomolbio.2012.10.002.

[36] T. White *et al.*, «Paediatric population neuroimaging and the Generation R Study: the second wave», *Eur. J. Epidemiol.*, vol. 33, n.º 1, pp. 99-125, ene. 2018, doi: 10.1007/s10654-017-0319-y.

[37] B. Fischl, «FreeSurfer», *NeuroImage*, vol. 62, n.º 2, pp. 774-781, ago. 2012, doi: 10.1016/j.neuroimage.2012.01.021.

[38] R. L. Muetzel *et al.*, «Tracking Brain Development and Dimensional Psychiatric Symptoms in Children: A Longitudinal Population-Based Neuroimaging Study», *Am. J. Psychiatry*, vol. 175, n.º 1, pp. 54-62, ene. 2018, doi: 10.1176/appi.ajp.2017.16070813.

[39] M. A. Hernán, S. Hernández-Díaz, M. M. Werler, y A. A. Mitchell, «Causal knowledge as a prerequisite for confounding evaluation: an application to birth defects epidemiology», *Am. J. Epidemiol.*, vol. 155, n.º 2, pp. 176-184, ene. 2002.

[40] L. R. Derogatis y N. Melisaratos, «The Brief Symptom Inventory: an introductory report», *Psychol. Med.*, vol. 13, n.º 3, pp. 595-605, ago. 1983.

[41] de Beurs E, «Brief Symptom Inventory, Handleiding (Dutch Manual)», *Leiden, The Netherlands: Swets & Zeitlinger*, 2004.

[42] P.J Tellegen, M.Winkel, B.J. Wijnberg-Williams, y J.A. Laros, «Snijders-Oomen Nonverbal Intelligence test», 2005.

[43] H. Jang, J. Y. Lee, K. I. Lee, y K. M. Park, «Are there differences in brain morphology according to handedness?», *Brain Behav.*, vol. 7, n.º 7, p. e00730, jul. 2017, doi: 10.1002/brb3.730.

[44] R. J. Simes, «An improved Bonferroni procedure for multiple tests of significance», *Biometrika*, vol. 73, n.º 3, pp. 751-754, 1986, doi: 10.1093/biomet/73.3.751.

[45] C. D. Nguyen, J. B. Carlin, y K. J. Lee, «Model checking in multiple imputation: an overview and case study», *Emerg. Themes Epidemiol.*, vol. 14, n.º 1, dic. 2017, doi: 10.1186/s12982-017-0062-6.

[46] G. T. Voelbel, M. E. Bates, J. F. Buckman, G. Pandina, y R. L. Hendren, «Caudate Nucleus Volume and Cognitive Performance: Are They Related in Childhood Psychopathology?», *Biol. Psychiatry*, vol. 60, n.º 9, pp. 942-950, nov. 2006, doi: 10.1016/j.biopsych.2006.03.071.

[47] C. U. Greven *et al.*, «Developmentally stable whole-brain volume reductions and developmentally sensitive caudate and putamen volume alterations in those with attention-deficit/hyperactivity disorder and their unaffected siblings», *JAMA Psychiatry*, vol. 72, n.º 5, pp. 490-499, may 2015, doi: 10.1001/jamapsychiatry.2014.3162.

[48] M. Hoogman *et al.*, «Subcortical brain volume differences in participants with attention deficit hyperactivity disorder in children and adults: a cross-sectional mega-analysis», *Lancet Psychiatry*, vol. 4, n.º 4, pp. 310-319, abr. 2017, doi: 10.1016/S2215-0366(17)30049-4.

[49] Y. Li, C. Shi, G. Lu, Q. Xu, y S. Liu, «Effects of electromagnetic radiation on spatial memory and synapses in rat hippocampal CA1», *Neural Regen. Res.*, vol. 7, n.º 16, pp. 1248-1255, jun. 2012, doi: 10.3969/j.issn.1673-5374.2012.16.007.

[50] S. Hussein, A.-A. El-Saba, y M. K. Galal, «Biochemical and histological studies on adverse effects of mobile phone radiation on rat's brain», *J. Chem. Neuroanat.*, vol. 78, pp. 10-19, dic. 2016, doi: 10.1016/j.jchemneu.2016.07.009.

[51] S. N. Narayanan, R. S. Kumar, B. K. Potu, S. Nayak, P. G. Bhat, y M. Mailankot, «Effect of radio-frequency electromagnetic radiations (RF-EMR) on passive avoidance behaviour and hippocampal morphology in Wistar rats», *Ups. J. Med. Sci.*, vol. 115, n.º 2, pp. 91-96, may 2010, doi: 10.3109/03009730903552661.

[52] S. N. Narayanan, R. S. Kumar, K. M. Karun, S. B. Nayak, y P. G. Bhat, «Possible cause for altered spatial cognition of prepubescent rats exposed to chronic radiofrequency electromagnetic radiation», *Metab. Brain Dis.*, vol. 30, n.º 5, pp. 1193-1206, oct. 2015, doi: 10.1007/s11011-015-9689-6.

[53] S. N. Narayanan *et al.*, «Radiofrequency electromagnetic radiation exposure effects on amygdala morphology, place preference behavior and brain caspase-3 activity in rats», *Environ. Toxicol. Pharmacol.*, vol. 58, pp. 220-229, mar. 2018, doi: 10.1016/j.etap.2018.01.009.

[54] M. Leszczynski, «How Does Hippocampus Contribute to Working Memory Processing?», *Front. Hum. Neurosci.*, vol. 5, 2011, doi: 10.3389/fnhum.2011.00168.

[55] J. L. McGaugh, «THE AMYGDALA MODULATES THE CONSOLIDATION OF MEMORIES OF EMOTIONALLY AROUSING EXPERIENCES», *Annu. Rev. Neurosci.*, vol. 27, n.º 1, pp. 1-28, jul. 2004, doi: 10.1146/annurev.neuro.27.070203.144157.

[56] A. J. Golby, «Material-specific lateralization in the medial temporal lobe and prefrontal cortex during memory encoding», *Brain*, vol. 124, n.º 9, pp. 1841-1854, sep. 2001, doi: 10.1093/brain/124.9.1841.

[57] S. P. Loughran, R. J. McKenzie, M. L. Jackson, M. E. Howard, y R. J. Croft, «Individual differences in the effects of mobile phone exposure on human sleep: Rethinking the problem», *Bioelectromagnetics*, vol. 33, n.º 1, pp. 86-93, ene. 2012, doi: 10.1002/bem.20691.

[58] C. Lustenberger *et al.*, «Inter-individual and intra-individual variation of the effects of pulsed RF EMF exposure on the human sleep EEG: Reproducibility of RF EMF Exposure Effects», *Bioelectromagnetics*, vol. 36, n.º 3, pp. 169-177, abr. 2015, doi: 10.1002/bem.21893.

[59] S. J. Regel *et al.*, «Pulsed radio-frequency electromagnetic fields: dose-dependent effects on sleep, the sleep EEG and cognitive performance», *J. Sleep Res.*, vol. 16, n.º 3, pp. 253-258, sep. 2007, doi: 10.1111/j.1365-2869.2007.00603.x.

[60] M. R. Schmid *et al.*, «Sleep EEG alterations: effects of different pulse-modulated radio frequency electromagnetic fields: Different pulse-modulated RF EMF and sleep EEG», *J. Sleep Res.*, vol. 21, n.º 1, pp. 50-58, feb. 2012, doi: 10.1111/j.1365-2869.2011.00918.x.

[61] E. M. Taveras, S. L. Rifas-Shiman, K. L. Bub, M. W. Gillman, y E. Oken, «Prospective Study of Insufficient Sleep and Neurobehavioral Functioning Among School-Age Children», *Acad. Pediatr.*, vol. 17, n.º 6, pp. 625-632, ago. 2017, doi: 10.1016/j.acap.2017.02.001.

[62] A. Sawangjit, C. N. Oyanedel, N. Niethard, C. Salazar, J. Born, y M. Inostroza, «The hippocampus is crucial for forming non-hippocampal long-term memory during sleep», *Nature*, vol. 564, n.º 7734, pp. 109-113, dic. 2018, doi: 10.1038/s41586-018-0716-8.

[63] I. Koyanagi, K. Akers, P. Vergara, S. Srinivasan, T. Sakurai, y M. Sakaguchi, «Memory consolidation during sleep and adult hippocampal neurogenesis», *Neural Regen. Res.*, vol. 14, n.º 1, p. 20, 2019, doi: 10.4103/1673-5374.243695.

[64] S. Thomas *et al.*, «Use of mobile phones and changes in cognitive function in adolescents», *Occup. Environ. Med.*, vol. 67, n.º 12, pp. 861-866, dic. 2010, doi: 10.1136/oem.2009.054080.

[65] I. Calvente *et al.*, «Does exposure to environmental radiofrequency electromagnetic fields cause cognitive and behavioral effects in 10-year-old boys?: Neurobehavioral Effects of RF-EMFs in Children», *Bioelectromagnetics*, vol. 37, n.º 1, pp. 25-36, ene. 2016, doi: 10.1002/bem.21951.

Study IV: Association between estimated whole-brain RF-EMF doses and cognitive function in preadolescents and adolescents

Alba Cabré-Riera, Luuk van Wel, Ilaria Liorni, Arno Thielens, Laura Ellen Birks, Livia Pierotti, Wout Joseph, Llucia Gonzalez, Jesús Ibarluzea, Amparo Ferrero, Anke Huss[5], Joe Wiart, Loreto Santa-Marina, Maties Torrent, Tanja Vrijkotte, Myles Capstick, Roel Vermeulen, Martine Vrijheid, Elisabeth Cardis, Martin Röösli, Mònica Guxens

Under review at the *International Journal of Hygiene and Environmental Health*

Abstract

Objective: To investigate the association between estimated whole-brain radiofrequency electromagnetic fields (RF-EMF) dose, using an improved integrated RF-EMF exposure model, and cognitive function in preadolescents and adolescents.

Methods: Cross-sectional analysis in preadolescents aged 9-11 years and adolescents aged 17-18 years from the Dutch Amsterdam Born Children and their Development Study (n=1,664 preadolescents) and the Spanish INfancia y Medio Ambiente Project (n=1,288 preadolescents and n=261 adolescents), two population-based birth cohort studies. Overall whole-brain RF-EMF doses (mJ/kg/day) were estimated for several RF-EMF sources together including mobile and Digital Enhanced Cordless Telecommunications phone calls (named phone calls), other mobile phone uses than calling, tablet use, laptop use (named screen activities), and far-field sources. We also estimated whole-brain RF-EMF doses in these three groups separately (i.e. phone calls, screen activities, and far-field) that lead to different patterns of RF-EMF exposure. We assessed non-verbal intelligence in the Dutch and Spanish preadolescents, speed of information processing, attentional function, and cognitive flexibility in the Spanish preadolescents, and working memory and semantic fluency in the Spanish preadolescents and adolescents using validated neurocognitive tests.

Results: Estimated overall whole-brain RF-EMF dose was 90.1 mJ/kg/day (interquartile range (IQR) 42.7; 164.0) in the Dutch and Spanish preadolescents and 105.1 mJ/kg/day (IQR 51.0; 295.7) in the Spanish adolescents. Higher overall estimated whole-brain RF-EMF doses from all RF-EMF sources together and from phone calls were associated with lower non-verbal intelligence score in the Dutch and Spanish preadolescents (-0.10 points, 95% CI -0.19; -0.02 and -0.10 points, 95% CI -0.19; -0.02, respectively). However, none of the whole-brain RF-EMF doses was related to any other cognitive function outcome in the Spanish preadolescents or adolescents.

Conclusions: Our results suggest that higher brain exposure to RF-EMF is related to lower non-verbal intelligence but not to other cognitive function outcomes. Given the cross-sectional nature of the study, the small effect sizes, and the unknown biological mechanisms, we cannot discard that our results might be due to chance finding or reverse causality. Longitudinal studies on RF-EMF brain exposure and cognitive function are needed.

Introduction

Mobile communication devices such as phones or tablets emit electromagnetic fields (EMF) in the radiofrequency (RF) range (3 kHz to 300 GHz). The exposure to RF-EMF has become ubiquitous with the enormous increase of the use of these devices in recent years, especially in late childhood [1]–[6]. Adolescents might be more vulnerable to the potential RF-EMF health effects than adults as they are in a stage of life that is still a sensitive period of brain development [7]–[9].

Animal studies in mice and rats suggested that the exposure to RF-EMF increases permeability of the blood brain barrier, impairs the intracellular calcium homeostasis, alters neurotransmitters' regulation, increases neuronal lose, and damages brain tissue including cerebral cortex [10]. Moreover, experimental studies in humans showed both positive and negative cognitive effects after or during exposure to RF-EMF [11]–[14]. However, the available evidence is not sufficient to draw any definite biological mechanism. Several epidemiological studies investigated the association between RF-EMF exposure and cognitive function at ages between5 and 18 years old, showing mixed results [15]–[24]. Most of these previous studies have assessed brain RF-MF exposure using proxies of exposure such as maternal- or self-reported mobile or Digital Enhanced Cordless Telecommunications (DECT) phone calls [15]–[22], and only one cohort study estimated the actual whole-brain dose received from some RF-EMF sources [15], [25], [24]. This cohort study found that higher whole-brain RF-EMF dose was related to lower figural memory [15], [24] but not to concentration capacity [25] at ages between 12 and17 years. In our study, we used a recently developed whole-brain RF-EMF dose estimation based on a similar approach than the previous one [26] but with the advantage that it integrates a larger number of RF-EMF sources leading to a more complete dose estimation. Patterns of mobile communication devices use are different between ages during adolescence [27]. Therefore, a broader assessment of RF-EMF exposure to the brain by integrating all RF-EMF sources according to usage patterns will result in a more accurate and comprehensive dose estimation. .

Therefore, the aim of this study was to investigate the association between estimated overall whole-brain RF-EMF dose and specific whole-brain RF-EMF doses from three RF-EMF exposure patterns, using an improved integrated RF-EMF exposure model, and cognitive function in two brain developmental periods including preadolescents aged 9-11 years and adolescents aged 17-18 years.

Methods

Study design and population

This cross-sectional analysis used data from two population-based birth cohort studies, the Dutch Amsterdam Born Children and their Development (ABCD) Study (www.abcd-study.nl) and the Spanish INfancia y Medio Ambiente (INMA) Project [29] for which we included four INMA sub-cohorts (Valencia, Sabadell, Gipuzkoa, and Menorca). Between 1997 and 2004, depending on the cohort, pregnant women were invited to participate. A total number of 8,266 pregnant women for ABCD and 2,752 for INMA enrolled and their children have been followed through childhood. RF-EMF exposure and cognitive function were assessed in preadolescents at 9-11 years in ABCD (i.e. Dutch preadolescents) and in the Valencia, Sabadell, and Gipuzkoa sub-cohorts of INMA (i.e. Spanish preadolescents), and in adolescents at 17-18 years in the Menorca sub-cohort of INMA (i.e. Spanish adolescents). We included preadolescents and adolescents with information on RF-EMF exposure and with at least one cognitive test available (n=1,664 (20.1%) Dutch preadolescents, n=1,288 (56.7%) Spanish preadolescents, and n=261 (54.1%) Spanish adolescents) (Supplementary Figure S1).

Estimated whole-brain RF-EMF dose

We applied an integrative RF-EMF exposure model to estimate whole-brain RF-EMF dose from several RF-EMF exposure sources [30]–[32]. This model is built using information on the use of mobile communication devices (i.e. near-field RF-EMF sources) and estimations of exposure to environmental RF-EMF sources (i.e. far-field RF-EMF sources).

Near-field RF-EMF sources

Information of the use of mobile communication devices close to the body was collected using maternal-reported questionnaires in the Dutch and Spanish preadolescents and self-reported questionnaires in the Spanish adolescents. Duration of i) use of mobile phone for calling, ii) use of DECT phone for calling, iii) mobile phone use for internet browsing, e-mailing, and text messaging (named other mobile phone uses), iv) tablet use while wirelessly connected to internet, and v) laptop use while wirelessly connected to internet were collected in minutes/day.

Information on the proportion of network use for calling, and type of screen activity while other mobile phone uses, laptop use, or tablet use was not collected. Based on the mobile phone use in preadolescents, adolescents, and young adults in

Europe collected in the same period of time than in our study, we assumed a proportion of 35% 2G calls, 65% 3G calls, and no hands-free devices use [33]. During the timeslots where preadolescents and adolescents were using tablet or laptop while wirelessly connected to internet, we assumed that preadolescents and adolescents were 40% of that time playing video games, 40% of that time streaming video, and 20% of that time browsing the internet or checking social media based on expert opinion.

Far-field RF-EMF sources

We estimated RF-EMF exposure to different environmental RF-EMF sources (mobile phone base stations, FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) based on the microenvironments where preadolescents and adolescents spend most of their time such as home, school, commuting, and outdoors.

To estimate RF-EMF exposure from mobile phone base stations at home, a validated 3D geospatial radio wave propagation model NISMap was used [34]–[37]. In brief, NISMap computes the field strengths of mobile phone base stations for any location in 3D-space using detailed characteristics of the antennas and the 3D geometry of the urban environment. The model has been validated with outside, inside, and personal measurements showing reliable rank-order predictions [35], [36], [38]. We assessed the emission of the three mobile phone communication systems in use at the time of the study (GSM900, GSM1800, and UMTS) using a country-wide mobile phone base stations data set from 2015. These systems operated in the following downlink frequency bands: 925-960 MHz, 1805-1880 MHz, and 2110-2170 MHz, respectively. Using the geo-coded address of each participant and the floor level of his/her bedroom at the time of the cognitive function assessment, we computed the RF-EMF exposure from mobile phone base stations at each participant's bedroom.

RF-EMF exposure from mobile phone base stations in the other microenvironments besides home and from the other far-field RF-EMF sources (FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) in all microenvironments was approximated using the average of the personal RF-EMF measurements done over up to 72 hours by 56 preadolescents from the Dutch cohort and by 191 preadolescents and 53 adolescents from the Spanish cohort [2].

Integrated RF-EMF exposure model

We applied the integrated RF-EMF exposure model to estimate overall and source-specific whole-brain RF-EMF doses [30]–[32]. Briefly, the model combines three types of information: i) the estimated ratio of the absorbed power to the mass in which it is absorbed of each specific RF-EMF source which already takes into account the protection role of the head and individual characteristics (e.g. sex, age, height, weight), known as specific absorption rate (SAR, in Watts (W)/kilogram (kg)), normalized to 1 W output power [30], ii) the output power of each RF-EMF source (in W), and iii) the daily duration of use or exposure to each RF-EMF source (in minutes (min)/day). First, the model estimated a specific RF-EMF dose (millijoules (mJ)/kg/day) to each RF-EMF source (mobile phone calls, DECT phone calls, other mobile phone uses, tablet use, laptop use, and far-field RF-EMF sources) as follows:

Equation 1: Specific whole-brain RF-EMF dose $(\mathrm{mJ/kg/day})_{\mathrm{source}}$

$$= \left(\mathbf{SAR}\left(\frac{\mathrm{W}}{\mathrm{Kg}}\right) source \text{ x } \mathbf{Output\ power}\ (\mathrm{W})\ source \text{ x } \mathbf{Duration}\left(\frac{\mathrm{min}}{\mathrm{day}}\right) source\right)$$

Then, overall whole-brain RF-EMF dose was calculated combining the specific RF-EMF doses of all RF-EMF sources:

Equation 2: Overall whole-brain RF-EMF dose (mJ/kg/day)

$$= \sum_{\mathrm{source}} \left(\mathbf{SAR}\left(\frac{\mathrm{W}}{\mathrm{Kg}}\right) source \text{ x } \mathbf{Output\ power}\ (\mathrm{W})\ source \text{ x } \mathbf{Duration}\left(\frac{\mathrm{min}}{\mathrm{day}}\right)\ source\right)$$

Moreover, we combined the RF-EMF sources in three groups that lead to different exposure patterns to the brain: i) high RF-EMF doses from peak exposures very close to the head but for short periods of time (i.e. mobile and DECT phone calls, named phone calls), ii) low RF-EMF doses that might mainly represent a variety of social or individual factors related to the use of mobile communication devices (i.e. mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop use while wirelessly connected to the internet, named screen activities), and iii) low RF-EMF doses received continuously throughout the day (i.e. far-field sources such as mobile phone base stations, FM radio and TV broadcast antennas, and WiFi, named far-field).

