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Estimated all-day and evening whole-brain radiofrequency electromagnetic fields doses, and sleep in preadolescents

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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:** All-day whole-brain RF-EMF doses were not associated with self-reported sleep disturbances and objective sleep measures. Regarding evening doses, preadolescents with high evening whole-brain RF-EMF dose from phone calls had a shorter total sleep time compared to preadolescents with zero evening whole-brain RF-EMF dose from phone calls [-11.9 min (95%CI -21.2; -2.5)].

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 or reasons motivating the phone calls rather than the RF-EMF exposure itself or due to chance finding.

Abbreviations: Radiofrequency electromagnetic fields, RF-EMF.

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1. 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 (Owens, 2014). Several biological, social, and environmental factors play a role in determining sleep patterns and have been related to insufficient sleep duration (Crowley et al., 2018). The use of mobile communication devices such as mobile phones and tablets has been described as a potential factor impairing adolescents' sleep (Adams et al., 2013; Cain and Gradisar, 2010; Gradisar et al., 2013). 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 (Schoeni et al., 2017). However, studies that assessed the use of mobile communication devices for activities that lead to RF-EMF exposure using reported questionnaires found an association of higher use with daytime sleepiness and higher symptoms of sleep disturbances in 14–24 years olds (Jiang et al., 2015; Brunetti et al., 2016; Mak et al., 2014; Durusoy et al., 2017; Liu et al., 2019). Moreover, studies that assessed environmental RF-EMF exposure at home or school find associations with tiredness and exhaustibility (Schoeni et al., 2016) but did not find any association with sleep disturbances (Durusoy et al., 2017) 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 objective sleep measures with actigraphy (Fobian et al., 2016). The authors reported that higher evening use was related to more symptoms of sleep disturbances (Calamaro et al., 2009; Lemola et al., 2015) and lower objective sleep efficiency (Fobian et al., 2016) 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 i) the cross-sectional association between estimated overall and source-specific all-day whole-brain RF-EMF doses with sleep disturbances and objective sleep measures, and ii) the longitudinal association between 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.

2. Methods

2.1. Study design and population

This analysis used data from two population-based birth cohorts: the Dutch Generation R Study (Kooijman et al., 2016) and the Spanish

Infancia y Medio Ambiente (INMA) Project (Guxens et al., 2012) 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 9901 pregnant women for Generation R and 1415 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 1842 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 1599 of them, we collected information on all-day mobile communication devices use, and sleep disturbances with a general questionnaire completed by the mother or the preadolescent. We additionally collected information on objective sleep measures using a wrist accelerometer (GENEActiv; Activinsights, UK) for 7 consecutive days in 1080 preadolescents. We estimated whole-brain RF-EMF doses during a day, named "all-day whole-brain RF-EMF dose". In a sub-study sample of the INMA cohort ($n = 335$), during the 7 consecutive days that we assessed objective sleep measures using a wrist accelerometer we also collected information on the use of mobile communication devices after 7 p.m. and before falling asleep with sleep diaries reported by preadolescents and we estimated the daily evening whole-brain RF-EMF doses.

2.2. 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 (Liorni et al., 2020; van Wel et al., 2021). 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).

2.2.1. 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). 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 (Supplementary Table S2).

2.2.2. 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 and we consider them constant for the 7 consecutive days.

To estimate RF-EMF exposure from mobile phone base stations at home, a validated 3D geospatial radio wave propagation model NISMap was used (Bürgi et al., 2009; Beekhuizen et al., 2013, 2014; Huss et al., 2015). 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 (Beekhuizen et al., 2013, 2014; Martens et al., 2015). We assessed the emission of the three mobile phone communication systems in use at the time of the study

(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:

$$\text{Source-specific all-day whole brain RF-EMF dose}(mJ/kg/day)_{\text{source}} = \left(\frac{\text{SAR} \left(\frac{W}{kg} \right)_{\text{source}}}{\text{normalized output power } 1 W} \times \text{Output power}(W)_{\text{source}} \times \text{Duration} \left(\frac{\text{min}}{\text{day}} \right)_{\text{source}} \right) \quad (1)$$

$$\text{Source-specific evening whole-brain RF-EMF dose}(mJ/kg/day)_{\text{source,day}} = \left(\frac{\text{SAR} \left(\frac{W}{kg} \right)_{\text{source}}}{\text{normalized output power } 1 W} \times \text{Output power}(W)_{\text{source}} \times \text{Duration} \left(\frac{\text{min}}{\text{evening}} \right)_{\text{source,day}} \right) \quad (2)$$

(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 h between 2014 and 2015 (Birks et al., 2018). 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.

