Health symptoms and cognitive function in Swiss adolescents in relation to mobile phone use and radiofrequency electromagnetic field exposure

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Science cannot solve the ultimate mystery of nature. And that is because, in the last analysis, we ourselves are part of nature and therefore part of the mystery that we are trying to solve.

Max Planck (1858-1947)

Table of Contents

Acknowledgements

This thesis is part of the HERMES study (Health Effects Related to Mobile phonE use in adolescentS). The HERMES study was funded by the Swiss National Science Foundation (project number 138190). This thesis was carried out at the Swiss Tropical and Public Health Institute in Basel, Switzerland.

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Summary

Introduction and Background

Within the last 15 years the use of mobile phones has increased remarkably in adults as well as in adolescents. This increase has been accompanied by a growing public concern that radio frequency electromagnetic fields (RF-EMF), which are emitted from such devices, might be associated with adverse health effects or cognitive function in adolescents. In particular, young people have become the focus of increased attention since the lifetime exposure will be longer than that of present-day adults. Potential effects of RF-EMF on health and cognitive function in adolescents are of high public interest since the use of mobile phones is an essential part of the daily life of adolescents.
To date, epidemiological research in this field is scarce and the Research Agenda of the World Health Organization (WHO) considers additional research in this age group as a high research priority. There have been several studies so far that investigated whether health, cognitive function and behavior in adolescents are affected by RF-EMF exposure from mobile phones. The majority of these studies however had some methodological limitations such as a cross-sectional study design and self-reported mobile phone use data. Additionally, there is not only RF-EMF emitted by mobile phones, but there are a lot of other RF-EMF sources in our everyday life which have to be considered when dealing with RF-EMF exposure. No study so far has ever tried to differentiate between effects due to RF-EMF radiation and to non-radiation related effects, which are mediated by regularly using the mobile phone and other wireless devices.

Objectives

The aim of the work for this thesis was to evaluate how adolescents' perceived health and how cognitive function are affected by various aspects of mobile phone use and other wireless devices including radiofrequency electromagnetic field exposure.

Methods

In the framework of the HERMES (**H**ealth **E**ffects **R**elated to **M**obile phon**E** use in adolescent**S**) study, 439 students aged 12 to 17 years and attending 7th, 8th or 9th grade in schools in Central Switzerland were recruited to participate in the baseline investigation, which was conducted from June 2012 until February 2013. During a school visit the adolescents filled in a questionnaire with questions, amongst others, on health symptoms, use of mobile phones and other wireless devices, socio-demographics, and other relevant covariables and two cognitive tests using a standardized, computerized cognitive testing system were performed. Additionally a questionnaire for the parents was distributed. The questionnaire for the parents included questions, amongst others, on the behavior of their children, on socio-economic factors, on wireless technology at home and on child development. This procedure was repeated one year later with the same study participants (participation rate: 96.8%).

From 234 study participants objectively recorded mobile phone use data from the three Swiss mobile phone operators for the time period up to six months prior to the baseline investigation until follow-up was received.

A subgroup of 95 study participants took part in personal measurements. The adolescents carried a portable measurement device, a so-called exposimeter, and kept a diary on a timeactivity diary application installed on a mobile phone in flight-mode for about three consecutive days. Far-field exposure from fixed site transmitters (radio and TV broadcast transmitters and mobile phone base stations) at home and in school was modelled using a geospatial propagation model. RF-EMF dose measures were computed for the brain and the whole body by combining questionnaire data with objectively recorded mobile phone use data, personal measurements and propagation model outputs.

Results

We could demonstrate that mobile phone use during night is common among adolescents. In a cross-sectional design, poor perceived health was shown when adolescents were being awakened by an incoming text message or call during night. Similar results were found when considering objectively recorded mobile phone use during night. The cognitive tests on concentration capacity and memory performance were not related to mobile phone use during night.

An integrative exposure surrogate combining exposure from near-field (use of wireless devices) and far-field (environmental sources) RF-EMF sources to one single whole body and brain exposure measure was developed. Most relevant contributors for the brain dose, based on self-reported mobile phone call duration, were calls on the mobile phone (on average 93.3%) followed by calls with the cordless phones (4.2%). For the whole body dose, calls on the mobile phone (on average 66.9%), the use of computer/laptop/tablet connected to WLAN (12.0%) and data traffic on mobile phones over WLAN (8.1%) counted for the most part. Less important for the dose measures were exposure from radio and TV broadcast transmitters (brain dose: 0.1%; whole body dose: 0.3%) and mobile phone base stations (brain dose: 0.6%; whole body dose: 2.0%).