The output power depends on the characteristics of the network. We assumed that other mobile phone uses, laptop use, and tablet use while wirelessly connected to the internet occur using WiFi at 2.4 GHz [32] and that WiFi data transfer rates were 54 Megabits per second. Moreover, the brain SAR depends on the relative distance to the device. SAR values were estimated in an previous study [30] and we used averaged SAR values from different available positions of use to obtain one SAR value per device and activity that could be inserted in Equation 1 and Equation 2.

Cognitive function

Cognitive function measured as non-verbal intelligence, speed of information processing, attentional function, cognitive flexibility, working memory, and semantic fluency were assessed at 9-11 years in the Dutch and Spanish preadolescents or at 17-18 years in the Spanish adolescents using a battery of validated neurocognitive tests (Table1).

Non-verbal intelligence

Non-verbal intelligence describes thinking skills and problem-solving abilities that do not fundamentally require verbal language production and comprehension [40]. In this study, non-verbal intelligence was assessed using a Raven-like test [41] in the Dutch preadolescents and the Raven test [42] in the Spanish preadolescents. These tests consist of a matrix of figural patterns in which one pattern is missing. Preadolescents must choose a potential match for the missing pattern from different given options. Over the course of the test, participants were exposed to different matrices, and the task consists on discovering the rules governing the configuration of the patterns and to apply them to select the correct option. The number of correct responses were collected for each cohort, converted into standard deviation units (z-score equals raw score subtracted from mean and divided by the standard deviation) and then standardized to a mean of 100 and a standard deviation of 15 (new score = 100 + 15 x z-score) to homogenize the scores between cohorts. A lower score indicates lower non-verbal intelligence.

Speed of information processing

Speed of information processing is how quick and individual can identify, discriminate, integrate, make decisions, and respond to visual and verbal information [43]. In this study, speed of information processing was measured by the coding and the symbol search subtests of the Wechsler Intelligence Scale for Children IV (WISC-IV) in the Spanish preadolescents [44]. In the coding subtest, a clue in which 9 numbers from 1 to 9 are paired with 9 different symbols is given to the preadolescents. Then, preadolescents had to go through a random list of numbers between 1 and 9 and place the corresponding symbol below each number based on the clue given to them at the beginning. They had to do it as fast as possible during a maximum of 120 seconds. In the symbol search subtest, several rows of 7 symbols, divided in 2 target symbols on the left and 5 other symbols on the right are given to the preadolescents. The preadolescents had to go through each row and identify if one of the 2 target symbols on the left is repeated in the group of 5 symbols on the right as fast as possible during a maximum of

120 seconds. Scores of the coding and symbol search subsets were summed to form the processing speed index. The processing speed index was converted into standard deviation units (z-score equals raw score subtracted from mean and divided by the standard deviation) and then standardized to a mean of 100 and a standard deviation of 15 (new score = 100 + 15 x z-score). A lower processing speed index indicates lower speed of information processing.

Attentional function

Attentional function is the capacity to focus on a stimulus over a period of time while ignoring other perceivable information [45]. In this study, attentional function was assessed in the Spanish preadolescents and adolescents using the Attention Network Task [46]. The test consists of responding to whether a central fish placed in the screen is pointing to the left or to the right by pressing the corresponding button on the mouse while ignoring all the flanking fishes (i.e. the other 4 fish located to the left and right of the central fish), which point in either the same or opposite direction than the central fish. Our primary outcomes of interest were the hit reaction time (HRT, the mean response time in milliseconds (ms) for all correct answer), the standard error of the HRT (HRT (SE), the standard error of the reaction time for responses to all correct answers), the number of omission errors (the number of times the individual did not respond to a stimuli), and the number of commission errors (the number of times that the individual respond incorrectly). Higher omission errors reflect poorer orientation and a slower response. Higher omission errors and/or commission errors together with a fast HRT reflect impulsivity while higher omissions and/or commission errors together with a slow HRT indicate inattention. HRT (SE) is a measure of the consistency of the response time, such that higher values indicate inattention.

Visual attention

Visual attention mediates the selection of relevant and the filtering out of irrelevant information from cluttered visual scenes [47]. Visual attention was assessed in the Spanish preadolescents using the part A of the Trail Making Test (TMTA) [48]. Preadolescents were instructed to draw lines connecting 25 consecutive encircled numbers distributed on a computer screen as quickly and accurately as possible. Time to complete the task (in ms) was recorded and higher (i.e. slower) time to complete the task indicates a lower visual attention [49].

Cognitive flexibility

Cognitive flexibility is the ability to switch between thinking about two different concepts, and to think about multiple concepts simultaneously, and can happen unconsciously (task switching) or consciously (task shifting) [50]. Cognitive flexibility was assessed in the Spanish preadolescents using the TMTA (detailed in the previous paragraph) and the part B of the Trail Making Test (TMTB) [48]. In the TMTB preadolescents were instructed to draw lines alternating between 13 encircled numbers and 12 letters (from A to L) in an ascending number-letter sequence (1–A–2–B– etc.) distributed on a computer screen as quickly and accurately as possible. Time to complete the task (in ms) was recorded and higher (i.e. slower) time to complete task B indicates a lower task switching capacity. A task shifting score was calculated as follows: *[TMTB(ms) – TMTA(ms)] / TMTA(ms)]* [48], [51]. A higher score indicates a lower task shifting capacity.

Working memory

Working memory is the retention of a small amount of information in a readily accessible form [52]. Working memory was assessed in the Spanish preadolescents and adolescents using the N-back test [53]. Participants were required to respond whenever a stimuli (number) was presented on the screen that matched the one presented 3 trials back. Primary outcomes of interest were HRT (the mean response time in ms for all correct answer), and d prima (d’) which allows the distinction of signal and noise taking into account the number of correct rejections, the number of false alarms, the number of hits, and the number of misses [54]. d’ is indicative of accuracy of the performance of the test and higher HRT and lower d’ values indicate lower working memory.

Semantic verbal fluency

Semantic verbal fluency involves retrieval of words from conceptual memory [55]. Semantic fluency was assessed in the Spanish preadolescents and adolescents using the Semantic Verbal Fluency Test [56]. Participants had to name in 60 seconds as many words of animals as they could [57]. The outcome is the number of words that do not repeat. Animals were considered valid if their change of gender or age implied a change of word, or if they referred to fantastic or extinct animals, but animals from the same family scored fewer points. Less number of words indicates a lower semantic fluency.

Potential confounding variables

The potential confounding variables were a *priori* defined with a Directed Acyclic Graph (DAG) according to the existing literature [58]. Maternal educational level (primary or lower (low), secondary (medium), or university or higher (high)), maternal social class based on the international standard classification of occupations (managers and technicians (high), skilled manual/non-manual (medium), or semi-skilled and unskilled (low)), maternal country of birth (country of the cohort, or others), and maternal smoking during pregnancy (yes or no) were assessed at birth of the child. Maternal anxiety and depressive symptoms were assessed at 5 years of the child using the Depression Anxiety Stress Scale (DASS) [59] in the Dutch cohort and the Symptom Checklist-90-Revised [60] in the Spanish sub-cohorts of Valencia, Sabadell, and Gipuzkoa. Sex of the child was collected at birth, and age, physical activity, weight, and height were collected or measured at the cognitive function assessment. In the Dutch cohort, physical activity was scored by calculating the Metabolic Equivalent (MET) score for the various reported activities using the compendium of physical activities [61] and categorized as low/medium (<percentile 80th) or high (≥percentile 80th). In the Spanish cohort, physical activity was collected in minutes of overall physical activity and categorized as low/medium (≤90 minutes/day) or high (>90 minutes/day). Body mass index was calculated as weight/height^2.

Statistical analysis

After checking that all assumptions of the models were fulfilled, we used a linear mixed-effects model with cohort (including ABCD, INMA-Valencia, INMA Sabadell, and INMA-Gipuzkoa) as random intercept to assess the association between estimated overall and source-specific whole-brain RF-EMF doses and non-verbal intelligence score. We used linear regression models to assess the association between estimated overall and source-specific whole-brain RF-EMF doses and processing speed index, HRT and HRT (SE) of the Attentional Network Task, visual attention score, task switching score, task shifting score, and HRT and d' of the N-back test, and semantic fluency score. We used negative binomial regression models to assess the association between estimated whole-brain RF-EMF doses and omission errors, and commission errors of the Attentional Network Task. All models were adjusted for potential confounding variables specified in the previous section. Additionally, linear and negative regression models were adjusted for INMA sub-cohort. To assess the influence of the assumptions of the integrated RF-EMF exposure model on our results, we estimated overall whole-brain RF-EMF dose based on two new scenarios slightly modifying our original assumptions and assessed their association with cognitive outcomes in the Dutch and Spanish preadolescents and in the Spanish adolescents. In one scenario (i.e. scenario that lead to a higher RF-EMF exposure), we assumed a proportion of 45% 2G calls, 55% 3G calls, and no hands-free used, and that preadolescents and adolescents were 35% playing video games, 50% streaming video, and 15% browsing the internet or checking social media when using tablet or laptop while wirelessly connected to the internet. In the other scenario (i.e. scenario that lead to a lower RF-EMF exposure), we assumed a proportion of 25% 2G calls, 75% 3G calls, and no hands-free used, and that preadolescents and adolescents were 45% playing video games, 30% streaming video, and 25% browsing the internet or checking social media when using tablet or laptop while wirelessly connected to the internet.

Multiple imputation of missing confounding variables for each cohort/sub-cohort was performed using chained equations where 25 completed datasets were generated and analysed [62] (Supplementary Table S1). The distributions of the imputed datasets were similar to the non-imputed datasets (data not shown). Of the mother-child pairs recruited initially in the Dutch and Spanish cohorts, Dutch and Spanish preadolescents included in this analysis (n=1,664 and n=1,288, respectively) were more likely to have had higher weight and gestational age at birth, to have mothers with high level of education and social class at child’s birth, and mothers from the country of the cohort, and that had smoked less during pregnancy compared to preadolescents excluded from the Dutch cohort (n=6,227) and from the Spanish cohort (n=982) (Supplementary Table S2-S3). Spanish adolescents included in this analysis (n=261) were more likely to have mothers from high social class and that had smoked less during pregnancy compared to adolescents from the Spanish cohort not included (n=221) (Supplementary Table S4). Thus, we used inverse probability weighting to correct for loss to follow-up and account for potential selection bias when including only preadolescents or adolescents with available data compared to the full cohort recruited at pregnancy. Variables used to calculate the weights are in Supplementary Table S5.

All analyses were performed using Stata version 15 (StataCorp, College Station, TX).

Results

Descriptive analysis

Dutch and Spanish preadolescents of our population had mothers with high level of education, from high social classes, and from the country of the cohort, while Spanish adolescents had mothers with low level of education and from medium social classes (Table 2). Spanish adolescents had a higher estimated overall whole-brain RF-EMF dose (105.4 mJ/kg/day) than the Dutch and Spanish preadolescents (90.1 mJ/kg/day) (Table 3). For Dutch and Spanish preadolescents, and Spanish adolescents, the primary contributor to the overall whole-brain RF-EMF dose was phone calls (70.3% in preadolescents and 96.0% in adolescents), followed by far-field sources (28.4% in preadolescents and 4.7% in adolescents), and screen activities (1.3% in preadolescents and 0.5% in adolescents). Overall whole-brain RF-EMF dose was highly correlated with specific whole-brain RF-EMF dose from phone calls (r=0.79 in preadolescents and r=0.88 in adolescents) and specific whole-brain doses had a low correlation between each other (between -0.05 and 0.15 in the Dutch and Spanish preadolescents and between -0.18 and -0.03 in the Spanish adolescents) (Supplementary Table S6). Cognitive outcomes were poorly to moderately correlated with each other in the Dutch and Spanish preadolescents (Supplementary Table S7) and semantic fluency was poorly correlated with working memory in the Spanish adolescents (Supplementary Table S8).

Dutch and Spanish preadolescents having higher overall whole-brain RF-EMF dose, higher dose from phone calls, and higher dose from screen activities were more likely to be older and have mothers from high social class, from foreign countries, and with less anxiety and depressive symptoms (Supplementary Table S9). Dutch and Spanish preadolescents having higher whole-brain RF-EMF dose from far-field sources were more likely to have mothers with a low level of education and from low social class. In the Spanish adolescents, those with higher overall whole-brain RF-EMF dose and higher whole-brain RF-EMF dose from phone calls were more likely to be females and have mothers that smoked during pregnancy (Supplementary Table S10).

Estimated whole-brain RF-EMF doses and cognitive function

In the Dutch and Spanish preadolescents, higher estimated overall whole-brain and specific RF-EMF dose from phone calls were associated with lower non-verbal intelligence score [-0.10 points (95%CI -0.19; -0.01), and -0.10 points (95%CI -0.19; -0.01) per each increase in 100 mJ/kg/day, respectively] (Table 4). Specific whole-brain

RF-EMF doses from screen activities or from far-field sources were not related to non-verbal intelligence score.

Overall and source-specific whole-brain RF-EMF doses were not associated with speed of information processing, attentional function, visual attention, and cognitive flexibility in preadolescents, or with working memory and semantic fluency in the Spanish preadolescents and adolescents (Figure 1, and Supplementary Table S11-13). Effect estimates showed both positive and negative associations, although they were far from reaching statistical significance

Sensitivity analysis

Estimated overall whole-brain RF-EMF dose based on the assumptions of the higher-exposure scenario was 98.8 mJ/kg/day (IQR 50.0; 170.6) in preadolescents and 121.9 mJ/kg/day (IQR 55.0; 362.9) in adolescents and of the lower-exposure scenario was 53.4 mJ/kg/day (IQR 27.2; 118.4) in preadolescents and 78.8 mJ/kg/day (IQR 37.2; 216.1) in adolescents (Supplementary Table S14). All association between the new estimated overall whole-brain RF-EMF doses and cognitive function in the Dutch and Spanish preadolescents and in the Spanish adolescents remained materially unchanged (data not shown).

Table 1. Details of cognitive function assessment.

Cognitive ability	Test	Outcome of interest name	Outcome of interest calculation	Interpretation	Cohort and age
Non-verbal intelligence	Raven's Test	Non-verbal intelligence score	Number of correct items	↓n of correct items; lower non-verbal intelligence	Spanish preadolescents
	Raven-like test				Dutch preadolescents
Speed of information processing	Coding and symbol search subtests of the WISC -IV	Processing speed index	Coding subtest score + symbol search subtest score	↓index; lower speed of information processing	Spanish preadolescents
Attentional function	Atentional Network Task	Hit Reaction Time	Mean response time for all correct answer (ms)	↑HRT and ↑omission/commission errors; inattention ↓HRT and ↑omission/commission errors; impulsivity ↑HRT(SE); inattention	
		Hit Reaction Time (Standard Error)	Standard error of the reaction time for responses to all correct answers		
		Omission errors	Number of times the individual did not respond to a stimuli		
		Commission errors	Number of times that the individual respond wrongly		
Visual attention	Trail Making Test-part A	Visual attention score	Time to complete the task (ms)	↑time; lower visual attention	
Cognitive flexibility	Trail Making Test-part B	Task switching score	Time to complete the task (ms)	↑time; lower task switching capacity	
	Trail Making Test-part A and Trail Making Test-part B	Task shifting score	(Time to complete the TMTB (ms) – Time to complete the TMTA (ms)) / Time to complete the TMTA (ms))	↑score; lower task shifting capacity	
Semantic Verbal Fluency	Semantic Verbal Fluency Test	Semantic verbal fluency score	Number of words of animals that do not repeat	↓n of words; lower semantic fluency	Spanish preadolescents and adolescents
Working memory	N-back	Hit Reaction Time	Mean response time for all correct answer (ms)	↑HRT and ↓*d'*; lower working memory	
		d'	z (hit rate) – z (false alarm rate)		

ms, milliseconds; TMTA, Trail Making Test Part A; TMTB, Trail Making Test Part B; WISC-IV, Wechsler Intelligence Scale for Children-IV.

Table 2. Maternal and individual characteristics of the Dutch and Spanish preadolescents, and Spanish adolescents included in our study population.

	Dutch and Spanish preadolescents (n=2,952)	Spanish adolescents (n=261)
Maternal characteristics		
Educational level during pregnancy or at child's birth		
High	60.1	16.7
Medium	27.8	31.3
Low	12.1	52.0
Social class based on occupation during pregnancy or at child's birth		
High	54.4	20.8
Medium	23.4	65.9
Low	22.2	13.3
Country of birth (country of the cohort vs. others)	88.6	97.7
Anxiety symptoms at child's 5 years old		
(no symptoms vs. at risk or pathological)	47.3	na
Depressive symptoms at child's 5 years old		
(no symptoms vs. at risk or pathological)	37.9	na
Smoking during pregnancy (yes vs. no)	16.3	32.0
Individual characteristics		
Sex (female vs. male)	50.1	52.2
Age at cognitive function assessment, in years	10.0 (1.2)	17.6 (0.2)
Physical activity at cognitive function assessment (low/medium vs. high)	78.9	68.9
BMI at cognitive function assessment, in kg/m2	17.0 (2.5)	22.5 (3.6)

BMI, body mass index; na, data not available. Values are percentages for categorical variables and mean (SD) for continuous variables.

Table 3. Median of the estimated whole-brain RF-EMF doses (mJ/kg/day) and contribution of each source-specific dose to the overall whole-brain dose (mean/overall dose, in %) in the Dutch and the Spanish preadolescents, and in the Spanish adolescents.

	Dutch and Spanish preadolescents (n=2,952)		**Spanish adolescents (n=261)**	
Whole-brain RF-EMF doses	**Median,** in mJ/kg/day		**Median,** in mJ/kg/day	
Overall dose	90.1 (42.7; 164.0)		105.4 (51.0; 295.7)	
Source-specific doses		**%**		**%**
Phone calls[a]	24.9 (2.1; 80.6)	70.3	83.6 (33.5; 269.8)	96.0
Screen activities[b]	1.4 (0.6; 2.5)	1.3	1.3 (0.1; 2.4)	0.5
Far-field[c]	13.4 (10.1; 32.9)	28.4	11.2 (11.2; 11.2)	3.5

RF-EMF, Radiofrequency Electromagnetic Fields; mJ, millijoules; kg, kilograms. Values are medians (interquartile range, IQR).

[a] Phone calls refer to mobile and DECT phone calls.

[b] Screen activities refer to screen activities with mobile communication devices including mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop while wirelessly connected to the internet.

[c] RF-EMF exposure from different environmental RF-EMF sources (mobile phone base stations, FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) from different microenvironments (home, school, commuting, and outdoors).

Table 4. Association between estimated overall and source-specific whole-brain RF-EMF doses and non-verbal intelligence in the Dutch and the Spanish preadolescents (n=2,952).

Whole-brain RF-EMF doses (Δ100 mJ/kg/day)	**B (95% CI)**
Overall dose	-0.10 (-0.19; -0.02)
Source-specific doses	
Phone calls[a]	-0.10 (-0.19; -0.02)
Screen activities[b]	-18.13 (-37.09; 0.82)
Far-field[c]	0.27 (-0.11; 0.65)

B, Beta Coefficient ; CI, confidence interval; kg, kilograms; mJ, millijoules; RF-EMF, Radiofrequency Electromagnetic Fields.