2.2.3. Integrated RF-EMF exposure model

We applied the integrated RF-EMF exposure model to estimate all-day and evening whole-brain RF-EMF doses (Liorni et al., 2020; van Wel et al., 2021). 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)), for 1 W of output power (i.e. normalized output power 1 W), 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

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 their use (Langer et al., 2017). The output power depends on the characteristics of the network. We assumed that all screen activities with mobile communication devices occurred using WiFi at 2.4 GHz (Joseph et al., 2013) and that WiFi data transfer rates were 54 Megabits per second, instead of using 3G. Moreover, the brain SAR depends on the relative distance to the device. SAR values were simulated in a previous study (Liorni et al., 2020) 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) and (2). Finally, we assigned output powers to each mobile communication device and activity based on expert opinion (Supplementary Tables S1 and S2). As we previously pointed out, evening brain RF-EMF dose from far-field was constant for the 7 days of measurements (Equation (2)).

Second, we summed all source-specific all-day whole-brain RF-EMF doses to get the overall all-day whole-brain RF-EMF dose and all source-specific evening whole-brain RF-EMF doses for each day of measurement to get the overall daily evening whole-brain RF-EMF dose for each day (Equations (3) and (4)):

$$\text{Overall all-day whole-brain RF-EMF dose}(mJ/kg/day) = \sum_{\text{source}} \left(\frac{\text{SAR} \left(\frac{W}{kg} \right)_{\text{source}}}{\text{normalized output power } 1 W} \times \text{Output power}(W)_{\text{source}} \times \text{Duration} \left(\frac{\text{min}}{\text{day}} \right)_{\text{source}} \right) \quad (3)$$

$$= \sum_{\text{source, day}} \left(\frac{\text{Overall daily evening whole-brain RF-EMF dose (mJ/kg/evening)day}}{\text{SAR} \left(\frac{\text{W}}{\text{kg}} \right)_{\text{source}} \times \text{Output power (W)}_{\text{source}} \times \text{Duration} \left(\frac{\text{min}}{\text{evening}} \right)_{\text{source, day}}} \right) \quad (4)$$

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. Overall and source-specific all-day whole-brain RF-EMF doses, overall evening whole-brain RF-EMF dose, and evening whole-brain RF-EMF dose from screen activities were analysed as continuous variables. Since only 15–20% of the pre-adolescents reported phone calls in the evening, we categorized the evening whole-brain RF-EMF dose from phone calls as null dose (0 mJ/kg/evening), low dose (preadolescents with evening phone calls dose of or below the median of the mobile phone calls users (0–2.3 mJ/kg/evening)), and high dose (preadolescents with evening phone calls dose above the median of the mobile phone calls users (>2.3 mJ/kg/evening)).

2.3. Sleep disturbances

Sleep disturbances were assessed using the Sleep Disturbance Scale for Children (SDSC) (Bruni et al., 1996) 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. A higher score indicates more sleep problems. 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.

2.4. 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 (Koopman-Verhoeff et al., 2019; Koopman-Verhoeff et al., 2019). We did not use the new version of the device, which allowed for streaming function. After all days of measurement of each child, the fieldworkers downloaded the data of each device. Measurements were processed using the R-package GGIR (van Hees et al., 2015). 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.