By applying these RF-EMF dose measures to the prospective HERMES cohort study, we investigated whether adolescents' perceived health and cognitive function such as memory performance are affected by the use of mobile phones or other wireless devices per se or by RF-EMF exposure. We observed that rather the use of mobile phones or other wireless devices than RF-EMF exposure affect adolescents' health. In contrast we found that memory performance was more strongly associated with RF-EMF exposure than with the use of mobile phones or other wireless devices per se. This may indeed indicate that RF-EMF exposure affect memory performance in adolescents.

Using the geospatial propagation model we observed highest total exposure from fixed site transmitter to be 376 µW/m^2 (=0.38 V/m), which easily complies with current ICNIRP guidelines, as well as with the precautionary reference levels for Switzerland, which are 10 times lower than the ICNIP's. We observed an association between RF-EMF exposure from fixed site transmitters and tiredness in Swiss adolescents whereas other health symptoms were not related. The observed associations however have to be interpreted with caution and might represent a chance finding.

Conclusions and Outlook

In the HERMES study we we used the most comprehensive exposure assessment methods considering most relevant RF-EMF sources and exposure relevant behaviors. The integrative RF-EMF dose measures for the brain and the whole body are worldwide unique and have not been applied ever before.

We were able to demonstrate that rather the use of mobile phones or other wireless devices than RF-EMF exposure affect the health of adolescents. In contrast we found that memory performance was more strongly associated with RF-EMF exposure than with the use of mobile phones or other wireless devices per se.

Based on the results we conclude that precautionary measures to reduce the mobile phone use and thus personal exposure to RF-EMF should be applied.

Due to the massive growth in connecting devices, exposure assessment in the near future will become even more complex but also inevitably necessary in order to establish evidence-based management measures and effective health risk communication programs.

List of abbreviations and definitions

Abbreviations

95% CI	95% confidence interval
DECT	Digital enhanced cordless telecommunication
DNA	Deoxyribonucleic acid
EMF	Electromagnetic field
GSM	Global System for Mobile communications (2nd generation)
HERMES	Health Effects Related to Mobile phonE use in adolescentS
HIT-6	Headache Impact Test
Hz	Hertz (1/s)
IARC	International Agency for Research on Cancer
ICNIRP	International Commission on Non-Ionizing Radiation Protection
IQR	Interquartile range
LTE	Long-Term Evolution (4th generation network)
OR	Odds ratio
RF-EMF	Radiofrequency electromagnetic field
SAR	Specific absorption rate (W/kg)
TV	Television
UMTS	Universal Mobile Telecommunications System (3rd generation)
WHO	World Health Organization
WLAN	Wireless Local Area Network (wireless internet)

Definitions

Downlink	Communication from mobile phone base station to mobile phone handset.
Exposimeter	Portable exposure meter for measuring RF-EMF.
Handover	During an active call the mobile phone informs the network about changes in its location area.
Location area update	The mobile phone in stand-by mode informs the network about changes in its location area.
Uplink	Communication from mobile phone handset to mobile phone base station.

1 Introduction and background

In the modern society, health hazards by a variety of sources are of growing concern. The range of potential dangerous sources is broad: food, air pollution, water contaminations, pesticides, elemental toxic waste, radiation, environmental noise and a lot more. All are investigated for implications of harm on animal's and human's health. In the recent fast expanding field of using low radiating instruments, which are used day and night, a growing interest for research preferential comes from communication tools, in special for mobile phones and other wireless devices. The focus is set to look for short and long term damage to a variety of body functions. In the health and medical community possible interferences are discussed for harmful damages i.e. to the blood building system and especially to brain functions.

1.1 The electromagnetic spectrum

The electromagnetic spectrum (Figure 1) is the range of all possible frequencies of electromagnetic radiation and can be divided into ionizing and non-ionizing radiation. The division into these two categories is made according to its frequency. The frequency is measured in Hertz (Hz), whereas 1 Hz corresponds to 1 oscillation per second. Electromagnetic waves with a lower frequency are less energetic than electromagnetic waves with a higher frequency.

Ionizing radiation such as x-rays or gamma radiation have higher frequencies and contain enough energy to liberate electrons from molecules or atoms thereby modifying biological components, e.g. induction of DNA (Deoxyribonucleic acid) damage (Ward 1988).