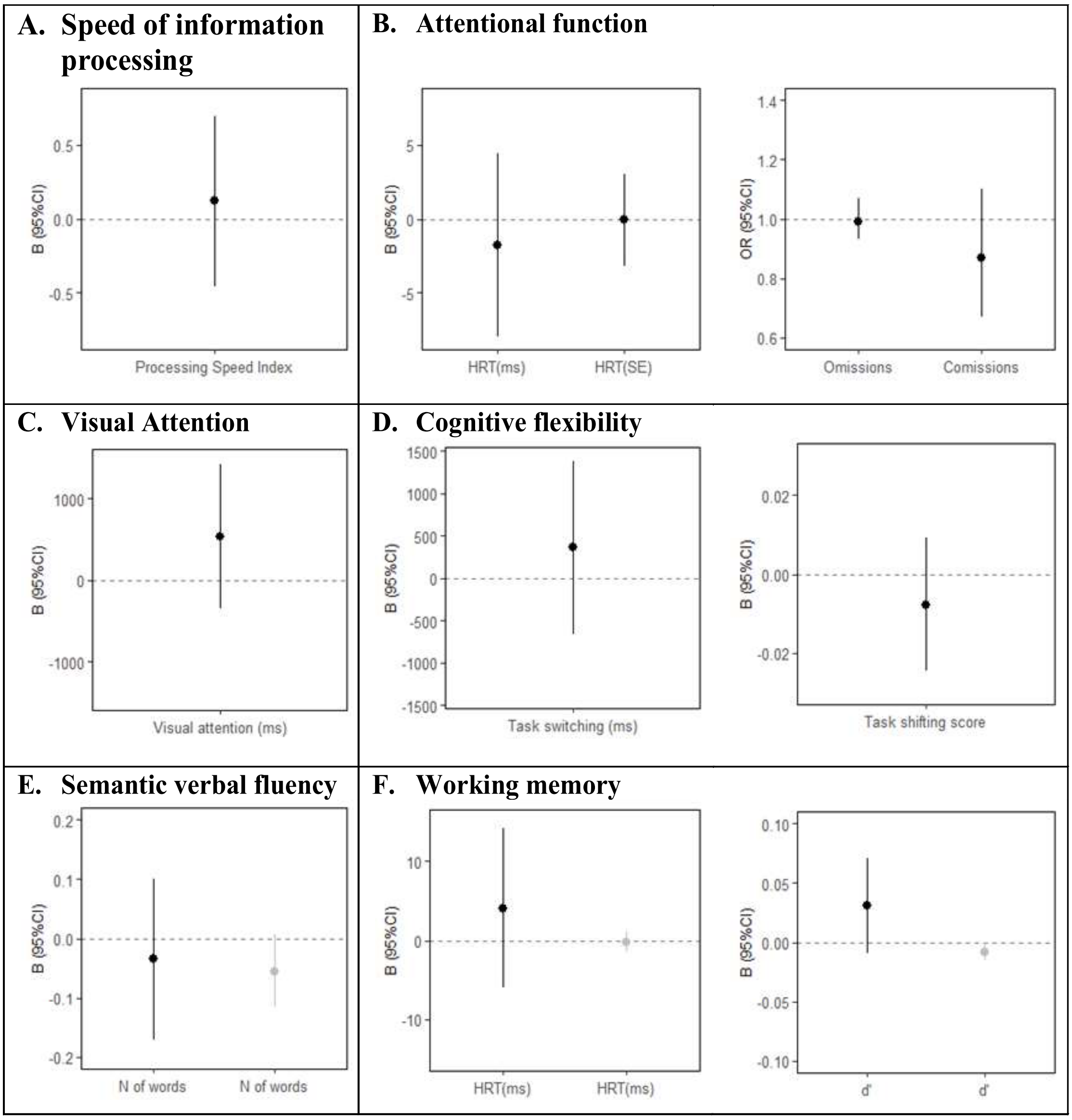
[a] Phone calls refer to mobile and DECT phone calls

[b] Screen activities refer to screen activities with mobile communication devices includes mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop while wirelessly connected to the internet.

[c] RF-EMF exposure from different environmental RF-EMF sources (mobile phone base stations, FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) from different microenvironments (home, school, commuting, and outdoors).

Linear mixed-effects regression models with cohort (ABCD, INMA-Valencia, INMA-Sabadell, INMA-Gipuzkoa) as random intercept adjusted for maternal educational level at child's birth, maternal social class based on occupation at child's birth, maternal country of birth, maternal anxiety and depressive symptoms at 5 years of the child, maternal smoking during pregnancy, and child sex, age, body mass index, and physical activity at cognitive function assessment.

Figure 1. Association between estimated overall whole-brain RF-EMF dose (per increase of 100 mJ/kg/day) and speed of information processing, attentional function, visual attention, cognitive flexibility, semantic verbal fluency, and working memory in the Spanish preadolescents (black lines, n = 1,288) and adolescents (light grey lines, n = 261).



B, Beta Coefficient; Comissions, commission errors; CI, confidence interval; d', detectability; HRT, Hit Reaction Time (in milliseconds (ms)); HRT (SE), Hit Reaction Time (Standard Error); Omissions, omission errors; OR, odd ratio; TMTA, time to complete part A of the trail making test (in ms); TMTB, time to complete part B of the trail making test (in ms); N of words, number of words.

Linear regression models adjusted for maternal educational level, maternal social class based on occupation, maternal country of birth, maternal smoking during pregnancy, child sex, age, body mass index, and physical activity. In preadolescents, linear regression models additionally adjusted for INMA sub-cohort (Valencia, Sabadell, Gipuzkoa) and maternal anxiety and depressive symptoms

Discussion

This study investigated the relationship of overall estimated whole-brain RF-EMF dose and specific doses from different RF-EMF sources that lead to three types of exposure patterns to the brain with cognitive function in preadolescents and adolescents. We found that higher overall whole-brain RF-EMF dose and specific whole-brain RF-EMF dose from mobile and DECT phone calls were associated with lower non-verbal intelligence in preadolescents. However, none of the whole-brain RF-EMF doses were related tospeed of information processing, attentional function, visual attention, and cognitive flexibility in preadolescents or to working memory and semantic fluency in both preadolescents and adolescents.

The ability to properly estimate the RF-EMF brain dose from several RF-EMF exposure sources represents an important step forward in the evaluation of the potential health effects of RF-EMF exposure. Most of the exposure assessment approaches used in previous studies investigating the relationship of RF-EMF exposure and cognitive function did not take into account important factors such as the organ of interest (i.e. the brain), other RF-EMF sources than phone calls such as tablets or laptops use, the position of the RF-EMF source in relation to the body, or personal characteristics (e.g. sex, age, weight, and height) that make individuals with the same amount of RF-EMF exposure to receive different RF-EMF doses to a specific organ. Given that the whole-brain RF-EMF dose approach is a recently developed method, only one previous cohort study has assessed its association with cognitive function in preadolescents and adolescents at 12-17 years of age [15], [24], [25]. They found in a longitudinal analysis that higher whole-brain RF-EMF dose was not associated with concentration capacity [25] but was associated with lower figural memory [15], [24]. Although in a previous study we did not find any association between whole-brain RF-EMF doses and volume alterations in the hippocampus or the amygdala, subcortical brain regions involved in memory performance [63], higher RF-EMF exposure induced brain alterations such as denditric remodelling and decreased viable cells in these subcortical structures in rats [64]–[68]. We did not assess figural memory in our study but non-verbal intelligence involves, among other cognitive skills, the ability to recognize visual sequences and remember them to understand and interpret the meaning of visual information. Therefore, figural memory, which also implies remembering visual information, might be essential to optimally develop non-verbal intelligence and we would expect that memory impairments shape deficits in non-verbal intelligence or that if there is a true effect of RF-EMF exposure on the brain, as suggested in some experimental studies, these cognitive abilities that share common neural substrates would be similarly affected. However, experimental studies assessing cognitive performance in adults exposed to RF-EMF have shown inconclusive results [11]–[14]. And in our study we found very small effect estimates in the associations between whole-brain RF-EMF dose and non-verbal intelligence. Therefore, we cannot discard that our results might be due to chance.

No previous studies have assessed the relationship of brain RF-EMF exposure and non-verbal intelligence but several studies have investigated the association between brain RF-EMF exposure using reported mobile and DECT phone calls, the primary contributors of RF-EMF exposure to the brain [2], [32], and other cognitive tasks similar to those included in our study [16]–[20], [22]. In line with our results, two studies did not observe any relationship of number of phone calls with speed of information processing [19] or minutes of phone calls with inattention [22] in children and preadolescents at 5-13 years of age. However, in contrast to our findings, other studies suggested that higher number of phone calls were related to poorer working memory [16], [18], poorer spatial and executive ability [20], and poorer cognitive flexibility [19] in children and preadolescents at 5-13 years of age. The association between number of phone calls and inhibitory control and visual recognition has also been investigated in previous studies and they showed mixed results in children and preadolescents at 5-13 years of age [16], [17], [19], [20]. The assessment of brain RF-EMF exposure using reported mobile and DECT phone calls might underestimate the actual brain RF-EMF exposure since this approach do not take into account other RF-EMF sources that also contribute to the whole-brain RF-EMF dose such as screen activities with mobile communication devices (i.e. mobile phones, tablets, or laptops wirelessly connected to the internet) or far-field sources. This underestimation might be more pronounced in preadolescents than in adolescents since preadolescents call less but use more mobile communication devices for screen activities [2], [27]. The different activity patterns and personal behavior related to the use of mobile communication devices explains dissimilarities in the whole-brain RF-EMF doses from phone calls and screen activities between ages [27]. However, the exposure to RF-EMF from far-field sources is mostly explained by distinct characteristics between regions (e.g. deployment of the antennas or type of buildings) [27]. In our study, adolescents were from Menorca, a Spanish Balearic island, which had low levels of exposure from far-field sources compared to other regions of Spain [2], which explained the big differences on the contribution from far-field sources to the overall whole-brain RF-EMF dose between preadolescents and adolescents (28.4% in preadolescents and 4.7% in adolescents). We did not find any relationship of whole-brain RF-EMF dose from far-field sources with cognitive function. However, one study found that higher residential RF-EMF exposure from mobile phone base stations was associated with improved inhibitory control and cognitive flexibility, and reduced visuomotor coordination in children at 5-6 years old [19]. Since all these previous studies did not estimate the RF-EMF dose received by the brain from the different RF-EMF exposure sources, it is not possible to know whether their findings might be related to the RF-EMF exposure to the brain or to social or individual factors related to the use of mobile and DECT phones or to the presence of far-field sources in the environment. In our study, we could not independently assess whole-brain RF-EMF dose from mobile and DECT phone calls and use of mobile and DECT phones because whole-brain dose from mobile and DECT phone calls and minutes of phone calls were highly correlated (r>0.80). Moreover, there is growing evidence that mobile communication devices, when used prudently, can be beneficial for some cognitive abilities [69]. This could masque potential negative effects of RF-EMF on cognitive function. Consequently, it is key to investigate, first, whether it is the whole-brain RF-EMF dose from phones calls or the phone use itself (e.g. mental arousal, displacement of other activities more beneficial for brain development, or phone dependency) what is behind the observed associations between phone calls and cognitive function [21], [24], [25], [70] and, second, whether the potential association between phone calls and cognitive function differs between children, preadolescents, and adolescents.

Strengths of this study are the availability of data in almost 3,000 preadolescents from two population birth-based cohort studies, the assessment of multiple mobile communication devices and cognitive function following similar protocols, and the use of a battery of validated neurocognitive tests. The main limitation of this study is its cross-sectional design. Preadolescents with lower non-verbal intelligence might be more prone to use mobile communication devices thus to have a higher whole-brain RF-EMF dose. To our knowledge there are no previous studies showing a longitudinal association between lower cognitive function and higher use of mobile communication devices. However, we cannot entirely discard reverse causality. Second, cognitive function in the Dutch cohort was only assessed in preadolescents and only as non-verbal intelligence and in the Spanish cohort non-verbal intelligence could not be assessed in adolescents. Therefore, we could not investigate whether whole-brain RF-EMF dose was also related to non-verbal intelligence at adolescence when they are more exposed to RF-EMF to the brain as they call more than in preadolescence. Third, we used an innovative and comprehensive tool to estimate whole-brain RF-EMF doses but it builds on some assumptions which could lead to non-differential misclassification of the exposure leading to a potential underestimation of the effect estimates. Forth, the use of mobile communication devices was self-reported or reported by the mother. Although a recent study showed that reported mobile phone use was a valid measure to distinguish between low and high exposed to RF-EMF from mobile phone use [71], objective measures such as validated applications installed in participants' mobile communication devices tracking their actual use could be used in new studies to improve accuracy on the measurements of the use of these devices.

Conclusion

Our results suggest that overall estimated whole-brain RF-EMF dose and specific dose from phone calls were related to lower non-verbal intelligence in preadolescents. However, our findings also indicate that whole-brain RF-EMF doses were not related to speed of information processing, attentional function, visual attention, and cognitive flexibility in preadolescents or to working memory and semantic fluency in both preadolescents and adolescents. Given the cross-sectional nature of the study, the small effect sizes, and the unknown biological mechanisms, we cannot discard that our results might be due to chance finding or reverse causality. Adolescence is a cognitive demanding stage of life, and one of the most rapid phases of human development. Consequently, impairments of cognitive abilities in adolescence can compromise their development. Further studies with longitudinal data on RF-EMF brain exposure and cognitive function are needed.

Acknowledgements

The authors would like to thank Reinout Wiersand Linda Vodegel-Matzen for implementation of the Raven-like test in the ABCD cohort.

We acknowledge support from the Spanish Ministry of Science and Innovation, and State Research Agency through the "Centro de Excelencia Severo Ochoa 2019-2023" Program (CEX2018-000806-S), and support from the Generalitat de Catalunya through the CERCA Program.

Source of financial support

This work was supported by the European Union Seventh Framework Program (FP7/2007–2013 No. 603794 GERoNiMO project).

INMA-Menorca: This study was funded by grants from Instituto de Salud Carlos III (Red INMA G03/176; CB06/02/0041; 97/0588; 00/0021-2; PI061756; PS0901958; PI14/00677 incl. FEDER funds), CIBERESP, Beca de la IV convocatoria de Ayudas a la Investigación en Enfermedades Neurodegenerativas de La Caixa, and EC Contract No. QLK4-CT-2000-00263.

INMA-Valencia: This study was funded by Grants from UE (FP7-ENV-2011 cod 282957 and HEALTH.2010.2.4.5-1), Spain: ISCIII (G03/176; FIS-FEDER: PI11/01007, PI11/02591, PI11/02038, PI12/00610, PI13/1944, PI13/2032, PI14/00891, PI14/01687, PI16/1288, and PI17/00663; Miguel Servet-FEDER CP11/00178, CP15/00025, and MSII16/00051), Generalitat Valenciana: FISABIO (UGP 15-230, UGP-15-244, and UGP-15-249), and Alicia Koplowitz Foundation 2017.

INMA-Sabadell: This study was funded by grants from Instituto de Salud Carlos III (Red INMA G03/176; CB06/02/0041; PI041436; PI081151 incl. FEDER funds; PI12/01890 incl. FEDER funds; CP13/00054 incl. FEDER funds, MS13/00054, CPII18/00018; PI17/01340 incl. FEDER funds), CIBERESP, Generalitat de Catalunya-CIRIT 1999SGR 00241, Generalitat de Catalunya-AGAUR (2009 SGR 501, 2014 SGR 822), Fundació La Marató de TV3 (090430), Spanish Ministry of Economy and Competitiveness (SAF2012-32991 incl. FEDER funds), French Agency for Food, Environmental and Occupational Health & Safety (EST-2016 RF-21), EU Commission (261357, 308333, 603794 and 634453).

INMA-Gipuzkoa: This study was funded by grants from Instituto de Salud Carlos III (FIS-PI13/02187), CIBERESP, Department of Health of the Basque

Government (2015111065), and the Provincial Government of Gipuzkoa (DFG15/221) and annual agreements with the municipalities of the study area (Zumarraga, Urretxu, Legazpi, Azkoitia y Azpeitia y Beasain).

The ABCD Study: This work is supported by the Netherlands Organization for Health Research and Development (grant 2100.0076) and within the programme Electromagnetic Fields and Health Research (grants 85600004 and 85800001) and Sarphati Amsterdam.

Supplementary material

Figure S1. Flowchart of the study

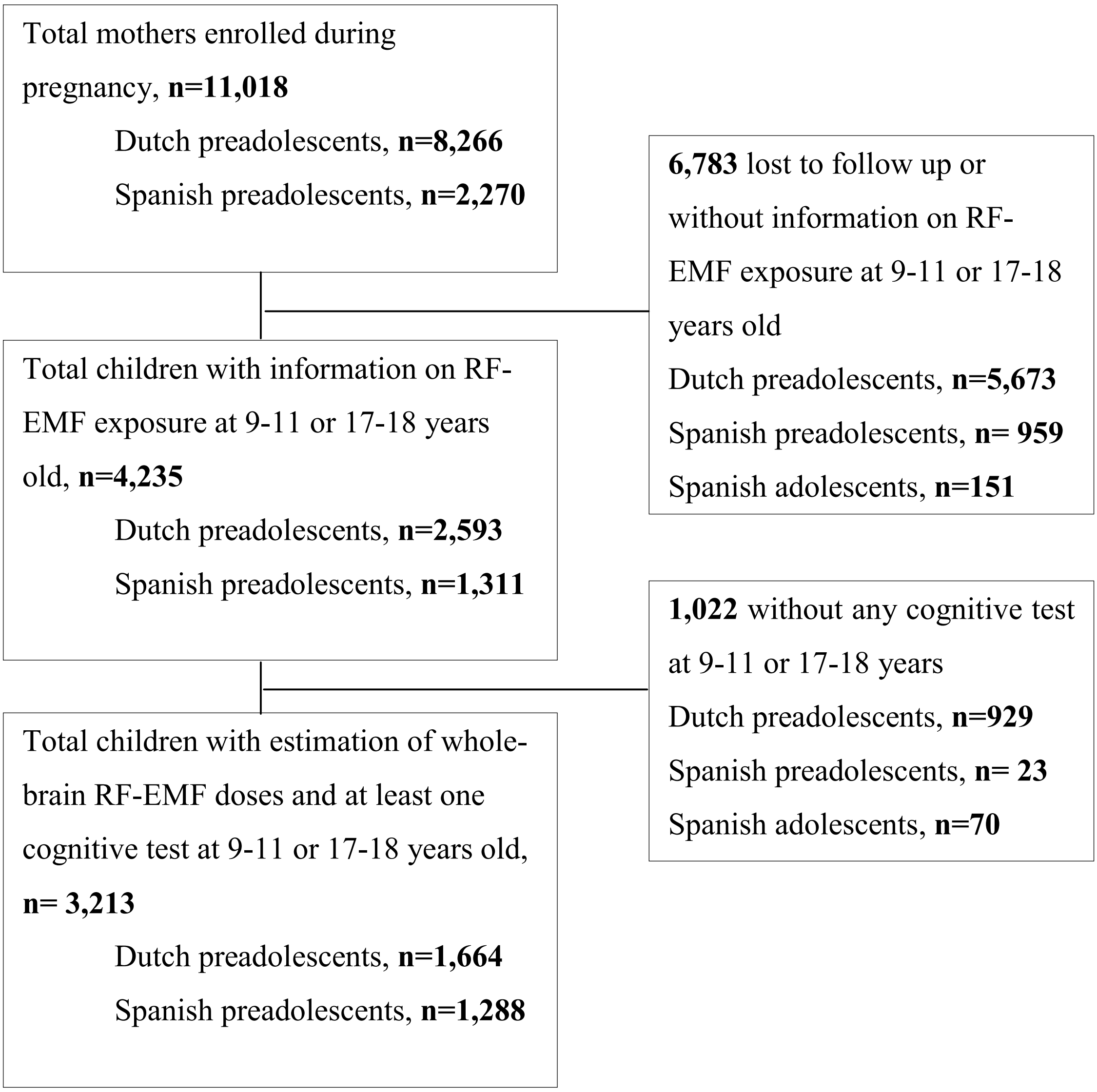


Table S1. Details of the imputation modelling.