2.5. Potential confounding variables

The potential confounding variables were *a priori* defined with a Directed Acyclic Graph (DAG) (Hernán et al., 2002). Maternal characteristics included, maternal country of birth collected in pregnancy, and maternal educational level (low, medium, or high) collected at 5–12 years of the child. Preadolescent characteristics included sex, age, body mass index (kg/m²), minutes of television watching, and self-perceived general health (very bad, bad, good, very good, or excellent) assessed at 9–12 years. 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).

2.6. Statistical analysis

Preadolescents included in at least one of the analyses (n = 1842) 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 = 9474). 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.

We also used multiple imputation of missing values using chained equations to impute missing potential confounding variables among all participants with available data on the exposure and the outcome. We ran this procedure twice, for the overall sample and for the sub-study sample. For each study sample, we obtained 25 completed datasets and we analysed them using standard procedures for multiple imputation (i.e., Rubin’s rules) (Rubin, 1987; Sterne et al., 2009). 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 visually identified as outliers (<0.5%) to achieve linearity.

To address our first research objective (i.e. cross-sectional

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

	Study sample ^a (n = 1599)	Sub-study sample ^b (n = 335)
Maternal characteristics		
Maternal education		
High	56.8	42.8
Medium	35.8	35.9
Low	7.4	21.2
Maternal country of birth (country of the cohort vs. others)	88.1	96.8
Preadolescents' characteristics		
Sex (female vs. male)	52.0	52.2
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 all-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 across 7 days.

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

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 (Espelt et al., 2016). 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. longitudinal 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 multinomial logistic mixed effects models using repeated

Table 2
Estimated overall and source-specific all-day and evening whole-brain RF-EMF doses in preadolescents.

	All-day dose (mJ/kg/day)		Evening dose (mJ/kg/evening) ^a		% ^b
	(n = 1599)		(n = 335)		
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
Overall dose	166 (700)	60 (20; 118)	283 (1046)	68 (11; 185)	
Source-specific doses					% ^b
Phone calls ^c	129 (692)	21 (2; 72)	78 (1046)	2 (0; 71)	77
Screen activities ^d	2 (2)	2 (1; 3)	1 (3 (11))	0 (0; 1)	1
Far-field sources ^e	35 (82)	11 (7; 25)	21 (63 (118))	13 (5; 66)	22

IQR, interquartile range; kg, kilograms; mJ, millijoules; RF-EMF, Radio-frequency Electromagnetic Fields; SD, standard deviation.

^a Average of the evening brain RF-EMF doses across 7 days.

^b Contribution of each source-specific dose to the overall dose, calculated as the mean source-specific dose divided by the mean overall dose.

^c Phone calls refer to mobile and DECT phone calls.

^d 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.

^e 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) for the all-day brain RF-EMF dose estimation and only from home for the evening brain RF-EMF dose estimation.

Table 3
Distribution of sleep disturbances and objective sleep measures in preadolescents.

	Study sample (n = 1599)	Sub-study sample (n = 335)
Sleep disturbances		
Problems with initiating and maintaining sleep^a	4.3 (3.4)	–
Excessive somnolence^b	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 onset latency (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) for continuous variables.

^a Higher scores indicate more sleep disturbances. Range = 0–20.

^b Higher scores indicate more sleep disturbances. Range = 0–28.

overall and source-specific evening whole-brain RF-EMF doses in relation to repeated measures of sleep quality and restfulness across 7 days. Since far-field exposure was considered as constant for the 7 days of measurement, evening whole-brain RF-EMF dose from far-field sources across the 7 days 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, self-perceived general health, and preadolescents' habits after 7 p.m. including minutes of console/computer gaming, minutes of television watching, caffeinated drinks intake, and sleeping alone in preadolescents' bedroom.

Analyses were corrected for multiple testing. We applied false discovery rating, first, to a total of 12 tests for sleep disturbances outcomes and, second, to a total of 32 tests for objective sleep measures. We obtained critical p-values for each association. All analyses were performed using Stata version 15 (StataCorp, College Station, TX) and R version 3.6.1.