Non-ionizing radiation, ubiquitously distributed throughout our everyday environment, originates from various sources such as small electrical devices (mobile phones) to large power lines and base stations. Non-ionizing radiation can be subdivided into four main categories based on their frequency: static fields (0 Hz), extremely low-frequency electromagnetic fields (0 to ~300 Hz), intermediate frequency electromagnetic fields (300 Hz to ~100 kHz), and radiofrequency electromagnetic fields (up to 300 GHz). Unlike ionizing radiation, non-ionizing radiation does not contain enough energy to directly modify molecules or atoms but above a certain intensity it can induce currents and electrical fields inside the body thereby stimulating muscle or nerve cells and the induction of retinal phosphenes (low frequency range) (International Commission on Non-Ionizing Radiation 2010). The absorption of high-frequency electromagnetic fields with mobile phone radiation belonging to it, can lead to heating effects (International Commission on Non-Ionizing Radiation 1998).

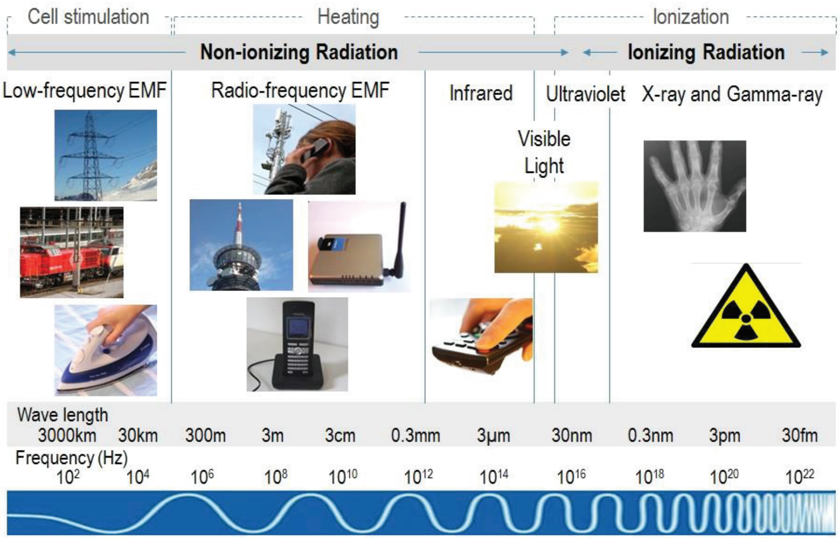

Figure 1: The electromagnetic spectrum

1.2 Characteristics and sources of radiofrequency electromagnetic fields

Exposure to radiofrequency electromagnetic fields (RF-EMF) can occur from personal devices (e.g. mobile or cordless phones) or from environmental sources such as mobile phone base stations and broadcast transmitters (radio and TV). Radiofrequency electromagnetic fields are used to transmit signals over long distances.

The strength of an electromagnetic field is usually measured in Volt per meter (V/m), although values in Volt per meter are not additive and root-mean-square calculations have to be done to sum up values. Another measure, which is additive, is the power flux density in Watt per square meter (W/m^2). To convert one unit into the other, the following formula can be applied, whereas the electrical field strength E is in [V/m] and the power flux density S in [W/m^2].

$$S = \frac{E^2}{Z_0}$$

$$E = \sqrt{S * Z_0}$$

Z_0 is the impedance of free space with a value of approximately 377 Ω. It describes the property of wave propagation through the air and stays constant (International Commission on Non-Ionizing Radiation 1998).

The thermal effect of radiofrequency electromagnetic fields is a well-known principle and beyond dispute. The reference quantity is the specific absorption rate (SAR). The SAR is measured in Watts per kilogram (W/kg) and depends on the field strength, on the physiological characteristics of the absorbing tissue and on the frequency of the source. It defines the power absorbed per kilogram of body mass. In general, the lower the frequency of RF-EMF, the farther it penetrates into biological tissue. Reference values are set so that the radiation never increases the human body temperature by more than 1˚C in order to prevent interferences with numerous body functions. Exposure to RF-EMF corresponding to a SAR value of 4 W/kg results in an increase in temperature of 1˚C. The International Commission of non-Ionizing Radiation (ICNIRP) therefore issued an average whole body SAR limit of 0.08 W/kg and a SAR limit of 4 W/kg and 2 W/kg for localized exposures in the head/ trunk and in limbs, respectively (International Commission on Non-Ionizing Radiation 1998).