Software used and key settings:

STATA 14.0 Software (Stata Corporation, College Station, Texas) - Ice Command (10 cycles)

Number of imputed datasets created: 25

Variables included in the imputation procedure:

We included all the variables collected in the Dutch and the Spanish cohorts at birth of the child or at the 9-18 years follow-up, depending on the cohort, that will be used in studies assessing radiofrequency electromagnetic fields exposure and several health and developmental outcomes (i.e. behavioral problems, cognitive performance, sleep problems, non-specific symptoms, and brain morphology). These variables are:

i) Individual characteristics: sex, birth weight, handedness, physical activity, number of siblings, intelligence quotient, height, and weight.

ii) Maternal characteristics: body mass index, marital status, age at intake, ethnicity, educational level, parity, breastfeeding, social class based on occupation, social class based on financial situation, interpersonal sensitivity, depression symptoms, anxiety symptoms, hostility, intelligence quotient, smoking use, and alcohol use.

iii) Paternal characteristics: body mass index, age at intake, ethnicity, educational level, social class based on occupation, social class based on financial situation, depression symptoms, anxiety symptoms, hostility, and smoking use

Treatment of categorical variables: logistic and multinomial models

Statistical interactions included in imputation models: none

Table S2. Comparison of maternal and individual characteristics of included (n=1,664) vs. excluded (n=6,227) Dutch preadolescents.

	Included (n=1,664)	Excluded (n=6,227)	p-value
Individual characteristics			
Sex (female vs. male)	50.7	49.4	0.502
Birth weight	3511(542)	3389 (632)	<0.001
Gestational age at birth	39.5 (1.6)	39.0 (3.0)	<0.001
Maternal characteristics			
Educational level at child's birth			<0.001
High	72.0	43.3	
Medium	20.6	43.5	
Low	7.4	27.2	
Social class based on occupation at child's birth			<0.001
High	82.3	69.1	
Medium	16.9	27.6	
Low	0.8	3.3	
Country of birth			<0.001
Country of the cohort vs. others	84.0	55.8	
Age at child's birth	32.4 (4.0)	30.2 (5.4)	<0.001
Parity at child's birth			<0.001
0 child	59.2	54.4	
1 child	32.4	31.1	
≥2 children	8.4	14.5	
Smoking during pregnancy			<0.001
Yes vs. No	7.0	10.0	
Body mass index at child's birth	22.6 (3.4)	23.2 (4.2)	<0.001
Family financial situation			<0.001
A lot to spare	28.5	21.1	
A little to spare	41.1	36.4	
Just enough	20.0	27.8	
To use the savings or go in red	10.4	14.7	

Values are percentages for categorical variables and mean (SD) for continuous variables. P-values are based on chi-square and t-student

Table S3. Comparison of maternal, paternal, and individual characteristics of included (n=1,288) vs. excluded (n=982) Spanish preadolescents.

	Included (n=1,288)	Excluded (n=982)	p-value
Individual characteristics			
Sex(female vs. male)	49.3	47.5	0.437
Birth weight	3273 (454)	3228 (523)	0.038
Gestational age at birth	39.7 (1.5)	39.5 (1.9)	0.018
Maternal characteristics			
Educational level at child's birth			<0.001
High	38.9	23.9	
Medium	40.7	40.9	
Low	20.4	35.2	
Social class based on occupation at child's birth			<0.001
High	25.6	14.7	
Medium	30.2	22.1	
Low	44.2	63.2	
Ethnicity			<0.001
Country of the cohort vs. others	94.8	84.3	
Age at child's birth	30.5 (4.1)	29.1 (4.9)	<0.001
Parity at child's birth			0.001
0 child	58.3	52.3	
1 child	36.9	39.2	
≥2 children	4.8	8.4	
Alcohol use during pregnancy			0.780
Yes vs. No	22.6	22.1	
Smoking during pregnancy			<0.001
Yes vs. No	28.9	38.2	
Body mass index at child's birth			0.838
<25 kg/m2	74.5	74.0	
25-30 kg/m2	17.9	18.1	
>30 kg/m2	7.6	7.9	
Paternal characteristics			
Educational level at child's birth			<0.001
High	24.0	14.9	
Medium	44.1	40.4	
Low	31.9	44.7	
Social class based on occupation at child's birth			<0.001
High	23.1	14.0	
Medium	17.2	16.6	
Low	59.7	69.4	
Country of birth			<0.001
Country of the cohort vs. others	93.1	81.2	
Age at child's birth	32.2 (4.7)	31.4 (5.6)	0.002
Body mass index at child's birth			0.838
<25 kg/m2	46.4	45.3	
25-30 kg/m2	42.6	43.1	
>30 kg/m2	11.0	11.6	

kg, kilograms. Values are percentages for categorical variables and mean (SD) for continuous variables. P-values are based on chi-square and t-student.

Table S4. Comparison of maternal, paternal, and individual characteristics of included (n=261) vs. excluded (n=221) Spanish adolescents.

	Included (n=261)	Excluded (n=221)	p-value
Individual characteristics			
Sex (female vs. male)	52.1	42.4	0.158
Birth weight	3197 (467)	3174 (540)	0.619
Gestational age at birth	39.2 (1.5)	39.3 (2.0)	0.591
Maternal characteristics			
Educational level at child's birth			0.242
High	16.7	9.3	
Medium	31.3	29.2	
Low	52.0	61.5	
Social class based on occupation at child's birth			0.002
High	20.8	9.2	
Medium	65.9	64.4	
Low	13.3	26.4	
Country of birth			0.261
Country of the cohort vs. others	97.6	94.9	
Age at child's birth	30.2 (4.5)	29.5 (4.5)	0.132
Parity at child's birth			0.028
0 child	45.3	64.5	
1 child	46.3	29.0	
≥2 children	8.4	6.5	
Alcohol use during pregnancy			0.185
Yes vs. No	10.7	7.2	
Smoking during pregnancy			0.011
Yes vs. No	32.5	43.8	
Body mass index at child's birth			0.003
<25 kg/m2	78.9	82.6	
25-30 kg/m2	17.5	11.3	
>30 kg/m2	3.6	6.1	
Paternal characteristics			
Educational level at child's birth			0.316
High	9.7	6.5	
Medium	26.8	22.4	
Low	63.5	71.1	
Social class based on occupation at child's birth			0.318
High	19.6	13.1	
Medium	68.6	73.8	
Low	11.8	13.1	
Country of birth			0.353
Country of the cohort vs. others	97.6	96.7	
Age at child's birth	33.5 (5.2)	32.1 (4.9)	0.003
Body mass index at child's birth			0.631
<25 kg/m2	43.8	48.6	
25-30 kg/m2	47.6	43.3	
>30 kg/m2	8.6	8.1	

kg, kilograms. Values are percentages for categorical variables and mean (SD) for continuous variables. P-values are based on chi-square and t-student.

Table S5. Variables used in forward selection logistic regression model to calculate inverse probability of attrition weights.

	Dutch cohort		**Spanish cohort**			
Variables	**Preadolescents**		**Preadolescents**		**Adolescents**	
	Explored	**Included**	**Explored**	**Included**	**Explored**	**Included**
Gestational age at birth	x	x	x		x	
Maternal social class based on occupation	x		x		x	x
Maternal educational level at child’s birth	x	x	x	x	x	x
Maternal country of birth	x	x	x	x	x	x
Maternal age at child’s birth	x	x	x	x	x	x
Maternal parity at child’s birth	x	x	x	x	x	x
Maternal alcohol use during pregnancy	X		x	x	x	x
Maternal smoking during pregnancy	x	x	x	x	x	x
Maternal body mass index at child’s birth			x	x	x	x
Paternal social class based on occupation			x	x	x	
Paternal educational level at child’s birth			x	x	x	x
Paternal country of birth			x	x	x	x
Paternal age at child’s birth			x	x	x	x
Paternal body mass index at child’s birth			x	x	x	x
Child’s sex	x		x	x	x	x
Child’s birth weight	x	x	x		x	
Family financial status	x	x				

Table S6. Spearman correlations between estimated whole-brain RF-EMF doses in the Dutch and the Spanish preadolescents, and the Spanish adolescents.

	Preadolescents				**Adolescents**			
	1	**2**	**3**	**4**	**1**	**2**	**3**	**4**
Overall dose **(1)**	1.00				1.00			
Phone calls[a] **(2)**	**0.79**	1.00			**0.88**	1.00		
Screen activities[b] **(3)**	**0.57**	**0.15**	1.00		**0.23**	-0.09	1.00	
Far-field[c] **(4)**	**0.06**	**-0.05**	**0.05**	1.00	**-0.21**	**-0.18**	-0.03	1.00

Values are rho coefficients from spearman correlations. **Bold:** p-value<0.05.

[a] Phone calls refer to mobile and DECT phone calls

[b] Screen activities refer to screen activities with mobile communication devices includes mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop while wirelessly connected to the internet.

[c] RF-EMF exposure from different environmental RF-EMF sources (mobile phone base stations, FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) from different microenvironments (home, school, commuting, and outdoors).

Table S7. Correlations between cognitive outcomes in the Dutch and the Spanish preadolescents.

		(1)	**(2)**	**(3)**	**(4)**	**(5)**	**(6)**	**(7)**	**(8)**	**(9)**	**(10)**	**(11)**	**(12)**
Non-verbal intelligence	Non-verbal intelligence score **(1)**	1.00											
Speed of processing information	Processing speed index **(2)**	**0.23**	1.00										
Attentional function	Hit Reaction Time (ms) **(3)**	**-0.28**	**-0.26**	1.00									
	Hit Reaction Time (Standard Error) **(4)**	**-0.31**	**-0.26**	**0.72**	1.00								
	Omission errors **(5)**	**-0.32**	**-0.25**	**0.62**	**0.69**	1.00							
	Commission errors **(6)**	**-0.09**	-0.05	0.02	**0.13**	0.06	1.00						
Visual attention	Visual attention score, in ms **(7)**	**-0.30**	**-0.45**	**0.43**	**0.33**	**0.33**	0.02	1.00					
Task switching	Task switching score, in ms **(8)**	**-0.25**	**0.43**	**0.35**	**0.31**	**0.31**	0.01	**0.63**	1.00				
Task shifting	Task shifting score**(9)**	0.03	0.00	**-0.08**	-0.02	-0.01	-0.01	**-0.40**	**0.38**	1.00			
Semantic fluency	Semantic verbal fluency score **(10)**	**0.29**	**0.23**	**-0.34**	**-0.29**	**-0.26**	-0.02	**-0.34**	**-0.27**	**0.09**	1.00		
Working memory	Hit Reaction Time, in ms **(11)**	0.01	**-0.06**	**0.14**	**0.11**	0.07	-0.00	**0.08**	0.05	0.03	**-0.12**	1.00	
	d' **(12)**	**0.18**	**0.23**	**-0.15**	**-0.17**	**-0.17**	-0.01	**-0.18**	**-0.19**	0.01	**0.15**	**-0.11**	1.00

d´, detectability; ms, miliseconds. Values are rho coefficients from spearman correlations. **Bold:** p-value<0.05.

Table S8. Correlations between cognitive outcomes in the Spanish adolescents.

		(1)	**(2)**	**(3)**
Semantic fluency	Number of words **(1)**	1.00		
Working memory	Hit Reaction Time, in ms **(2)**	-0.02	1.00	
	d' numbers **(3)**	**0.16**	0.05	1.00

Ms, milliseconds. Values are rho coefficients from spearman correlations. **Bold:** p-value<0.05.

Table S9. Association between maternal, family, and preadolescents' characteristics, and estimated whole-brain RF-EMF doses (mJ/kg/day) in the Dutch and Spanish preadolescents.

	Overall dose		Phone calls[a]		Screen activities[b]		Far-field [c]	
Maternal characteristics	**Mean (SD)/ ρ**	**p-value**	**Mean (SD)/ ρ**	**p-value**	**Mean (SD)/ ρ**	**p-value**	**Mean (SD)/ ρ**	**p-value**
Educational level		0.022		0.318		<0.001		0.001
High	185.3 (420.8)		110.5 (408.4)		14.3 (13.4)		41.8 (77.7)	
Medium	143.1 (298.0)		87.3 (278.8)		12.2 (15.4)		51.3 (103.9)	
Low	150.8 (324.6)		96.7 (300.0)		11.4 (12.2)		58.4 (117.0)	
Social class		<0.001		<0.001		<0.001		<0.001
High	185.2 (342.1)		108.9 (333.3)		14.9 (13.7)		41.1 (78.8)	
Medium	168.2 (527.1)		105.0 (497.1)		11.8 (11.9)		55.5 (104.0)	
Low	83.0 (121.9)		42.5 (114.6)		9.6 (11.4)		58.4 (115.3)	
Country of birth		<0.001		<0.001		<0.001		0.080
Country of the cohort	156.5 (310.2)		90.7 (295.3)		13.2 (13.5)		46.4 (91.3)	
Others	321.3 (747.4)		241.4 (746.8)		16.1 (17.4)		37.2 (69.5)	
Anxiety symptoms	-0.3	<0.001	-0.2	<0.001	-0.2	<0.001	0.0	0.021
Depressive symptoms	-0.1	<0.001	-0.1	<0.001	-0.1	<0.001	-0.0	0.823
Smoking during pregnancy		0.001		0.030		<0.001		<0.001
Yes	123.1 (225.6)		72.6 (212.8)		10.8 (11.8)		59.2 (112.7)	
No	183.6 (410.5)		113.2 (399.7)		14.0 (14.3)		42.5 (79.2)	
Individual characteristics								
Sex		<0.001		<0.001		0.483		0.483
Female	198.2 (476.9)		139.1 (477.0)		11.7 (12.4)		44.5 (90.7)	
Male	147.6 (262.6)		72.9 (225.5)		15.2 (15.1)		46.9 (89.0)	
Age, in years	0.6	<0.001	0.5	<0.001	0.3	<0.001	-0.0	0.858
Physical activity		0.022		0.035		0.253		0.197
Low/medium	174.9 (413.9)		107.4 (396.9)		13.3		45.4 (89.6)	
High	134.1 (196.0)		71.2 (186.3)		12.6		51.1 (101.4)	
Body mass index, in kg/m2	-0.0	0.743	0.0	0.410	-0.1	<0.001	-0.1	0.005

Values are means (SD) or rho coefficients (ρ). P-values are based on one-way anova or spearman correlations.

[a] Phone calls refer to mobile and DECT phone calls

[b] Screen activities refer to screen activities with mobile communication devices including mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop while wirelessly connected to the internet.

[c] RF-EMF exposure from different environmental RF-EMF sources (mobile phone base stations, FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) from different microenvironments (home, school, commuting, and outdoors).

Table S10. Association between maternal, family, and adolescent characteristics, and estimated whole-brain RF-EMF doses (mJ/kg/day) in the Spanish adolescents.

	Overall dose		Phone calls[a]		Screen activities[b]		Far-field [c]	
Maternal characteristics	**Mean (SD)/ ρ**	**p-value**	**Mean (SD)/ ρ**	**p-value**	**Mean (SD)/ ρ**	**p-value**	**Mean (SD)/ ρ**	**p-value**
Educational level		0.431		0.322		0.899		0.034
High	549.3 (1333.4)		529.0 (1354.8)		10.4 (8.0)		11.1 (0.4)	
Medium	325.6 (497.6)		263.9 (490.9)		11.3 (9.2)		11.2 (0.1)	
Low	448.3 (997.0)		403.1 (1002.4)		10.9 (12.2)		11.2 (0.1)	
Social class		0.936		0.841		0.295		0.081
High	465.7 (1353.5)		453.6 (888.5)		11.0 (13.7)		11.1 (0.4)	
Medium	432.0 (864.7)		392.6 (888.5)		10.3 (9.4)		11.2 (0.2)	
Low	382.0 (486.8)		315.4 (457.1)		13.9 (13.4)		11.2 (0.0)	
Country of birth		0.895		0.844		0.635		0.010
Country of the cohort	455.5 (1040.4)		411.3 (1049.7)		10.7 (10.6)		11.2 (0.2)	
Others	511.3 (414.6)		495.7 (475.7)		12.8 (7.5)		10.9 (0.6)	
Smoking during pregnancy		0.003		0.002		0.948		0.899
Yes	743.6 (1545.8)		714.8 (1571.9)		10.7 (13.3)		11.2 (0.2)	
No	331.9 (646.2)		287.4 (657.2)		10.8 (9.2)		11.2 (0.2)	
Individual characteristics								
Sex		0.305		0.377		0.056		0.007
Female	528.0 (1086.2)		477.1 (1086.5)		12.0 (12.2)		11.1 (0.2)	
Male	393.6 (984.0)		358.9 (1006.4)		9.5 (8.3)		11.2 (0.2)	
Age, in years	0.1	0.093	0.1	0.098	0.0	0.941	-0.1	0.066
Physical activity		0.516		0.475		0.762		0.124
Low/medium	494.1 (1212.9)		452.4 (1211.3)		10.9 (10.9)		11.1 (0.2)	
High	399.0 (580.8)		348.2 (574.2)		10.4 (10.2)		11.2 (0.1)	
Body mass index, in kg/m2	-0.0	0.611	0.1	0.327	-0.3	<0.001	-0.1	0.264

Values are means (SD) or rho coefficients (ρ). P-values are based on one-way anova or spearman correlations.

[a] Phone calls refer to mobile and DECT phone calls

[b] Screen activities refer to screen activities with mobile communication devices including mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop while wirelessly connected to the internet.

[c] RF-EMF exposure from different environmental RF-EMF sources (mobile phone base stations, FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) from different microenvironments (home, school, commuting, and outdoors).

Table S11. Association between estimated whole-brain RF-EMF doses and speed of information processing and attentional function in the Spanish preadolescents.

	Speed of information processing	Attentional function			
Whole-brain RF-EMF doses (Δ100 mJ/kg/day)	**PSI** **B (95% CI)**	**HRT (ms)** **B (95% CI)**	**HRT(SE)** **B (95% CI)**	**Omission errors** **IRR (95% CI)**	**Comission errors** **IRR (95% CI)**
Overall dose	0.12 (-0.45; 0.69)	-1.75 (-7.97; 4.45)	-0.05 (-3.14; 3.03)	0.99 (0.93; 1.07)	0.87 (0.67; 1.1)
Source-specific doses					
Phone calls[a]	-0.13 (-1.10; 0.84)	1.08 (-9.30; 11.45)	1.77 (-3.38; 6.92)	1.01 (0.90; 1.12)	0.81 (0.49; 1.35)
Screen activities[b]	3.85 (-4.77; 12.47)	-35.80 (-130.72; 59.12)	11.52 (-35.10; 58.14)	0.79 (0.28; 2.28)	0.14 (0.01; 3.68)
Far-field[c]	0.24 (-0.46; 0.94)	-3.14 (-10.98; 4.71)	-1.20 (-5.05; 2.65)	0.99 (0.90; 1.08)	0.91 (0.69; 1.18)

B, Beta Coefficient; CI, confidence interval; HRT, Hit Reaction Time; HRT (SE), Hi Reaction Time (Standard Error); kg, kilograms; ms, milliseconds; mJ, milijoules; PSI, Processing Speed Index; RF-EMF, Radiofrequency Electromagnetic Fields.

[a] Phone calls refer to mobile and DECT phone calls.