3. Results

3.1. Descriptive analysis

About 52% of preadolescents of our population were female, 56% of preadolescents in the full 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 min/day using mobile communication devices for screen activities and 2.5 min/day making phone calls (Supplementary Table S3). The median of the overall estimated all-day whole-brain RF-EMF dose was 60 (interquartile range (IQR) 20; 118) mJ/kg/day and the main contributor to the all-day whole-brain RF-EMF dose were phone calls (78%) (Table 2). In the sub-study sample, the median of the all-day phone calls dose was 6 (IQR 0; 55) mJ/kg/day and the median (IQR) of the evening phone calls dose was 2 (IQR 0; 71) mJ/kg/evening (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 mJ/kg/day in Generation R, 375 mJ/kg/day in INMA-Sabadell, and 104 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 h, sleep efficiency was 84%, and wake after sleep onset was 71.4 min in the study sample (Table 3). 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).

3.2. Cross-sectional association between 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 (Tables 4 and 5). However, higher all-day whole-brain RF-EMF dose from screen activities was associated with higher symptoms of excessive somnolence [2.2 symptom score (95%CI 0.1; 4.3) 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 [0.3 min (95%CI 0.1; 0.5) 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 associated 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 [0.3 min (95%CI 0.0; 0.4) per increase in 100 mJ/kg/day]. None of these associations survive correction for multiple testing.

3.3. Longitudinal association between 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 [-11.9 min (95%CI -21.2 ; -2.5) and] 0.3 min (95%CI 0.0; 0.7), respectively] (Table 6). However, the latter

Table 4

Cross-sectional association between estimated overall and source-specific all-day whole-brain RF-EMF doses ($\Delta 100$ mJ/kg/day) and sleep disturbances in preadolescents ($n = 1599$).

	Problems with initiating and maintaining sleep^d	Excessive somnolence^d	Arousal problems (yes vs. no)
	B (95% CI)	B (95% CI)	PR (95% CI)
Overall dose	0.0 (−0.0; 0.0)	0.0 (−0.0; 0.0)	1.0 (0.9; 1.0)
Source-specific doses			
Phone calls ^a	0.0 (−0.0; 0.0)	0.0 (−0.0; 0.0)	0.9 (0.9; 1.0)
Screen activities ^b	1.6 (−0.3; 3.6)	2.2 (0.1; 4.3)	2.2 (0.1; 68.8)
Far-field sources ^c	0.0 (−0.0; 0.1)	−0.0 (−0.1; 0.1)	1.0 (0.9; 1.1)

Linear or Poisson with robust variance regression models adjusted for cohort, maternal education, and country of birth, and preadolescent sex, age at sleep assessment, body mass index at sleep assessment, minutes of television watching, and self-perceived general health.

In bold, statistical significant associations (p -value < 0.05).

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.

Table 5

Cross-sectional association between estimated overall and source-specific all-day whole-brain RF-EMF doses ($\Delta 100$ mJ/kg/day) and objective sleep measures in preadolescents ($n = 1080$).

	<u>Total sleep time (min)</u>	<u>Sleep efficiency (%)</u>	<u>Wake After Sleep Onset (min)</u>	<u>Sleep onset latency^c</u>
	B (95% CI)	B (95% CI)	B (95% CI)	B (95% CI)
Overall dose	0.0 (-0.4; 0.5)	-0.0 (-0.1; 0.0)	-0.0 (-0.3; 0.2)	0.0 (-0.0; 0.0)
Source-specific doses				
Phone calls ^a	0.0 (-0.4; 0.4)	-0.0 (-0.1; 0.0)	-0.0 (-0.3; 0.2)	0.0 (-0.0; 0.0)
Screen activities ^b	-30.7 (-162.3; 100.9)	10.3 (-3.5; 24.2)	-69.9 (-149.7; 10.0)	-0.5 (-8.1; 7.1)
Far-field sources ^c	0.1 (-3.6; 3.7)	0.2 (-0.2; 0.5)	-0.3 (-2.5; 1.8)	0.3 (0.1; 0.5)

^d Square root transformed.

Linear regression models adjusted for cohort, maternal education, and country of birth, and preadolescent sex, age at sleep assessment, body mass index at sleep assessment, minutes of television watching, and self-perceived general health.