In our everyday environment we are exposed to numerous sources that emit RF-EMF. The exposure sources can be divided into near-field and far-field sources. The former include mobile and cordless phones, also called close to body sources, whereas the latter include mobile phone base stations and broadcast transmitters, also called environmental far-field sources. Near-field sources are in general responsible for higher exposure levels than far-field sources, however, when exposed to far-field sources, the whole body is continuously exposed and the duration can be longer (Frei et al. 2009b; Regel et al. 2006). Depending on the distance to the body, exposure from mobile phones from nearby persons or from wireless internet (WLAN) sources can be regarded as far-field exposure.
In order to prevent the public from RF-EMF exposure, the International Commission on Non-Ionizing Radiation Protection (ICNIRP) published guidelines for reference levels in 1998 (International Commission on Non-Ionizing Radiation 1998). Reference levels are frequency-dependent and range from 42 V/m to 61 V/m. Switzerland additionally introduced precautionary limits for places with sensitive use and places of residence which range from 4 V/m to 6 V/m, about 10 times below the ICNIRP reference values (FOEN 2012).

1.2.1 Characteristics of mobile phone radiation

Mobile phones play an integral part in our life and have become more than a tool for communication. According to the International Telecommunication Union (ITU) the use of mobile phones has increased remarkably worldwide. It is estimated that in the year 2014 there were approximately 6.9 billion mobile phone subscriptions worldwide. In Switzerland 11.4 million mobile phone subscriptions were registered, which results in 140.5 mobile phone subscriptions in 100 habitants. At present there are at least two different mobile phone networks, which are mostly used for mobile phone communication, working in Switzerland: The 2nd generation Global System for Mobile Communications (GSM) network and the 3rd generation Universal Mobile Telecommunications System (UMTS) network. There is currently a further network generation being established, the so-called Long-Term Evolution (LTE). This network is being established due to the rapid increase of mobile data traffic.

Mobile phones on the GSM network emit radiation in the frequency range of 880-915 MHZ and in the range of 1710-1785 MHZ, whereas mobile phones on the UMTS network emit radiation in the frequency range of 1920-1980 MHZ. The LTE is using the frequency bands of 800 MHZ and 2.6 GHZ (OFCOM 2011). The radiation emitted by mobile phones depends on the network technology being used. The output power of mobile phones and thus exposure to its radiofrequency electromagnetic fields working on the GSM network is distinct from the mobile phone working on the UMTS network due to a different adaptive power control (Gati et al. 2009; Vrijheid et al. 2009b). Mobile phones working on the GSM network start the call always with the maximum output power. Unless a good connection to the base station is provided, the output power is decreased during a call, just sufficient for good-quality reception. However, while walking or driving around during a phone call, the mobile phone has to reconnect with different base stations (so called handovers) and thus the output power goes up to the maximum at each handover (Erdreich et al. 2007; Gati et al. 2009; Vrijheid et al. 2009b).

Mobile phones working on the UMTS network instead, start every call with the minimum output power. The output power is increased as much as needed for maintaining a good-quality reception. The mobile phones on the UMTS network almost never reach their maximum output power. Therefore, the radiation exposure of mobile phones working on the UMTS network is several times reduced compared to mobile phones working on the GSM network (Gati et al. 2009).

Due to location updates, mobile phones can also emit radiation in stand-by mode (Lin et al. 2002; Urbinello and Röösli 2013). A location update happens when a mobile phone is in stand-by mode and changing from one radio cell (area covered by a mobile phone base station) to another radio cell. The mobile phone is in constant communication with mobile phone base stations and during such a location update, the mobile phone informs the network whenever it changes from one radio cell to another, which leads to the emission of radiation.

Depending on the direction of communication between mobile phone and mobile phone base station, uplink and downlink exposure can be distinguished. Uplink exposure represents the communication from a mobile phone to a mobile phone base station whereas downlink exposure represents the communication from the mobile phone base station to the mobile phone.

1.3 Potential implications on health and cognitive function in children and adolescents

The rapid increase in mobile phone use in the last few years has been accompanied by a growing public concern that radiofrequency electromagnetic fields, emitted by such devices, might be associated with adverse health effects, reduced cognitive function or behavioral problems among children and adolescents. It has even been proposed that children and adolescents may be more vulnerable to RF-EMF due to their still developing nervous system and since lifetime exposure will be longer compared to today's adults (Kheifets et al. 2005; Wiart et al. 2005; Wiart et al. 2011).

To respond to these concerns, the World Health Organization (WHO) mounted an important research effort over the past years. The WHO established the International Electromagnetic Fields Project in 1996 to assess possible adverse health effects due to electromagnetic fields. A formal risk assessment of all studied health outcomes from radiofrequency electromagnetic fields by 2016 is planned. Additionally, a WHO specialized agency, the International Agency for Research on Cancer (IARC), classified RF-EMF as possibly carcinogenic to humans in May 2011 (Baan et al. 2011).

Various studies have been conducted in the last few years in order to address the research question whether the mobile phone use and thus exposure to RF-EMF is associated with adverse health effects or reduced cognitive function among children and adolescents.