[b] Screen activities refer to screen activities with mobile communication devices including mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop while wirelessly connected to the internet.

[c] RF-EMF exposure from different environmental RF-EMF sources (mobile phone base stations, FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) from different microenvironments (home, school, commuting, and outdoors).

Table S12. Association between estimated whole-brain RF-EMF doses and visual attention, task switching, and task shifting in the Spanish preadolescents.

	Visual attention	**Task switching**	**Task shifting**
Whole-brain RF-EMF doses	**Time (ms)**	**Time (ms)**	**Time (ms)**
(Δ100 mJ/kg/day)	**B (95% CI)**	**B (95% CI)**	**B (95% CI)**
Overall dose	528.25 (-353.76; 1410.27)	360.98 (-661.70; 1383.67)	-0.01 (-0.02; 0.01)
Source-specific doses			
Phone calls	475.36 (-971.94; 1922.67)	406.54 (-1317.56; 2130.64)	-0.01 (-0.04; 0.01)
Screen activities[b]	-3533.13 (-17174.05; 10107.79)	-4763.34 (-20797.30; 11270.62)	-0.02 (-0.28; 0.24)
Far-field[c]	571.39 (-532.40; 1675.17)	358.94 (-910.41; 1628.29)	0.00 (-0.02; 0.02)

B, Beta Coefficient; CI, confidence interval; kg, kilograms; ms, milliseconds; mJ, milijoules; RF-EMF, Radiofrequency Electromagnetic Fields.

[a] Phone calls refer to mobile and DECT phone calls

[b] Screen activities refer to screen activities with mobile communication devices including mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop while wirelessly connected to the internet.

[c] RF-EMF exposure from different environmental RF-EMF sources (mobile phone base stations, FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) from different microenvironments (home, school, commuting, and outdoors).

Table S13. Association between estimated whole-brain RF-EMF doses, and semantic fluency and working memory in the Spanish preadolescents and adolescents.

	Preadolescents			**Adolescents**		
	Semantic fluency	**Working memory**		**Semantic fluency**	**Working memory**	
Whole-brain RF-EMF doses	**Number of words**	**HRT (ms)**	**d'**	**Number of words**	**HRT (ms)**	**d'**
(Δ100 mJ/kg/day)	**B (95% CI)**	**B (95% CI)**	**B (95% CI)**	**B (95% CI)**	**B (95% CI)**	**B (95% CI)**
Overall dose	-0.03 (-0.17; 0.10)	4.08 (-5.97; 14.15)	0.03 (-0.01; 0.07)	-0.05 (-0.11; 0.01)	-0.14 (-1.39; 1.10)	-0.01 (-0.01; -0.00)
Source-specific doses						
Phone calls[a]	0.01 (-0.22; 0.25)	-5.10 (-21.17; 10.97)	0.05 (-0.01; 0.12)	-0.06 (-0.12; 0.00)	-0.06 (-1.31; 1.20)	-0.01 (-0.01; 0.00)
Screen activities[b]	0.35 (-1.68; 2.39)	37.64 (-107.07; 182.35)	-0.10 (-0.74; 0.54)	-3.29 (-9.52; 2.93)	-8.16 (-134.46; 118.15)	0.13 (-0.63; 0.90)
Far-field[c]	-0.06 (-0.23; 0.10)	9.11 (-3.10; 21.32)	0.02 (-0.03; 0.07)	-142.74 (-427.74; 142.26)	4676.24 (-1010.92; 10363.39)	1.59 (-33.22; 36.40)

B, Beta Coefficient; CI, confidence interval; d', detectability; HRT, Hit Reaction Time; kg, kilograms; ms, milliseconds; mJ, milijoules; RF-EMF, Radiofrequency Electromagnetic Fields.

[a] Phone calls refer to mobile and DECT phone calls

[b] Screen activities refer to screen activities with mobile communication devices including mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop while wirelessly connected to the internet.

[c] RF-EMF exposure from different environmental RF-EMF sources (mobile phone base stations, FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) from different microenvironments (home, school, commuting, and outdoors).

Table S14. Estimated overall and source-specific whole-brain RF-EMF doses (mJ/kg/day) based on the assumptions of the higher- and lower-exposure scenarios in the Dutch and Spanish preadolescents, and the Spanish adolescents

	Dutch and Spanish preadolescents (n=2,952)		**Spanish adolescents (n=261)**	
Higher-exposure scenario	**Median,** in mJ/kg/day		**Median,** in mJ/kg/day	
Overall dose	98.8 (50.0; 170.6)		121.9 (55.0; 362.9)	
Source-specific doses		**%**		**%**
Phone calls[a]	31.2 (2.1; 102.3)	74.9	110.2 (42.4; 350.5)	98.4
Screen activities[b]	1.6 (0.6; 2.7)	1.1	1.4 (0.7; 2.3)	0.4
Far-field[c]	13.4 (10.1; 32.9)	24.0	11.2 (11.2; 11.2)	1.2
Lower-exposure scenario	**Median,** in mJ/kg/day		**Median,** in mJ/kg/day	
Overall dose	53.4 (27.2; 118.4)		78.8 (37.2; 216.1)	
Source-specific doses		**%**		**%**
Phone calls[a]	18.48 (2.1; 58.8)	63.7	66.4 (24.7; 203.8)	97.4
Screen activities[b]	1.3 (0.5; 2.3)	1.4	1.4 (0.7; 2.3)	0.6
Far-field[c]	13.4 (10.1; 32.9)	34.9	11.2 (11.2; 11.2)	2.0

RF-EMF, Radiofrequency Electromagnetic Fields; mJ, millijoules; kg, kilograms. Values are medians (interquartile range, IQR).

[a] Phone calls refer to mobile and DECT phone calls.

[b] Screena ctivities refer to screen activities with mobile communication devices including mobile phone use for internet browsing, e-mailing, and text messaging, tablet use, and laptop while wirelessly connected to the internet.

[c] RF-EMF exposure from different environmental RF-EMF sources (mobile phone base stations, FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi) from different microenvironments (home, school, commuting, and outdoors).

References

[1] ICT, “ICT Facts and Figures (Internet). International Telecommunication Union (2017).,” 2017.

[2] L. E. Birks *et al.*, “Spatial and temporal variability of personal environmental exposure to radio frequency electromagnetic fields in children in Europe,” *Environ. Int.*, vol. 117, pp. 204–214, Aug. 2018, doi: 10.1016/j.envint.2018.04.026.

[3] IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, “Non-ionizing radiation, Part 2: Radiofrequency electromagnetic fields,” *IARC Monogr. Eval. Carcinog. Risks Hum.*, vol. 102, no. Pt 2, pp. 1–460, 2013.

[4] E. van Deventer, E. van Rongen, and R. Saunders, “WHO research agenda for radiofrequency fields,” *Bioelectromagnetics*, vol. 32, no. 5, pp. 417–421, Jul. 2011, doi: 10.1002/bem.20660.

[5] C. Sage and E. Burgio, “Electromagnetic Fields, Pulsed Radiofrequency Radiation, and Epigenetics: How Wireless Technologies May Affect Childhood Development,” *Child Dev.*, vol. 89, no. 1, pp. 129–136, Jan. 2018, doi: 10.1111/cdev.12824.

[6] E. A. Crone and E. A. Konijn, “Media use and brain development during adolescence,” *Nat. Commun.*, vol. 9, no. 1, Dec. 2018, doi: 10.1038/s41467-018-03126-x.

[7] L. Kheifets, “The Sensitivity of Children to Electromagnetic Fields,” *PEDIATRICS*, vol. 116, no. 2, pp. e303–e313, Aug. 2005, doi: 10.1542/peds.2004-2541.

[8] D. Rice and S. Barone, “Critical periods of vulnerability for the developing nervous system: evidence from humans and animal models,” *Environ. Health Perspect.*, vol. 108 Suppl 3, pp. 511–533, Jun. 2000.

[9] A. J. Gerber *et al.*, “Anatomical Brain Magnetic Resonance Imaging of Typically Developing Children and Adolescents,” *J. Am. Acad. Child Adolesc. Psychiatry*, vol. 48, no. 5, pp. 465–470, May 2009, doi: 10.1097/CHI.0b013e31819f2715.

[10] J. H. Kim, D.-H. Yu, Y. H. Huh, E. H. Lee, H.-G. Kim, and H. R. Kim, “Long-term exposure to 835 MHz RF-EMF induces hyperactivity, autophagy and demyelination in the cortical neurons of mice,” *Sci. Rep.*, vol. 7, p. 41129, Jan. 2017, doi: 10.1038/srep41129.

[11] E. Valentini, M. Ferrara, F. Presaghi, L. D. Gennaro, and G. Curcio, “Systematic review and meta-analysis of psychomotor effects of mobile phone electromagnetic fields,” *Occup. Environ. Med.*, vol. 67, no. 10, pp. 708–716, Oct. 2010, doi: 10.1136/oem.2009.047027.

[12] A. Verrender, S. P. Loughran, A. Dalecki, R. McKenzie, and R. J. Croft, “Pulse modulated radiofrequency exposure influences cognitive performance,” *Int. J. Radiat. Biol.*, vol. 92, no. 10, pp. 603–610, Oct. 2016, doi: 10.1080/09553002.2016.1213454.

[13] A. Barth, I. Ponocny, T. Gnambs, and R. Winker, “No effects of short-term exposure to mobile phone electromagnetic fields on human cognitive performance: A meta-analysis,” *Bioelectromagnetics*, vol. 33, no. 2, pp. 159–165, Feb. 2012, doi: 10.1002/bem.20697.

[14] Z. Vecsei, B. Knakker, P. Juhász, G. Thuróczy, A. Trunk, and I. Hernádi, “Short-term radiofrequency exposure from new generation mobile phones

reduces EEG alpha power with no effects on cognitive performance," *Sci. Rep.*, vol. 8, no. 1, Dec. 2018, doi: 10.1038/s41598-018-36353-9.

[15] A. Schoeni, K. Roser, and M. Röösli, "Memory performance, wireless communication and exposure to radiofrequency electromagnetic fields: A prospective cohort study in adolescents," *Environ. Int.*, vol. 85, pp. 343–351, Dec. 2015, doi: 10.1016/j.envint.2015.09.025.

[16] M. J. Abramson *et al.*, "Mobile telephone use is associated with changes in cognitive function in young adolescents," *Bioelectromagnetics*, vol. 30, no. 8, pp. 678–686, Dec. 2009, doi: 10.1002/bem.20534.

[17] M. Redmayne *et al.*, "Use of mobile and cordless phones and cognition in Australian primary school children: a prospective cohort study," *Environ. Health Glob. Access Sci. Source*, vol. 15, p. 26, Feb. 2016, doi: 10.1186/s12940-016-0116-1.

[18] S. Thomas *et al.*, "Use of mobile phones and changes in cognitive function in adolescents," *Occup. Environ. Med.*, vol. 67, no. 12, pp. 861–866, Dec. 2010, doi: 10.1136/oem.2009.054080.

[19] M. Guxens *et al.*, "Outdoor and indoor sources of residential radiofrequency electromagnetic fields, personal cell phone and cordless phone use, and cognitive function in 5–6 years old children," *Environ. Res.*, vol. 150, pp. 364–374, Oct. 2016, doi: 10.1016/j.envres.2016.06.021.

[20] C. R. Bhatt *et al.*, "Use of mobile and cordless phones and change in cognitive function: a prospective cohort analysis of Australian primary school children," *Environ. Health*, vol. 16, no. 1, Dec. 2017, doi: 10.1186/s12940-017-0250-4.

[21] A. Schoeni, K. Roser, and M. Röösli, "Symptoms and Cognitive Functions in Adolescents in Relation to Mobile Phone Use during Night," *PloS One*, vol. 10, no. 7, p. e0133528, 2015, doi: 10.1371/journal.pone.0133528.

[22] F. Zheng *et al.*, "Association between mobile phone use and inattention in 7102 Chinese adolescents: a population-based cross-sectional study," *BMC Public Health*, vol. 14, p. 1022, Oct. 2014, doi: 10.1186/1471-2458-14-1022.

[23] S. Heinrich, S. Thomas, C. Heumann, R. von Kries, and K. Radon, "Association between exposure to radiofrequency electromagnetic fields assessed by dosimetry and acute symptoms in children and adolescents: a population based cross-sectional study," *Environ. Health*, vol. 9, no. 1, Dec. 2010, doi: 10.1186/1476-069X-9-75.

[24] M. Foerster, A. Thielens, W. Joseph, M. Eeftens, and M. Röösli, "A Prospective Cohort Study of Adolescents' Memory Performance and Individual Brain Dose of Microwave Radiation from Wireless Communication," *Environ. Health Perspect.*, vol. 126, no. 7, p. 077007, Jul. 2018, doi: 10.1289/EHP2427.

[25] K. Roser, A. Schoeni, and M. Röösli, "Mobile phone use, behavioural problems and concentration capacity in adolescents: A prospective study," *Int. J. Hyg. Environ. Health*, vol. 219, no. 8, pp. 759–769, Nov. 2016, doi: 10.1016/j.ijheh.2016.08.007.

[26] K. Roser, A. Schoeni, A. Bürgi, and M. Röösli, "Development of an RF-EMF Exposure Surrogate for Epidemiologic Research," *Int. J. Environ. Res. Public. Health*, vol. 12, no. 5, pp. 5634–5656, May 2015, doi: 10.3390/ijerph120505634.

[27] M. Eeftens *et al.*, "Personal exposure to radio-frequency electromagnetic fields in Europe: Is there a generation gap?," *Environ. Int.*, vol. 121, pp. 216–226, Dec. 2018, doi: 10.1016/j.envint.2018.09.002.

[28] A. H. Ciccia, P. Meulenbroek, and L. S. Turkstra, “Adolescent Brain and Cognitive Developments: Implications for Clinical Assessment in Traumatic Brain Injury,” *Top. Lang. Disord.*, vol. 29, no. 3, pp. 249–265, Jul. 2009, doi: 10.1097/TLD.0b013e3181b53211.

[29] M. Guxens *et al.*, “Cohort Profile: The INMA—INfancia y Medio Ambiente—(Environment and Childhood) Project,” *Int. J. Epidemiol.*, vol. 41, no. 4, pp. 930–940, Aug. 2012, doi: 10.1093/ije/dyr054.

[30] Ilaria Liorni, “Approximation Formulas for Evaluation of Specific Absorption Rate in the Far-Field, Near-to-Far Field and Near-Field Regions for Integrative Radiofrequency Exposure Assessment in Epidemiological Studies (under review).”

[31] Luuk van Wel, “Organ-specific integrative exposure assessment: Radio-frequency electromagnetic field exposure and contribution of sources in the general population (under review).”

[32] L. E. Birks *et al.*, “Radiofrequency Electromagnetic Fields from Mobile Communication: Description of Modeled Dose in Brain Regions and the Body in European Children and Adolescents (under review).”

[33] C. E. Langer *et al.*, “Patterns of cellular phone use among young people in 12 countries: Implications for RF exposure,” *Environ. Int.*, vol. 107, pp. 65–74, Oct. 2017, doi: 10.1016/j.envint.2017.06.002.

[34] A. Bürgi *et al.*, “A model for radiofrequency electromagnetic field predictions at outdoor and indoor locations in the context of epidemiological research,” *Bioelectromagnetics*, p. n/a-n/a, 2009, doi: 10.1002/bem.20552.

[35] J. Beekhuizen, R. Vermeulen, H. Kromhout, A. Bürgi, and A. Huss, “Geospatial modelling of electromagnetic fields from mobile phone base stations,” *Sci. Total Environ.*, vol. 445–446, pp. 202–209, Feb. 2013, doi: 10.1016/j.scitotenv.2012.12.020.

[36] J. Beekhuizen *et al.*, “Modelling indoor electromagnetic fields (EMF) from mobile phone base stations for epidemiological studies,” *Environ. Int.*, vol. 67, pp. 22–26, Jun. 2014, doi: 10.1016/j.envint.2014.02.008.

[37] A. Huss *et al.*, “Environmental Radiofrequency Electromagnetic Fields Exposure at Home, Mobile and Cordless Phone Use, and Sleep Problems in 7-Year-Old Children,” *PLOS ONE*, vol. 10, no. 10, p. e0139869, Oct. 2015, doi: 10.1371/journal.pone.0139869.

[38] A. L. Martens, J. F. B. Bolte, J. Beekhuizen, H. Kromhout, T. Smid, and R. C. H. Vermeulen, “Validity of at home model predictions as a proxy for personal exposure to radiofrequency electromagnetic fields from mobile phone base stations,” *Environ. Res.*, vol. 142, pp. 221–226, Oct. 2015, doi: 10.1016/j.envres.2015.06.029.

[39] W. Joseph *et al.*, “Determination of the duty cycle of WLAN for realistic radio frequency electromagnetic field exposure assessment,” *Prog. Biophys. Mol. Biol.*, vol. 111, no. 1, pp. 30–36, Jan. 2013, doi: 10.1016/j.pbiomolbio.2012.10.002.

[40] E. Anagnostou *et al.*, “Nonverbal Intelligence,” in *Encyclopedia of Autism Spectrum Disorders*, F. R. Volkmar, Ed. New York, NY: Springer New York, 2013, pp. 2037–2041.

[41] L. B. L. Vodegel Matzen, M. W. van der Molen, and A. C. M. Dudink, “Error analysis of raven test performance,” *Personal. Individ. Differ.*, vol. 16, no. 3, pp. 433–445, Mar. 1994, doi: 10.1016/0191-8869(94)90070-1.

[42] John and J. Raven, "Raven Progressive Matrices," in *Handbook of Nonverbal Assessment*, R. S. McCallum, Ed. Boston, MA: Springer US, 2003, pp. 223–237.

[43] J. A. Holdnack, A. Prifitera, L. G. Weiss, and D. H. Saklofske, "WISC-V and the Personalized Assessment Approach," in *WISC-V Assessment and Interpretation*, Elsevier, 2016, pp. 373–413.

[44] A. S. Kaufman, D. P. Flanagan, V. C. Alfonso, and J. T. Mascolo, "Test Review: Wechsler Intelligence Scale for Children, Fourth Edition (WISC-IV)," *J. Psychoeduc. Assess.*, vol. 24, no. 3, pp. 278–295, Sep. 2006, doi: 10.1177/0734282906288389.

[45] R. F. White, R. Campbell, D. Echeverria, S. S. Knox, and P. Janulewicz, "Assessment of neuropsychological trajectories in longitudinal population-based studies of children," *J. Epidemiol. Community Health*, vol. 63, no. Suppl 1, pp. i15–i26, Jan. 2009, doi: 10.1136/jech.2007.071530.

[46] J. Fan, B. D. McCandliss, T. Sommer, A. Raz, and M. I. Posner, "Testing the Efficiency and Independence of Attentional Networks," *J. Cogn. Neurosci.*, vol. 14, no. 3, pp. 340–347, Apr. 2002, doi: 10.1162/089892902317361886.

[47] S. A. McMains and S. Kastner, "Visual Attention," in *Encyclopedia of Neuroscience*, M. D. Binder, N. Hirokawa, and U. Windhorst, Eds. Berlin, Heidelberg: Springer Berlin Heidelberg, 2009, pp. 4296–4302.

[48] T. Tombaugh, "Trail Making Test A and B: Normative data stratified by age and education," *Arch. Clin. Neuropsychol.*, vol. 19, no. 2, pp. 203–214, Mar. 2004, doi: 10.1016/S0887-6177(03)00039-8.

[49] E. A. Gaudino, M. W. Geisler, and N. K. Squires, "Construct validity in the trail making test: What makes part B harder?," *J. Clin. Exp. Neuropsychol.*, vol. 17, no. 4, pp. 529–535, Aug. 1995, doi: 10.1080/01688639508405143.