In bold, statistical significant associations (p-value < 0.05).

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).

association did not survive correction for multiple testing. Overall evening whole-brain RF-EMF dose, and evening dose from screen activities were not associated with objective sleep measures (Table 6) and with sleep quality and restfulness (data not shown).

4. Discussion

4.1. 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 in preadolescents. We found that the all-day whole-brain RF-EMF doses were not associated with sleep disturbances and objective sleep measures. Regarding evening doses, preadolescents with a high evening whole-brain RF-EMF dose from phone calls had shorter total sleep time.

4.2. 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 (Birks et al., 2018, 2021). 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 (Durusoy et al., 2017; Huss et al., 2015; Küçer and Pamukçu, 2014). However, we did not find any association of all-day RF-EMF dose from phone calls with subjective/reported 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 (Tettamanti et al., 2020). 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 (Czeisler and Shanahan, 2016; He et al., 2020). 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 (Lemola et al., 2015; Fobian et al., 2016; Calamaro et al., 2009).

Table 6

Longitudinal association between estimated overall and source-specific evening whole-brain RF-EMF doses, and objective sleep measures across seven days ($n = 335$).

	<u>Total sleep time (min)</u>	<u>Sleep efficiency (%)</u>	<u>Wake After Sleep Onset (min)</u>	<u>Sleep onset latency^c</u>
	B (95% CI)	B (95% CI)	B (95% CI)	B (95% CI)
Overall dose ($\Delta 100$ mJ/kg/evening)	-0.1 (-0.2; 0.1)	0.0 (-0.0; 0.0)	-0.2 (-0.4; 0.1)	-0.0 (0.0; 0.0)
Source-specific doses				
Phone calls^a				
Null (0 mJ/kg/evening)	Ref.	Ref.	Ref.	Ref.
Low (0–2.3 mJ/kg/evening)	-6.2 (-14.8; 2.4)	0.2 (-0.8; 1.1)	0.4 (-6.5; 7.3)	0.0 (-0.3; 0.3)
High (>2.3 mJ/kg/evening)	-11.9 (-21.2; -2.5)*	-0.3 (-1.3; 0.7)	-0.3 (-7.4; 6.8)	0.3 (0.0; 0.7)
Screen activities^b ($\Delta 100$ mJ/kg/evening)	-11.8 (-32.5; 9.0)	-0.5 (-1.8; 0.8)	8.4 (-2.1; 18.8)	0.1 (-0.4; 0.6)

Linear regression mixed models with individuals as random intercept adjusted for cohort, maternal education, and country of birth, and preadolescent sex, age, body mass index, and 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).

In bold, statistical significant associations (p-value < 0.05).

*, association that remained statistically significant after correction for multiple testing (p-value < corrected critical p-value (0.002)).

^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.

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. Experimental studies in humans showed encephalogram (EEG) alterations induced by RF-EMF emitted by mobile phone for all common frequency bands of the EEG (Danker-Hopfe et al., 2019; Wallace and Selmaoui, 2019) and impairment of sleep-depending learning processes in those individuals exposed to RF-EMF during sleep (Lustenberger et al., 2013). 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. mental arousal or sleep displacement).

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

All-day and evening whole-brain RF-EMF dose from screen activities were not associated with subjective or objective sleep measures. 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 (Brunetti et al., 2016; Liu et al., 2019; Mak et al., 2014) and higher symptoms of sleep disturbances (Jiang et al., 2015; Kenney and Gortmaker, 2017; Liu et al., 2019; Söderqvist et al., 2008) 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 (Akçay and Akçay, 2018; Amra et al., 2017; Bartel et al., 2016; Bruni et al., 2015; Dube et al., 2017; Fobian et al., 2016; Johansson et al., 2016; Lemola et al., 2015; Murugesan et al., 2018; Nathanson and Beyens, 2018; Olorunmoteni et al., 2018). In our study we did not include the assessment of other factors related to the use of mobile communication devices beyond RF-EMF exposure, including light exposure or excitement based on the content watched or activity performed, that might affect sleep. We exclusively included in our estimations the time of use of mobile phone other than calling, tablet, and laptop while wirelessly connected to the internet, i.e. the times that the device was emitting RF-EMF exposure. Thus preadolescents could be using the devices, and being exposed to other factors, such as light exposure, for longer periods of time, which might explain the results found in other studies. A more comprehensive study needs to be designed to disentangle between all the potential factors related to the use of mobile communication devices that might affect sleep, including RF-EMF exposure. Also, of note, 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. 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.