[50] K. Archambeau and W. Gevers, "(How) Are Executive Functions Actually Related to Arithmetic Abilities?," in *Heterogeneity of Function in Numerical Cognition*, Elsevier, 2018, pp. 337–357.

[51] E. Camelo *et al.*, "Clinical and Cognitive Correlates of Insight in Bipolar Disorder," *Psychiatr. Q.*, vol. 90, no. 2, pp. 385–394, Jun. 2019, doi: 10.1007/s11126-019-09627-2.

[52] N. Cowan, "Working Memory Underpins Cognitive Development, Learning, and Education," *Educ. Psychol. Rev.*, vol. 26, no. 2, pp. 197–223, Jun. 2014, doi: 10.1007/s10648-013-9246-y.

[53] S. Pelegrina *et al.*, "Normative data on the n-back task for children and young adolescents," *Front. Psychol.*, vol. 6, Oct. 2015, doi: 10.3389/fpsyg.2015.01544.

[54] L. Deserno, P. Sterzer, T. Wustenberg, A. Heinz, and F. Schlagenhauf, "Reduced Prefrontal-Parietal Effective Connectivity and Working Memory Deficits in Schizophrenia," *J. Neurosci.*, vol. 32, no. 1, pp. 12–20, Jan. 2012, doi: 10.1523/JNEUROSCI.3405-11.2012.

[55] J. Patterson, "Verbal Fluency," in *Encyclopedia of Clinical Neuropsychology*, J. S. Kreutzer, J. DeLuca, and B. Caplan, Eds. New York, NY: Springer New York, 2011, pp. 2603–2606.

[56] H. Sauzéon, P. Lestage, C. Raboutet, B. N'Kaoua, and B. Claverie, "Verbal fluency output in children aged 7–16 as a function of the production criterion: Qualitative analysis of clustering, switching processes, and semantic network exploitation," *Brain Lang.*, vol. 89, no. 1, pp. 192–202, Apr. 2004, doi: 10.1016/S0093-934X(03)00367-5.

[57] A. Ardila, “A cross-linguistic comparison of category verbal fluency test (ANIMALS): a systematic review,” *Arch. Clin. Neuropsychol.*, vol. 35, no. 2, pp. 213–225, Feb. 2020, doi: 10.1093/arclin/acz060.

[58] M. A. Hernan, “Estimating causal effects from epidemiological data,” *J. Epidemiol. Community Health*, vol. 60, no. 7, pp. 578–586, Jul. 2006, doi: 10.1136/jech.2004.029496.

[59] P. F. Lovibond and S. H. Lovibond, “The structure of negative emotional states: comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories,” *Behav. Res. Ther.*, vol. 33, no. 3, pp. 335–343, Mar. 1995.

[60] González de Rivera JL *et al.*, “The spanish version of the SCL-90-R. Normative data in the general population,” *Clinical Psychometric Research*, 1989.

[61] B. E. Ainsworth *et al.*, “Compendium of physical activities: an update of activity codes and MET intensities,” *Med. Sci. Sports Exerc.*, vol. 32, no. 9 Suppl, pp. S498-504, Sep. 2000.

[62] C. D. Nguyen, J. B. Carlin, and K. J. Lee, “Model checking in multiple imputation: an overview and case study,” *Emerg. Themes Epidemiol.*, vol. 14, no. 1, Dec. 2017, doi: 10.1186/s12982-017-0062-6.

[63] A. Cabré-Riera *et al.*, “Estimated whole-brain and lobe-specific radiofrequency electromagnetic fields doses and brain volumes in preadolescents,” *Environ. Int.*, vol. 142, p. 105808, Sep. 2020, doi: 10.1016/j.envint.2020.105808.

[64] Y. Li, C. Shi, G. Lu, Q. Xu, and S. Liu, “Effects of electromagnetic radiation on spatial memory and synapses in rat hippocampal CA1,” *Neural Regen. Res.*, vol. 7, no. 16, pp. 1248–1255, Jun. 2012, doi: 10.3969/j.issn.1673-5374.2012.16.007.

[65] S. Hussein, A.-A. El-Saba, and M. K. Galal, “Biochemical and histological studies on adverse effects of mobile phone radiation on rat’s brain,” *J. Chem. Neuroanat.*, vol. 78, pp. 10–19, Dec. 2016, doi: 10.1016/j.jchemneu.2016.07.009.

[66] S. N. Narayanan, R. S. Kumar, B. K. Potu, S. Nayak, P. G. Bhat, and M. Mailankot, “Effect of radio-frequency electromagnetic radiations (RF-EMR) on passive avoidance behaviour and hippocampal morphology in Wistar rats,” *Ups. J. Med. Sci.*, vol. 115, no. 2, pp. 91–96, May 2010, doi: 10.3109/03009730903552661.

[67] S. N. Narayanan, R. S. Kumar, K. M. Karun, S. B. Nayak, and P. G. Bhat, “Possible cause for altered spatial cognition of prepubescent rats exposed to chronic radiofrequency electromagnetic radiation,” *Metab. Brain Dis.*, vol. 30, no. 5, pp. 1193–1206, Oct. 2015, doi: 10.1007/s11011-015-9689-6.

[68] S. N. Narayanan *et al.*, “Radiofrequency electromagnetic radiation exposure effects on amygdala morphology, place preference behavior and brain caspase-3 activity in rats,” *Environ. Toxicol. Pharmacol.*, vol. 58, pp. 220–229, Mar. 2018, doi: 10.1016/j.etap.2018.01.009.

[69] H. H. Wilmer, L. E. Sherman, and J. M. Chein, “Smartphones and Cognition: A Review of Research Exploring the Links between Mobile Technology Habits and Cognitive Functioning,” *Front. Psychol.*, vol. 8, p. 605, Apr. 2017, doi: 10.3389/fpsyg.2017.00605.

[70] A. Schoeni, K. Roser, and M. Röösli, “Symptoms and the use of wireless communication devices: A prospective cohort study in Swiss adolescents,” *Environ. Res.*, vol. 154, pp. 275–283, Jan. 2017, doi: 10.1016/j.envres.2017.01.004.

[71] M. O. Mireku *et al.*, “Total recall in the SCAMP cohort: Validation of self-reported mobile phone use in the smartphone era,” *Environ. Res.*, vol. 161, pp. 1–8, Feb. 2018, doi: 10.1016/j.envres.2017.10.034.

8 Discussion

The results of the different studies included in the present thesis have already been presented and discussed in detail in previous chapters (see section 7, *Results*). In this chapter, I will summarize the main findings and provide a more general discussion about methodological issues, implications of this research for public health and policy making, and several ideas and recommendations for future research directions.

Table 1. Main findings of this doctoral thesis.

Study	What is known	What this study adds	Main results	Main conclusions
I. Mobile communication devices use and sleep	• Insufficient and inadequate sleep is common • The use of mobile communication devices is a public health problem • The use of mobile communication devices is associated with sleep • Sleep is crucial for an optimal brain development	• Differentiation between all-day and bedtime use • Assessment of sleep using objective sleep measure	• DECT calls and tablet use are associated with poorer sleep • Problematic mobile phone use is associated with poorer sleep • Bedtime use is not associated with sleep	✓ The use rather than the RF-EMF exposure seems to drive the observed associations
II. Whole-brain RF-EMF doses and sleep		• Comprehensive assessment of RF-EMF exposure to the brain using a whole-brain RF-EMF dose approach • Differentiation between all-day and evening RF-EMF doses • Assessment of sleep using objective sleep measures	• Overall all-day whole-brain RF-EMF dose and all-day dose from phone calls were not associated with sleep • All-day whole-brain dose from screen activities was associated with excessive somnolence • High evening whole-brain RF-EMF dose from phone calls was associated with lower total sleep time and longer sleep onset latency	✓ The evening seems a relevant window of RF-EMF exposure for sleep ✓ We cannot discard that the observed associated are rather due to the use than the RF-EMF exposure

Table 1 continuation. Main findings of this doctoral thesis.

Study	What is known	What this study adds	Main results	Main conclusions
III. Whole-brain and lobe-specific RF-EMF doses and brain volumes	• The use of mobile communication devices is a public health problem	• Comprehensive assessment of RF-EMF exposure to the brain using a whole-brain and lobe-specific RF-EMF dose approach • Assessment of neurodevelopment using MRI	• Overall whole-brain RF-EMF dose, and dose from phone calls were not associated with brain volumes • Whole-brain RF-EMF dose from screen activities was associated with smaller caudate volume	✓ We cannot discard that the observed associated are rather due to the use than the RF-EMF exposure to the brain ✓ We cannot discard reverse causality
IV. Whole-brain RF-EMF doses and cognitive function	• The use of mobile communication devices is associated with cognitive function and behavioural problems	• Comprehensive assessment of RF-EMF exposure to the brain using a whole-brain RF-EMF dose approach • Inclusion of two developmental periods (preadolescents and adolescents)	• Overall whole-brain RF-EMF dose, and dose from phone calls were associated with non-verbal intelligence in preadolescents • Whole-brain RF-EMF doses were not related to other cognitive abilities in preadolescents and adolescents	✓ RF-EMF exposure to the brain seems to have specific effects on cognitive abilities

Main findings and interpretation

RF-EMF exposure and sleep

In **Study I**, we assessed associations between all-day and bedtime reported mobile communication devices use, and sleep disturbances and objective sleep measures in adolescents. We found that higher frequency of DECT calls and problematic mobile phone use were associated with lower reported sleep quality and that higher tablet use was related to lower objective sleep efficiency and higher wake time after sleep onset. However, all-day use of mobile phone, laptop, and bedtime use of any mobile communication device was not associated with sleep. In **Study II**, we were able to estimate overall and specific whole-brain RF-EMF doses from different RF-EMF sources during a day and in the evening. Moreover, we combined the source-specific whole-brain RF-EMF doses in three groups that lead to different exposure patterns to the brain: i) high RF-EMF doses from peak exposures very close to the head but for short periods of time (phone calls), ii) low RF-EMF doses that might mainly represent non-RF-EMF factors related to the use of mobile communication devices (screen activities), and iii) low RF-EMF doses received continuously throughout the day (far-field or environmental sources). We found that overall all-day whole-brain RF-EMF dose and all-day whole-brain RF-EMF dose from phone calls were not associated with sleep disturbances or objective sleep measures. Regarding evening doses, overall or whole-brain RF-EMF doses from phone calls were not related to sleep disturbances but high evening whole-brain RF-EMF dose from phone calls were associated with lower total sleep time and longer sleep onset latency.

The association between whole-brain RF-EMF doses, or overall RF-EMF exposure assessing different RF-EMF sources together, and sleep has not been investigated to date. Some epidemiological studies assessed associations between reported phone calls, the main contributor of RF-EMF exposure to the brain, and sleep in adolescents [1]–[9]. In line with our results in **Study I**, reported phone calls during the day were associated with daytime sleepiness and higher symptoms of sleep disturbances at 12-20 years old [3], [4], [9]. The all-day RF-EMF exposure to the brain may underestimate peak RF-EMF exposures at certain time of the day that are more relevant for sleep such as the evening window of exposure. In **Study I**, we did not find any association between bedtime mobile communication devices use and sleep. However, we only assessed if participants were using a device or not at bedtime (yes vs.

no), and we could not distinguish uses that lead to RF-EMF exposure from uses that did not. In **Study II**, we collected evening use (i.e. use after 7 p.m. and before falling asleep) of mobile communication device in minutes of use to estimate evening whole-brain RF-EMF doses. In line with our findings in **Study II**, three studies found that higher evening use of mobile communication devices for activities that lead to high RF-EMF exposure to the brain (i.e. that include mobile phone calls) were related to higher symptoms of sleep disturbances [2], [6] and lower objective sleep efficiency [8] at 12-18 years of age. Moreover, one randomized control trial in young adults found that restricting mobile phone use close to bedtime reduced sleep latency and pre-sleep arousal and increased sleep duration and working memory [10]. Unfortunately, these studies [2], [6], [8], [10] did not independently assess the relationship of evening phone calls and sleep, and in **Study II** we performed a large number of tests increasing the probability that chance produced our observed associations. Consequently, we cannot discard that the association between phone calls in the evening and sleep are due to other factors related to the use of these devices (e.g. mental arousal, sleep displacement, or exposure to blue light from screens) or chance finding.

In **Study II**, higher all-day whole-brain RF-EMF dose from far-field sources was associated with longer sleep onset latency. Previous studies that assessed the relationship of RF-EMF exposure levels at school, or at adolescents' bedroom and sleep found mixed results [1], [9], [11]. Higher RF-EMF exposure measured at school was not associated with sleep disturbances in adolescents at 15-18 years old [9] and young adults [1], but was related to shorter sleep duration and less sleep arousal problems in children at 5-7 years old [11].

RF-EMF exposure and neurodevelopment

The **Study III** was the first epidemiological study exploring the association between estimated overall and source-specific whole-brain and lobe-specific RF-EMF doses and brain volumes in preadolescents. We did not find a relationship of overall whole-brain or lobe-specific RF-EMF doses, or whole-brain or lobe-specific RF-EMF doses from phone calls, or from far-field sources with brain volumes in preadolescents. However, higher whole-brain RF-EMF dose from screen activities was associated with smaller caudate volume. In **Study IV**, we investigated the relationship of estimated overall and source-specific whole-brain RF-EMF doses and cognitive function in preadolescents and adolescents. We found that higher overall whole-brain RF-EMF dose and specific whole-brain RF-EMF dose from phone calls were associated with lower non-verbal intelligence in preadolescents. However, none of the whole-brain RF-EMF doses were related to other cognitive abilities such as speed of information processing, attentional function, visual attention, and cognitive flexibility in preadolescents or to working memory and semantic fluency in both preadolescents and adolescents.

Experimental studies in animals have showed that exposure to RF-EMF is related to brain morphology alterations. In particular, higher RF-EMF exposure induced dendritic remodelling and decreased viable cells in the hippocampus and the amygdala in rats [12]–[16]. However, we did not find an association between overall whole-brain RF-EMF dose, or dose from phone calls and the volume of the hippocampus or the amygdala in **Study III**. Among other functions, the hippocampus plays an important role in the formation of new memories [17] and the amygdala is involved in memory consolidation [18]. Interestingly, a longitudinal epidemiological study found that a higher estimated whole-brain RF-EMF dose in preadolescents and adolescents with right-side preference for the phone calls was related to a decreased figural memory performance, which involves mainly the right hemisphere [19], and not to verbal memory performance, which involves mainly the left hemisphere, after one year of follow-up [20]. In **Study IV**, we did not assess figural memory but non-verbal intelligence involves, among other cognitive skills, the ability to recognize visual sequences and remember them to understand and interpret the meaning of visual information. Therefore, figural memory, which also implies remembering visual information, might be essential to optimally develop non-verbal intelligence and we would expect that memory impairments shape deficits in non-verbal intelligence or that these cognitive abilities that share common neural substrates would be similarly affected. However, experimental studies assessing cognitive performance in adults during or after exposure to RF-EMF have shown inconclusive results [21]–[24], and in our study we found very small effect estimates in the associations between whole-brain RF-EMF doses and non-verbal intelligence. Consequently, the association between whole-brain RF-EMF doses and non-verbal intelligence needs confirmation in other population-based studies. These associations between RF-EMF brain dose and memory, or non-verbal intelligence could be driven by disturbed sleep [20], as previous studies found alterations in the electroencephalogram (EEG) during sleep in participants exposed to RF-EMF [25]–[28] and disturbed sleep have been related to poorer memory consolidation [29] and disturbed subcortical structures such as hippocampus [30], [31].

Methodological considerations

Studies included in this thesis were based on three prospective population-based cohort studies with a follow-up from fetal life onwards. They followed similar protocols to assess RF-EMF exposure to the brain, sleep, and cognitive function. We obtained large sample sizes combining individuals from these cohorts, which provided notable statistical power, and we were one of the first applying the integrative exposure model in population-based samples, and assessing the relationship of brain RF-EMF doses with brain volumes. However, the studies presented in this thesis also have several limitations, mainly with reference to study design, and to exposure and outcome assessments. These limitations will be discussed in the following sections.

Study design

Single time point data

The lack of repeated measures of the all-day RF-EMF exposure to the brain and the outcomes evaluated in our studies is one of the main limitations of this thesis. We only had repeated measures of the exposure and outcome in **Study IV**. However, these repeated measures were restricted to evening whole-brain RF-EMF doses in a sub-study sample which only included Sabadell and Gipuzkoa sub-cohorts. The lack of repeated measures in our studies does not allow us to discard reverse causality as a potential explanation for our findings. For example, regarding **Study III**, children and young adults with some psychiatric disorders such as attention-deficit/hyperactivity disorder have been shown to have a smaller caudate brain volume [32]–[34], and it could be hypothesized that individuals with these disorders have a higher use of mobile communication devices. Having repeated measurements of the exposure and outcome allows analyzing changes in the outcome related to changes in the exposure over time, therefore increasing the feasibility of causal inference. Future studies should look at repeated measures to better understand the complex association between RF-EMF exposure to the brain and sleep, and RF-EMF exposure to the brain and neurodevelopment. Longitudinal data will also allow the possibility to assess sleep as a potential mediator in the association between mobile communication devices and neurodevelopment or vice versa.

Confounding

It is not clear whether is the RF-EMF exposure to the brain or the use of mobile communication devices itself what is behind the associations of mobile communication devices and sleep, and mobile communication devices and neurodevelopment. In **Study I**, our results indicated that the use might be more relevant than the RF-EMF exposure. If the observed associations were driven by RF-EMF exposure, we would expect to find an association between duration of DECT and mobile phone calls with sleep in addition to the observed association between frequency of DECT phone calls and sleep. In **Study II**, **III**, and **IV** we were capable to estimate RF-EMF doses to the brain. However, given that the doses were estimated based on the reported minutes of use, brain RF-EMF doses and minutes of use were highly correlated ($r < 0.80$). Consequently, we could not independently assess associations with brain RF-EMF doses and mobile communication devices use. One way to distinguish between potential effects of RF-EMF exposure and mobile communication devices use is to assess the latter using problematic mobile phone use instead of minutes of use. There is growing evidence that mobile communication devices, when used prudently, can be beneficial for some cognitive abilities [35]. This could masque potential negative effects of RF-EMF exposure on brain development. Moreover, we missed relevant factors (e.g. type of content or activity performed with devices, psychological well-being, or family structure) to assess potential associations with mobile communication devices use. The collection of a complete set of covariates should be carefully considered in the study design phase to properly assess associations between mobile communication devices use and outcome.

Biological plausibility

There is scientific evidence that RF-EMF exposure can alter the brain by nerve stimulation, temperature rise, and change of permeability of cell membranes [36]. However, the lack of a defined biological mechanism behind the observed associations between RF-EMF exposure and sleep, and RF-EMF exposure and neurodevelopment complicates the interpretation of the results in epidemiological studies. Consequently, the results of the studies included in this thesis are rather hypothesis generating for further studies than conclusive evidence.

Exposure assessment

Exposure misclassification

In **Study I**, personal mobile communication devices use was self-reported by adolescents. In **Study II**, **III**, and **IV**, estimated brain RF-EMF doses from near-field sources (phone calls and screen activities) relied on information collected using maternal reported questionnaires in preadolescents and self-reported questionnaires in adolescents. Some studies suggested that self-reported questionnaires overestimate duration of mobile phone use [37] but others studies indicated that young people with low mobile phone use tend to underestimate their use and those with high mobile phone use tend to overestimate their use [38], [39]. Unfortunately, there are not studies validating the accuracy of maternal reported mobile phone use for calling, maternal and self-reported use of other mobile phone uses, tablet, or laptop, or daily diaries to assess evening use of mobile communication devices. New studies should assess personal use of mobile communication devices objectively. For example, by installing applications in participants' mobile communication devices which track the actual use. However, this is not always feasible in epidemiological studies with big sample sizes. Validated paper or on-line questionnaires and diaries to assess the use of mobile communication devices would give reliable and powerful tools to assess the personal use of mobile communication devices as an alternative to objective measures.

Spatial variability

Spatial variability occurs when a quantity that is measured at different spatial locations exhibits values that differ across the locations. The distribution of environmental exposure to RF-EMF, as many other environmental exposures, is different between countries or even between regions within a country [40]–[42]. Distinct characteristics (e.g. deployment of the antennas, type of buildings, or population density) lead to different amount of environmental RF-EMF exposure between countries or regions [43]. For example, in **Study IV**, adolescents were from Menorca, a Spanish Balearic island, which has low levels of environmental RF-EMF exposure compared to other regions of Spain [40]. This explains our observed disparities on the contribution from far-field sources to the overall whole-brain RF-EMF dose between preadolescents and adolescents (28.4% in preadolescents and 3.5% in adolescents). Moreover, environmental RF-EMF exposure differs between microenvironments in a given country (homes, school, commuting, outdoors). However, microenvironment contributions to the overall environmental exposure do not vary significantly between countries [40], [43], [44]. Previous studies assessing environmental RF-EMF exposure and its relationship with sleep and neurodevelopment partially captured the environmental exposure, assessing RF-EMF levels at school or home only [1], [9], [11], [45]. In **Studies II**, **III**, and **IV** we have tried a more accurate approach to assess environmental RF-EMF exposure and we included environmental exposure from different microenvironments such as home, school, commuting, and outdoors. We included measurements taken using portable exposure meters that allow for the inclusion of many sources (mobile phone base stations, FM radio and TV broadcast antennas, mobile phones, DECT phones, and WiFi), which can hardly be captured using a questionnaire-based approach. However, these measurements were assessed only in few participants of the INMA (n = 244) and the ABCD (n = 56) cohort studies. Generation R did not participate in these RF-EMF measurements. This small sample size could compromise the external validity of these measurements, which might not represent the general population, and might be exclusive for our study population and period of time. RF-EMF exposure at home from mobile phone base stations was modeled using a wave propagation model (NISMap) which allowed us to assess this type of exposure to all participants of our studies. However, there are also inaccuracies related to how participants move around rather than staying in one location (i.e. home) and we did not know how much time, on average, they spent at home.

Temporal variability

Temporal variability occurs when a quantity that is measured at different time points exhibits values that differ across time. The all-day assessment of RF-EMF exposure might underestimate high uses at a given time of the day that lead to peak exposures, masking potential association between RF-EMF exposure and an outcome in a defined window of exposure. For example, in **Study IV**, the evening seems to be a relevant window of exposure for sleep. The short-term RF-EMF exposure variability (different times within a day) is mostly determined by changes in personal mobile communication device use [43]. Studies assessing the relationship of personal mobile communication devices use that lead to RF-EMF exposure to the brain in different times of a day and the outcome are of interest. However, to assess potential associations between RF-EMF exposure to the brain at night while sleeping and sleep, environmental RF-EMF exposure at night should be considered. Personal mobile communication devices use is lower at night than during the day (i.e. few adolescents wake up by any mobile communication device, and use them, and the brain exposure from active but not directly being used mobile communication devices close the bed while sleeping is very low) [46], which might increase the contribution of environmental exposures to the overall brain RF-EMF dose at night. Moreover, to date, we do not know if peak exposures that occur at certain times of the day are more or less relevant for sleep and neurodevelopment than prolonged low levels of continuous exposure. Only in **Study IV**, we observed some associations between environmental exposure and outcome (sleep) in preadolescents. Long-term RF-EMF exposure variability (week-to-week, year-to-year) is not only defined by changes on personal mobile communication devices use but also by environmental RF-EMF exposure fluctuations, which might be determined by the microenvironment where we spend our time but also by other changes in network characteristics (e.g. implementation of 5G). In this case, repeated measures of RF-EMF exposure from personal mobile communication devices use, and far-field sources are equally important to understand potential associations between long-term changes of RF-EMF exposure over time (week, or years) and the outcome under study. Moreover, repeated measures of RF-EMF exposure over time are of interest to study cumulative RF-EMF effects to the brain.

Personal variability

Age is one of the main determinants of personal mobile communication devices use [43]. In **Study IV**, preadolescents and adolescents had different contributions to the whole-brain RF-EMF dose from phone calls (70.3% in preadolescents, and 96.0 % in adolescents) and screen activities (1.3% in preadolescents, and 0.5% in adolescents). However, we cannot discard that this difference might be explained by the different year of data collection in the cohorts included in our studies (2015-2019 for preadolescents of Valencia, Sabadell, Gipuzkoa, and ABCD and 2015-2016 for adolescents of Menorca). A better understanding of activity patterns of mobile communication devices use in different ages during adolescence will improve the quality of RF-EMF assessment in epidemiological studies, and thus, the accuracy of RF-EMF dose estimations. Moreover, questionnaires being developed for future population-based studies should incorporate new mobile communication functionalities such as virtual glasses that were not used by preadolescents or adolescents at the time of the set-up of the follow-up included in our studies.

RF-EMF dose approach

The ability to estimate the RF-EMF brain dose from several RF-EMF exposure sources represents an important step forward in the evaluation of the potential health effects of RF-EMF exposure. Previous studies have mostly used questionnaires to assess near-field RF-EMF exposure (phone calls and screen activities), and portable exposure meters, spot measurements, or modeling to assess far-field or environmental RF-EMF exposure. In **Study II**, **III**, and **IV**, we used a recently developed integrated exposure model to estimate overall and source-specific RF-EMF brain doses [47], [48]. However, this model requires the following high quality information (near-field sources, far-field sources, and personal characteristics) to accurately assess RF-EMF doses:

1. Near-field sources. Mobile communication devices used, and for each device:
   - Duration of use
   - Proportion of functions used (e.g. texting, streaming)
   - Output power for each function
   - Where the device was held in relation to the body during use (e.g. left, right, hands-free when calling, or in front of eyes)
   - Network type and frequency used
   - Nearby mobile communication devices not directly being used, but connected and active.
2. Far-field sources. Portable exposure meters measurements or propagation wave modeling with accurate location history
3. Personal characteristics to determine specific absorption energy at the target organ (e.g. brain): age, sex, body mass index

Some uncertainties can arise when this information is not provided. In our studies, information on the proportion of network use for calling, network used for screen activities, or type of screen activity while other mobile phone uses, laptop use, or tablet use was not collected (see **Study II, III** and **IV**). Based on a previous study and expert opinion, we made some assumptions, which could lead to errors on the estimation of the doses. However, these errors are shared or systematic (i.e. affecting equally all participants from the study), leading to non-differential misclassification and potential underestimation of effect estimates. Moreover, we did not collect information on nearby mobile communication devices not directly being used, but connected and active. Some preadolescents and adolescents sleep with mobile communication devices close to their heads, but the RF-EMF emission from inactive devices is very low, and when the device is more than 20 cm away from the head the RF-EMF emitted can be considered negligible [49]. In **Study I** and **II**, we collected information on being awaked by any mobile communication device at night (yes vs. no). In **Study I**, we could not use this data for our analyses because very few participants (<3%) reported to be awaked by a mobile communication device and use it in bed, and in **Study II** we missed relevant information to estimate RF-EMF doses from night use (e.g. duration of use). Studies assessing associations between RF-EMF exposure at night while sleeping and sleep should consider collecting whether participants wake up by any device, and if so, what type of activity they do and for how long.

We recommend estimating RF-EMF doses, which allow accounting for personal characteristics and organ of interest (e.g. the brain). The contribution from specific RF-EMF sources to the overall dose is different for each organ. Studies assessing associations between RF-EMF exposure with sleep, or neurodevelopment should focus on the brain.

Timing of data collection

Scientific publications often come out with results based on RF-EMF exposure information collected or measured some years ago. In our studies, we used information on RF-EMF exposure assessed between 2014 and 2019, depending on the cohort. Exposure patterns are quickly obsolete because of rapidly evolving mobile communication functionalities (e.g. video streaming, on-line gaming, WhatsApp). An up-to-date understanding of today’s patterns of RF-EMF exposure is crucial to translate evidence from epidemiological studies in current public health recommendations. In this sense, descriptive studies of RF-EMF exposure patterns for age ranges and time periods are missing. Private or telecommunication companies track the use of mobile communication devices of their clients and own information on characteristics of the antennas (e.g. exact location, position of the antenna etc.), and perform their far-field RF-EMF measurements and estimations. Unfortunately, this data is difficult to access and use for epidemiological studies.

Outcome assessment

Sleep assessment

In **Study I** and **II**, preadolescents' and adolescents' sleep disturbances were mother- or self-reported, respectively. The description of preadolescents' sleep by the parent appears appropriate as far as symptoms are concerned, but does not result in an accurate estimate of sleep onset latency or sleep duration [59]. In our studies, we combined reported sleep disturbances and objective sleep measures to have a more comprehensive assessment of preadolescents' and adolescents' sleep. Today, the only widely accepted method for clinically monitoring sleep is the polysomnography (PSG), which is, however, expensive to perform and influences the sleep [60]. The availability of digital technologies (e.g. actigraphy) for the measurement of sleep has significantly expanded in the last decade [61] and has become one of the most appropriate tools to assess sleep in participants' natural environment for epidemiological studies [62]. To date, very few studies assessed the association between RF-EMF exposure and sleep objectively measured with actigraphy [8], [63].

Neurodevelopment assessment

Most of the previous studies have assessed neurodevelopment as cognitive function or behavior problems using validated neuropsychological tests or questionnaires. The heterogeneity of available tests make sometimes the comparability between studies or the possibility of combining cohorts difficult. In **Study IV**, the cohorts used different test to assess preadolescents' non-verbal intelligence. We aimed to increase the comparability between the tests by standardizing the score to mean of 100 and a standard deviation of 15.

Given that **Study III** was the first study investigating potential associations between RF-EMF exposure to the brain and brain volumes using magnetic resonance imaging, further studies are needed to replicate our findings. Moreover, the brain is dynamic and responds to many external inputs, including environmental exposures. This dynamism might not always translate to detectable structural brain alterations but to small brain activity changes that could explain the observed associations between RF-EMF exposure and impaired cognitive function in previous studies [7], [20], [50]–[57], [45], [58], as well as the observed brain effects in animal studies [12]–[16]. Other approaches than structural imaging might be relevant for exploring the potential brain alterations related to RF-EMF exposure. For example, it would be interesting to investigate whether RF-EMF exposure induce changes in the activity of the brain using functional magnetic resonance imaging.

Implications for public health and for policy making

It was not until this year, 2020, that the ICNIRP published recommended SAR values. Basic restrictions for frequency ranges between 100 kHz and 6 GHz for local exposures (e.g. RF-EMF exposure to the brain) are that the temperature increase is not allowed to exceed 2ºC over 10 grams of tissue over 6 minutes of exposure. This avoid SAR to surpass 20 W/kg, the necessary level described by the ICNIRP to produce harm to human body [36]. After applying the recommended reduction factor - which is 10 - for general population, SAR levels recommended by the ICNIRP for general population are 2 W/kg. In our studies, none of the estimated brain RF-EMF doses exceed this value. Given that the capability to estimate RF-EMF doses in population-based studies is new, few studies have investigated the relationship of RF-EMF doses and health. The insufficient evidence makes basic restrictions of SAR values for RF-EMF exposure too conservative. And we would expect to observe health effects related to lower doses of RF-EMF as suggested in our studies. We cannot draw strong conclusions for public health recommendations or policy making only out of the studies included in this thesis. However, our studies provide experience to draw recommendations for future research on the field of RF-EMF exposure to the brain and health (see *Future research directions* section), which aim to better understand overall and source-specific brain RF-EMF doses at different ages during preadolescence and adolescence, and potential sleep and neurodevelopment effects related to these doses.

Future research directions

Evidence is limited for potential effects of RF-EMF exposure to the brain. Experimental studies in humans show inconsistent results and epidemiological studies that assessed RF-EMF exposure to the brain and its relationship with sleep and neurodevelopment are scarce. However, since mobile communication devices came to stay, it is important to comprehend how they affect our health (i.e. whether RF-EMF exposure is behind the observed associations). From my perspective, I list below some key points for future research studies on RF-EMF exposure to the brain, sleep, and neurodevelopment:

Related to the exposure:

- To assess problematic mobile phone use together with RF-EMF exposure to the brain (see *Confounding* section).
- To collect high quality data on personal use of mobile communication devices (see *RF-EMF dose approach* section).
- To collect location history when assessing far-field or environmental exposure (see *RF-EMF dose approach* section).
- To estimate brain RF-EMF doses.

Related to the outcome:

- To assess sleep using objective measures.
- To use functional magnetic resonance imaging as an approach to assess brain activity alterations that might not translate to structural brain alterations.
- To assess laterality of phone calls and conduct analysis stratifying by brain hemisphere when assessing associations between RF-EMF exposure to the brain and brain volumes, or cognitive function.

Related to the study design or the analysis plan:

- To collect repeated measures on RF-EMF exposure to the brain and outcome of interest.
- To include children in the study population. It could be that specific levels of RF-EMF doses do not have an effect in preadolescents and adolescents but do have it at younger ages, when the brain is more rapidly developing and, thus, more vulnerable.
- To replicate existing findings [20], [51] and our results in other population-based studies to increase the consistency of evidence.
- To study the role of sleep as a potential mediator in the association between RF-EMF exposure to the brain and cognitive function, or vice versa.

9 Conclusions

The results of this thesis suggest:

- that the use of mobile communication devices, in particular higher DECT phone use and problematic mobile phone use, is associated with poorer reported sleep quality in adolescents.
- that higher tablet use is associated with lower objective sleep efficiency and longer wake after sleep onset in adolescents.
- that estimated overall all-day whole-brain RF-EMF dose, and all-day whole-brain RF-EMF dose from phone calls are not associated with sleep disturbances or objective sleep measures in preadolescents.
- that high evening whole-brain RF-EMF dose from phone calls were associated with shorter total sleep time and longer sleep onset latency in preadolescents.
- that estimated overall whole-brain and lobe-specific RF-EMF doses, and whole-brain and lobe-specific RF-EMF doses from phone calls are not associated with brain volumes in preadolescents.
- that estimated whole-brain RF-EMF dose from screen activities are associated with smaller caudate volume in preadolescents.
- that estimated overall whole-brain RF-EMF dose, and whole-brain RF-EMF dose from phone calls are associated with lower non-verbal intelligence in preadolescents.
- that estimated overall whole-brain RF-EMF dose, and whole-brain RF-EMF dose from phone calls are not associated with speed of information processing, attentional function, visual attention, and cognitive flexibility in preadolescents or to working memory and semantic fluency in both preadolescents and adolescents.

10 References

[1] G. Berg-Beckhoff *et al.*, «Mobile phone base stations and adverse health effects: phase 2 of a cross-sectional study with measured radio frequency electromagnetic fields», *Occup. Environ. Med.*, vol. 66, n.º 2, pp. 124-130, feb. 2009, doi: 10.1136/oem.2008.039834.

[2] C. J. Calamaro, T. B. A. Mason, y S. J. Ratcliffe, «Adolescents Living the 24/7 Lifestyle: Effects of Caffeine and Technology on Sleep Duration and Daytime Functioning», *PEDIATRICS*, vol. 123, n.º 6, pp. e1005-e1010, jun. 2009, doi: 10.1542/peds.2008-3641.

[3] Y. W. Mak *et al.*, «Association between screen viewing duration and sleep duration, sleep quality, and excessive daytime sleepiness among adolescents in Hong Kong», *Int. J. Environ. Res. Public. Health*, vol. 11, n.º 11, pp. 11201-11219, oct. 2014, doi: 10.3390/ijerph111111201.

[4] V. C. Brunetti, E. K. O'Loughlin, J. O'Loughlin, E. Constantin, y É. Pigeon, «Screen and nonscreen sedentary behavior and sleep in adolescents», *Sleep Health*, vol. 2, n.º 4, pp. 335-340, dic. 2016, doi: 10.1016/j.sleh.2016.09.004.

[5] X. Jiang, L. L. Hardy, L. A. Baur, D. Ding, L. Wang, y H. Shi, «Sleep duration, schedule and quality among urban Chinese children and adolescents: associations with routine after-school activities», *PloS One*, vol. 10, n.º 1, p. e0115326, 2015, doi: 10.1371/journal.pone.0115326.

[6] S. Lemola, N. Perkinson-Gloor, S. Brand, J. F. Dewald-Kaufmann, y A. Grob, «Adolescents' Electronic Media Use at Night, Sleep Disturbance, and Depressive Symptoms in the Smartphone Age», *J. Youth Adolesc.*, vol. 44, n.º 2, pp. 405-418, feb. 2015, doi: 10.1007/s10964-014-0176-x.

[7] M. Redmayne *et al.*, «Use of mobile and cordless phones and cognition in Australian primary school children: a prospective cohort study», *Environ. Health Glob. Access Sci. Source*, vol. 15, p. 26, feb. 2016, doi: 10.1186/s12940-016-0116-1.

[8] A. D. Fobian, K. Avis, y D. C. Schwebel, «Impact of Media Use on Adolescent Sleep Efficiency», *J. Dev. Behav. Pediatr. JDBP*, vol. 37, n.º 1, pp. 9-14, ene. 2016, doi: 10.1097/DBP.0000000000000239.

[9] R. Durusoy, H. Hassoy, A. Özkurt, y A. O. Karababa, «Mobile phone use, school electromagnetic field levels and related symptoms: a cross-sectional survey among 2150 high school students in Izmir», *Environ. Health*, vol. 16, n.º 1, dic. 2017, doi: 10.1186/s12940-017-0257-x.

[10] J. He, Z. Tu, L. Xiao, T. Su, y Y. Tang, «Effect of restricting bedtime mobile phone use on sleep, arousal, mood, and working memory: A randomized pilot trial», *PLOS ONE*, vol. 15, n.º 2, p. e0228756, feb. 2020, doi: 10.1371/journal.pone.0228756.

[11] A. Huss *et al.*, «Environmental Radiofrequency Electromagnetic Fields Exposure at Home, Mobile and Cordless Phone Use, and Sleep Problems in 7-Year-Old Children», *PLOS ONE*, vol. 10, n.º 10, p. e0139869, oct. 2015, doi: 10.1371/journal.pone.0139869.

[12] Y. Li, C. Shi, G. Lu, Q. Xu, y S. Liu, «Effects of electromagnetic radiation on spatial memory and synapses in rat hippocampal CA1», *Neural Regen. Res.*, vol. 7, n.º 16, pp. 1248-1255, jun. 2012, doi: 10.3969/j.issn.1673-5374.2012.16.007.

[13] S. Hussein, A.-A. El-Saba, y M. K. Galal, «Biochemical and histological studies on adverse effects of mobile phone radiation on rat's brain», *J. Chem. Neuroanat.*, vol. 78, pp. 10-19, dic. 2016, doi: 10.1016/j.jchemneu.2016.07.009.

[14] S. N. Narayanan, R. S. Kumar, B. K. Potu, S. Nayak, P. G. Bhat, y M. Mailankot, «Effect of radio-frequency electromagnetic radiations (RF-EMR) on passive avoidance behaviour and hippocampal morphology in Wistar rats», *Ups. J. Med. Sci.*, vol. 115, n.º 2, pp. 91-96, may 2010, doi: 10.3109/03009730903552661.

[15] S. N. Narayanan, R. S. Kumar, K. M. Karun, S. B. Nayak, y P. G. Bhat, «Possible cause for altered spatial cognition of prepubescent rats exposed to chronic radiofrequency electromagnetic radiation», *Metab. Brain Dis.*, vol. 30, n.º 5, pp. 1193-1206, oct. 2015, doi: 10.1007/s11011-015-9689-6.