4.4. 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 (Birks et al., 2018, 2021). In our study, RF-EMF dose from far-field sources was not related to subjective or objective sleep measures. 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 (Durusoy et al., 2017), or daytime RF-EMF levels at preadolescents' bedroom (Berg-Beckhoff et al., 2009) 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 sleep arousal problems in children at 5–7 years old (Huss et al., 2015). RF-EMF exposure has a large spatial variability (Birks et al., 2018). 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.

4.5. 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 1600 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 and sleep diary, respectively). Mothers reported all-day use retrospectively which might have introduced recall bias, thus underestimating adolescents' use during a day. Moreover, we used a novel and integrative tool to estimate all-day and evening whole-brain RF-EMF doses. This tool allows the inclusion of the exposure received from all RF-EMF emitting sources and devices, those used by the preadolescents themselves (e.g. mobile phone, tablet) and those in the different microenvironments (e.g. school, public transportation, home) where the preadolescents spent their time (e.g. mobile phone antennas, WiFi). Uncertainties of the numerical simulations were used to develop the IEM (Liorni et al., 2020), and the sensitivity of the model to the different input parameters was quantified (Van Wel et al., 2020). However, several assumptions needed to be considered which could lead to non-differential misclassification of the exposure leading to a potential underestimation of the effect estimates. For example, one of these assumptions was related to the exposure to environmental RF-EMF sources in the different microenvironments. This exposure was measured in a subsample of preadolescents (Birks et al., 2018) but we assumed that exposure was the same for the rest of preadolescents of the same cohort for which measurements were not done. Also, at the moment of the study, there was no widely available data on output power in 4G networks. However, average output power of 4G is expected to be similar to 3G (Joshi et al., 2017), so our estimations of 3G exposure might have also represented 4G exposure. Thus we assigned output powers to each mobile communication device and activity based on expert opinion. Objective measures such as applications installed in preadolescents' mobile communication devices would improve the accuracy of RF-EMF dose estimations. We collected information on whether preadolescents slept with the mobile phone, tablet, or laptop switch on in the bedroom, whether they woke up if they received a message in the night, and whether they read or answer it. However, less than 5% of our population reported waking up if they received a message during the night. Thus unfortunately we could not estimate RF-EMF doses during the night. Although we adjusted for several potential confounding variables, we cannot completely discard residual confounding, in particular from variables related to uptake of mobile phone use in this age group. Thus our results might be due to chance finding and the results should be interpreted as hypothesis generating.

5. 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 adolescents' sleep.

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Author contribution

Alba Cabré-Riera: conceptualization, formal analysis, investigation, writing-original draft, visualization; **Luuk van Wel:** methodology, software, writing - Review & Editing; **Iliaria Liorni:** methodology, software, writing - Review & Editing; **M. Elisabeth Koopman-Verhoeff:** data curation, writing - Review & Editing; **Liher Imaz:** methodology, writing - Review & Editing; **Jesús Ibarluzea:** funding acquisition, writing - Review & Editing; **Anke Huss:** funding acquisition, writing - Review & Editing; **Joe Wiart:** methodology, writing - Review & Editing; **Roel Vermeulen:** methodology, funding acquisition, writing - Review & Editing; **Wout Joseph:** methodology, funding acquisition, writing - Review & Editing; **Myles Capstick:** methodology, funding acquisition, writing - Review & Editing; **Martine Vrijheid:** funding acquisition, writing - Review & Editing; **Elisabeth Cardis:** funding acquisition,

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envres.2021.112291>.

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