[16] S. N. Narayanan *et al.*, «Radiofrequency electromagnetic radiation exposure effects on amygdala morphology, place preference behavior and brain caspase-3 activity in rats», *Environ. Toxicol. Pharmacol.*, vol. 58, pp. 220-229, mar. 2018, doi: 10.1016/j.etap.2018.01.009.

[17] M. Leszczynski, «How Does Hippocampus Contribute to Working Memory Processing?», *Front. Hum. Neurosci.*, vol. 5, 2011, doi: 10.3389/fnhum.2011.00168.

[18] J. L. McGaugh, «THE AMYGDALA MODULATES THE CONSOLIDATION OF MEMORIES OF EMOTIONALLY AROUSING EXPERIENCES», *Annu. Rev. Neurosci.*, vol. 27, n.º 1, pp. 1-28, jul. 2004, doi: 10.1146/annurev.neuro.27.070203.144157.

[19] A. J. Golby, «Material-specific lateralization in the medial temporal lobe and prefrontal cortex during memory encoding», *Brain*, vol. 124, n.º 9, pp. 1841-1854, sep. 2001, doi: 10.1093/brain/124.9.1841.

[20] M. Foerster, A. Thielens, W. Joseph, M. Eeftens, y M. Röösli, «A Prospective Cohort Study of Adolescents’ Memory Performance and Individual Brain Dose of Microwave Radiation from Wireless Communication», *Environ. Health Perspect.*, vol. 126, n.º 7, p. 077007, jul. 2018, doi: 10.1289/EHP2427.

[21] E. Valentini, M. Ferrara, F. Presaghi, L. D. Gennaro, y G. Curcio, «Systematic review and meta-analysis of psychomotor effects of mobile phone electromagnetic fields», *Occup. Environ. Med.*, vol. 67, n.º 10, pp. 708-716, oct. 2010, doi: 10.1136/oem.2009.047027.

[22] A. Verrender, S. P. Loughran, A. Dalecki, R. McKenzie, y R. J. Croft, «Pulse modulated radiofrequency exposure influences cognitive performance», *Int. J. Radiat. Biol.*, vol. 92, n.º 10, pp. 603-610, oct. 2016, doi: 10.1080/09553002.2016.1213454.

[23] A. Barth, I. Ponocny, T. Gnambs, y R. Winker, «No effects of short-term exposure to mobile phone electromagnetic fields on human cognitive performance: A meta-analysis», *Bioelectromagnetics*, vol. 33, n.º 2, pp. 159-165, feb. 2012, doi: 10.1002/bem.20697.

[24] Z. Vecsei, B. Knakker, P. Juhász, G. Thuróczy, A. Trunk, y I. Hernádi, «Short-term radiofrequency exposure from new generation mobile phones reduces EEG alpha power with no effects on cognitive performance», *Sci. Rep.*, vol. 8, n.º 1, dic. 2018, doi: 10.1038/s41598-018-36353-9.

[25] S. P. Loughran, R. J. McKenzie, M. L. Jackson, M. E. Howard, y R. J. Croft, «Individual differences in the effects of mobile phone exposure on human sleep: Rethinking the problem», *Bioelectromagnetics*, vol. 33, n.º 1, pp. 86-93, ene. 2012, doi: 10.1002/bem.20691.

[26] C. Lustenberger *et al.*, «Inter-individual and intra-individual variation of the effects of pulsed RF EMF exposure on the human sleep EEG: Reproducibility of

RF EMF Exposure Effects», *Bioelectromagnetics*, vol. 36, n.º 3, pp. 169-177, abr. 2015, doi: 10.1002/bem.21893.

[27] S. J. Regel *et al.*, «Pulsed radio-frequency electromagnetic fields: dose-dependent effects on sleep, the sleep EEG and cognitive performance», *J. Sleep Res.*, vol. 16, n.º 3, pp. 253-258, sep. 2007, doi: 10.1111/j.1365-2869.2007.00603.x.

[28] M. R. Schmid *et al.*, «Sleep EEG alterations: effects of different pulse-modulated radio frequency electromagnetic fields: Different pulse-modulated RF EMF and sleep EEG», *J. Sleep Res.*, vol. 21, n.º 1, pp. 50-58, feb. 2012, doi: 10.1111/j.1365-2869.2011.00918.x.

[29] E. M. Taveras, S. L. Rifas-Shiman, K. L. Bub, M. W. Gillman, y E. Oken, «Prospective Study of Insufficient Sleep and Neurobehavioral Functioning Among School-Age Children», *Acad. Pediatr.*, vol. 17, n.º 6, pp. 625-632, ago. 2017, doi: 10.1016/j.acap.2017.02.001.

[30] A. Sawangjit, C. N. Oyanedel, N. Niethard, C. Salazar, J. Born, y M. Inostroza, «The hippocampus is crucial for forming non-hippocampal long-term memory during sleep», *Nature*, vol. 564, n.º 7734, pp. 109-113, dic. 2018, doi: 10.1038/s41586-018-0716-8.

[31] I. Koyanagi, K. Akers, P. Vergara, S. Srinivasan, T. Sakurai, y M. Sakaguchi, «Memory consolidation during sleep and adult hippocampal neurogenesis», *Neural Regen. Res.*, vol. 14, n.º 1, p. 20, 2019, doi: 10.4103/1673-5374.243695.

[32] G. T. Voelbel, M. E. Bates, J. F. Buckman, G. Pandina, y R. L. Hendren, «Caudate Nucleus Volume and Cognitive Performance: Are They Related in Childhood Psychopathology?», *Biol. Psychiatry*, vol. 60, n.º 9, pp. 942-950, nov. 2006, doi: 10.1016/j.biopsych.2006.03.071.

[33] C. U. Greven *et al.*, «Developmentally stable whole-brain volume reductions and developmentally sensitive caudate and putamen volume alterations in those with attention-deficit/hyperactivity disorder and their unaffected siblings», *JAMA Psychiatry*, vol. 72, n.º 5, pp. 490-499, may 2015, doi: 10.1001/jamapsychiatry.2014.3162.

[34] M. Hoogman *et al.*, «Subcortical brain volume differences in participants with attention deficit hyperactivity disorder in children and adults: a cross-sectional mega-analysis», *Lancet Psychiatry*, vol. 4, n.º 4, pp. 310-319, abr. 2017, doi: 10.1016/S2215-0366(17)30049-4.

[35] H. H. Wilmer, L. E. Sherman, y J. M. Chein, «Smartphones and Cognition: A Review of Research Exploring the Links between Mobile Technology Habits and Cognitive Functioning», *Front. Psychol.*, vol. 8, p. 605, abr. 2017, doi: 10.3389/fpsyg.2017.00605.

[36] International Commission on Non-Ionizing Radiation Protection (ICNIRP), «Guidelines for Limiting Exposure to Electromagnetic Fields (100 kHz to 300 GHz)»:, *Health Phys.*, vol. 118, n.º 5, pp. 483-524, may 2020, doi: 10.1097/HP.0000000000001210.

[37] G. Goedhart *et al.*, «Using software-modified smartphones to validate self-reported mobile phone use in young people: A pilot study», *Bioelectromagnetics*, vol. 36, pp. 538-543, oct. 2015, doi: 10.1002/bem.21931.

[38] M. O. Mireku *et al.*, «Total recall in the SCAMP cohort: Validation of self-reported mobile phone use in the smartphone era», *Environ. Res.*, vol. 161, pp. 1-8, feb. 2018, doi: 10.1016/j.envres.2017.10.034.

[39] M. Redmayne, E. Smith, y M. J. Abramson, «Patterns in wireless phone estimation data from a cross-sectional survey: what are the implications for

epidemiology?», *BMJ Open*, vol. 2, n.º 5, p. e000887, 2012, doi: 10.1136/bmjopen-2012-000887.

[40] L. E. Birks *et al.*, «Spatial and temporal variability of personal environmental exposure to radio frequency electromagnetic fields in children in Europe», *Environ. Int.*, vol. 117, pp. 204-214, ago. 2018, doi: 10.1016/j.envint.2018.04.026.

[41] S. Sagar *et al.*, «Radiofrequency electromagnetic field exposure in everyday microenvironments in Europe: A systematic literature review», *J. Expo. Sci. Environ. Epidemiol.*, vol. 28, n.º 2, pp. 147-160, abr. 2018, doi: 10.1038/jes.2017.13.

[42] M. Velghe, W. Joseph, S. Debouvere, R. Aminzadeh, L. Martens, y A. Thielens, «Characterisation of spatial and temporal variability of RF-EMF exposure levels in urban environments in Flanders, Belgium», *Environ. Res.*, vol. 175, pp. 351-366, ago. 2019, doi: 10.1016/j.envres.2019.05.027.

[43] M. Eeftens *et al.*, «Personal exposure to radio-frequency electromagnetic fields in Europe: Is there a generation gap?», *Environ. Int.*, vol. 121, pp. 216-226, dic. 2018, doi: 10.1016/j.envint.2018.09.002.

[44] D. Urbinello *et al.*, «Radio-frequency electromagnetic field (RF-EMF) exposure levels in different European outdoor urban environments in comparison with regulatory limits», *Environ. Int.*, vol. 68, pp. 49-54, jul. 2014, doi: 10.1016/j.envint.2014.03.007.

[45] M. Guxens *et al.*, «Outdoor and indoor sources of residential radiofrequency electromagnetic fields, personal cell phone and cordless phone use, and cognitive function in 5–6 years old children», *Environ. Res.*, vol. 150, pp. 364-374, oct. 2016, doi: 10.1016/j.envres.2016.06.021.

[46] E. Chiaramello *et al.*, «Radio Frequency Electromagnetic Fields Exposure Assessment in Indoor Environments: A Review», *Int. J. Environ. Res. Public. Health*, vol. 16, n.º 6, p. 955, mar. 2019, doi: 10.3390/ijerph16060955.

[47] C. M. Liorni I., «Specific Absorption Rate Transfer Algorithms for Integrative Radio-Frequency Exposure Assessment in Epidemiological Studies», 2019.

[48] V. R. van Wel L., «Organ-specific integrative exposure assessment: Radio-frequency electromagnetic field exposure and contribution of sources in the general population», 2019.

[49] S. Wall, Z.-M. Wang, T. Kendig, D. Dobraca, y M. Lipsett, «Real-world cell phone radiofrequency electromagnetic field exposures», *Environ. Res.*, vol. 171, pp. 581-592, abr. 2019, doi: 10.1016/j.envres.2018.09.015.

[50] F. Zheng *et al.*, «Association between mobile phone use and inattention in 7102 Chinese adolescents: a population-based cross-sectional study», *BMC Public Health*, vol. 14, p. 1022, oct. 2014, doi: 10.1186/1471-2458-14-1022.

[51] A. Schoeni, K. Roser, y M. Röösli, «Memory performance, wireless communication and exposure to radiofrequency electromagnetic fields: A prospective cohort study in adolescents», *Environ. Int.*, vol. 85, pp. 343-351, dic. 2015, doi: 10.1016/j.envint.2015.09.025.

[52] A. Schoeni, K. Roser, y M. Röösli, «Symptoms and Cognitive Functions in Adolescents in Relation to Mobile Phone Use during Night», *PloS One*, vol. 10, n.º 7, p. e0133528, 2015, doi: 10.1371/journal.pone.0133528.

[53] K. Roser, A. Schoeni, y M. Röösli, «Mobile phone use, behavioural problems and concentration capacity in adolescents: A prospective study», *Int. J. Hyg. Environ. Health*, vol. 219, n.º 8, pp. 759-769, nov. 2016, doi: 10.1016/j.ijheh.2016.08.007.

[54] M. J. Abramson *et al.*, «Mobile telephone use is associated with changes in cognitive function in young adolescents», *Bioelectromagnetics*, vol. 30, n.º 8, pp. 678-686, dic. 2009, doi: 10.1002/bem.20534.

[55] C. R. Bhatt *et al.*, «Use of mobile and cordless phones and change in cognitive function: a prospective cohort analysis of Australian primary school children», *Environ. Health*, vol. 16, n.º 1, dic. 2017, doi: 10.1186/s12940-017-0250-4.

[56] S. Heinrich, S. Thomas, C. Heumann, R. von Kries, y K. Radon, «Association between exposure to radiofrequency electromagnetic fields assessed by dosimetry and acute symptoms in children and adolescents: a population based cross-sectional study», *Environ. Health*, vol. 9, n.º 1, dic. 2010, doi: 10.1186/1476-069X-9-75.

[57] S. Thomas *et al.*, «Use of mobile phones and changes in cognitive function in adolescents», *Occup. Environ. Med.*, vol. 67, n.º 12, pp. 861-866, dic. 2010, doi: 10.1136/oem.2009.054080.

[58] I. Calvente *et al.*, «Does exposure to environmental radiofrequency electromagnetic fields cause cognitive and behavioral effects in 10-year-old boys?: Neurobehavioral Effects of RF-EMFs in Children», *Bioelectromagnetics*, vol. 37, n.º 1, pp. 25-36, ene. 2016, doi: 10.1002/bem.21951.

[59] D. Gozal, Dayyat, Spruyt, y Molfese, «Sleep estimates in children: parental versus actigraphic assessments», *Nat. Sci. Sleep*, p. 115, oct. 2011, doi: 10.2147/NSS.S25676.

[60] K. B. Mikkelsen *et al.*, «Accurate whole-night sleep monitoring with dry-contact ear-EEG», *Sci. Rep.*, vol. 9, n.º 1, p. 16824, dic. 2019, doi: 10.1038/s41598-019-53115-3.

[61] I. Perez-Pozuelo *et al.*, «The future of sleep health: a data-driven revolution in sleep science and medicine», *Npj Digit. Med.*, vol. 3, n.º 1, p. 42, dic. 2020, doi: 10.1038/s41746-020-0244-4.

[62] J. L. Martin y A. D. Hakim, «Wrist Actigraphy», *Chest*, vol. 139, n.º 6, pp. 1514-1527, jun. 2011, doi: 10.1378/chest.10-1872.

[63] K. K. Murdock, M. Horissian, y C. Crichlow-Ball, «Emerging Adults' Text Message Use and Sleep Characteristics: A Multimethod, Naturalistic Study», *Behav. Sleep. Med.*, vol. 15, n.º 3, pp. 228-241, may 2017, doi: 10.1080/15402002.2015.1120203.

11 Appendices

PhD portfolio

PhD Student	Alba Cabré-Riera
PhD Period	January 2017 –September 2020
Supervisor	Dr. Mònica Guxens

Courses	**Year**
• International Programme of Advanced Epidemiology and Statistics - Causal Inference with Directed Graphs	2017
• International Programme of Advanced Epidemiology and Statistics - Causal Mediation and Interaction Analysis	2017
• International Programme of Advanced Epidemiology and Statistics - Methods to deal with attrition and missing data	2017
• PRBB Intervals - Explaining your research to ANYONE	2018
• PRBB Intervals - Mindfulness	2018
• PRBB Intervals - Write it clearly: fundamentals of good scientific writing	2018
• PRBB Intervals - Pensar en imágenes: cómo usar la facilitación gráfica para solucionar problemas, innovar y trabajar en equipo	2018
• European Educational Programme in Epidemiology – Infeccious Diseases Epidemiology	2019
• European Educational Programme in Epidemiology – Advanced Statistics	2019
• PRBB Intervals – Peer mentoring	2020
• PRBB Intervals – Emotional Intelligence	2020

Conferences – oral presentations	**Year**
• XXXV Reunión Científica Anual de la Sociedad Española de Epidemiología. Barcelona, Spain. *Telecommunication devices use, screen time, and sleep in adolescents*.	2017
• ISGlobal PhD Symposim, Barcelona, Spain. *Telecommunication devices use, screen time, and sleep in adolescents*.	2017
• ISEE Young, Munich, Germany. *Estimated whole-brain RF-EMF dose and cognitive function in preadolescents and adolescents.*	2018
• ISEE, Utrecht. *Estimated whole-brain RF-EMF dose and cognitive function in preadolescents and adolescents.*	2018
• XXXVII Reunión Científica Anual de la Sociedad Española de Epidemiología. Oviedo, Spain. *Estimated whole-brain and lobe-specific RF-EMF doses and brain volumes in preadolescents*.	2019
• XXXVII Reunión Científica Anual de la Sociedad Española de Epidemiología. Oviedo, Spain. *Estimated whole-brain RF-EMF dose and cognitive function in preadolescents and adolescents*.	2019

Conferences – poster presentations	**Year**
• World Sleep Congress. Prague, Czech Republic. *Telecommunication devices use, screen time, and sleep in adolescents.*	2017
• 14ª Jornadas Científicas INMA, Granada: *Telecommunication devices use, screen time, and sleep in adolescents*	2017
• ISEE, Utrecht. *Estimated whole-brain and lobe-specific RF-EMF doses and brain volumes in preadolescents.*	2019

Others	**Year**
• LifeCycle fellowship Training Programme	2017
• Awared with the 2nd best oral communication – ISGlobal PhD Symposium	2017
• Awarded with one of the best chalk talk – ISGlobal PhD Symposium	2019

Agraïments

Quan era petita somiava ser astronauta i amb uns anys més bombera. De més gran vaig obsessionar-me sense èxit a viure de l'esport, volia ser jugadora professional de bàsquet. Quan estava acabant secundària volia obrir un forn. Amb la insistència dels meus pares**, Toni** i **Nani,** vaig obrir portes a altres opcions. Totes aquestes pàgines (no les he comptat) són gràcies a la vostra motivació constant i suport incondicional. També a la meva germana **Roser**, sempre (omni)present, observadora i sobretot imprevisible, capaç de donar-te el millor consell. A en **Marc**, company de vida que m'ha donat estabilitat i suport, gestionant a la perfecció els meus alts i baixos (superarem el confinament!). A l'**Àvia Roser**, exemple de superació, alegria i capacitat cognitiva (jo de gran vull ser com tu!). A tota la meva família i a les seves estrelles que de ben segur ens observen des del cel.

El 14 de setembre de 2016 la **Mònica** em comunicava que li havien donat un nou projecte, fet que li permetia contractar una investigadora predoctoral. Amb moltes ganes i il.lusió vaig acceptar el repte. Gràcies per confiar en la meva feina i brindar-me aquesta oportunitat. La teva excel.lència, exigència, detallisme i perfeccionisme han fet que aquestes pàgines siguin millors.

A totes les companyes i companys d'ISGlobal. Heu fet que el camí sigui més planer. És un plaer haver fet la tesi al vostre costat. En especial gràcies a la **Sala C** i a la **colla de dinars**, grup que ha anat canviat durant aquests tres anys i mig. Primer, ple de professionals amb experiència. Ara, plena d'incorporacions recents amb energia nova. Totes dues facetes importants i imprescindibles per superar un procés que pot ser feixuc en alguns moments.

A totes les meves **amigues** i **amics** per regalar-me els millors moments de desconnexió.

Després de tot, no sé si vull ser bombera, astronauta, jugadora de bàsquet o portadora d'un forn però passi el que passi tot haurà sigut gràcies a vosaltres.

Juny de 2020

About the author

Alba Cabré-Riera was born on September 29th, 1991 in Mataró, Spain. She received her Bachelor in Biomedical Sciences at the University of Barcelona and her Master degree in Public Health at the Pompeu Fabra University, in Barcelona. During her masters, she worked as a quality consultant at CSV experts and Roche Diagnostics in Mataró and Sant Cugat del Vallés. She started as a PhD student in 2017 at the Barcelona Institute for Global Health (ISGlobal) under the supervision of Dr. Mònica Guxens. During her PhD, most of her studies were embedded within ELFES, which was an ANSES (French Agency for food, environmental, occupational health & Safety) - funded research project (2017-2020) with the goal of exploring potential associations between radiofrequency electromagnetic fields exposure and sleep in adolescents. She is currently working as epidemiologist at the Epidemiological Surveillance and Public Health Emergency Response Service of the Generalitat de Catalunya.