Health:

Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity (WHO 1948). A basic prerequisite for general well-being is good sleep quality. In several epidemiological studies effects of mobile phone use on sleep have been investigated. In a 4-year longitudinal study of mobile phone use, increased fatigue was found (preliminary results) in children aged 5 to 12 years (Grigoriev 2011). A German study showed that owning a mobile phone was associated with going to bed after 9 pm among children aged 9 and 10 years and therefore not obtaining of at least 10 hours sleep as recommended by pediatricians (Heins et al. 2007). In a Belgian study in 2003, 26% of 13-year-old and 43% of 16-year-old children reported being disturbed in their sleep by incoming text messages, leading to an unhealthy sleep pattern (Van den Bulck 2003). In a one year follow-up in the same study collective, increased levels of tiredness were found for study participants who used the mobile phone more frequently during night (Van den Bulck 2007). Not only studies on the effects of mobile phone use on sleep but also on other health symptoms such as headache, tinnitus and depression among children and adolescents are available. In a large Swedish cross-sectional study of 2000 adolescents, self-reported use of mobile phones was related to self-reported health complaints such as tiredness, stress, headache, anxiety, concentration difficulties and sleep disturbances (Soderqvist et al. 2008). In a representative Finnish sample of 7300 adolescents the health status was better for non-mobile phone users than for mobile phone users (Koivusilta et al. 2007). Mobile phone use was found to be associated with headache (Chiu et al. 2014; Redmayne et al. 2013), feeling of discomfort (Byun et al. 2013), fatigue (Byun et al. 2013; Ikeda and Nakamura 2014) and dizziness (Byun et al. 2013). In a cohort study from Thomée et al. (2011), high frequency of self-reported mobile phone use at baseline was a risk factor for mental health outcomes after a 1-year follow-up.

Cognitive function:

Cognitive function can be defined as cerebral activities that lead to knowledge, including all means and mechanisms of acquiring information. Cognitive function encompasses reasoning, memory, attention, and language and lead directly to the attainment of information and, thus, knowledge (Naturex 2010). RF-EMF studies on cognitive function among children and adolescents have mostly been experimental (Haarala et al. 2005; Lee et al. 2003; Movvahedi et al. 2014; Preece et al. 2005; Riddervold et al. 2008). The results of these studies showed to be contradictory which might be due to a wide variety of methodologies used, such as different measurement tools and exposure durations and conditions. All these aspects hamper the interpretation of the results. Another major limitation in experimental studies are the small sample size and the short exposure duration, addressing acute effects only. From a public health perspective, however, effects of chronic exposure are more relevant and need to be investigated with epidemiological studies. There exist only a small number of epidemiological studies on cognitive function in children and adolescents. Lee et al. (2001) found that exposure to RF-EMF, emitted by mobile phones, may have a mild facilitating effect on human attention in Hong Kong Chinese teenagers. They reported better performance in one out of three attention measures in mobile phone users compared to non-mobile phone users. Another study showed that mobile phone ownership, the time spent on mobile phone per day, the position of the mobile phone during the day and the mode of the mobile phone at night were all significantly associated with inattention in Chinese adolescents (Zheng et al. 2014). The only longitudinal study so far done in 317 seventh grade students found that mobile phone use was associated with faster but less accurate response on a number of cognitive tasks (Abramson et al. 2009). The authors speculated that these behaviors may not be consequences from RF-EMF emitted from mobile phones but may have been learnt from the frequent use of a mobile phone. One year later, in a follow-up of 236 of those students, changes in response time rather than in accuracy were observed (Thomas et al. 2010a). These results, however, were mainly attributed to statistical artefacts.

1.4 Challenges in RF-EMF research

Most of the studies cited above have several methodological limitations. With a cross-sectional design long-term effects are not represented and one cannot differentiate between cause and effect since exposure and outcome are measured at the same time point. Hence, health effects for example could result in an increased mobile phone use and not vice versa. Another methodological limitation in all of these studies is the reliance on self-reported number or duration of mobile phone calls as an exposure proxy. Self-reported number or duration of mobile phone calls, however, is only modestly correlated with objectively recorded number or duration of mobile phone calls. Adolescents tend to considerably overestimate their amount of mobile phone use (recall bias) (Aydin et al. 2011b; Inyang et al. 2009) and since the network (GSM vs. UMTS) used for calls is a major factor influencing RF-EMF exposure (for details see chapter 1.2.1), it does not represent RF-EMF exposure properly. Additionally, there is not only RF-EMF emitted by mobile phones, but there are a lot of other RF-EMF sources such as other wireless devices (cordless phones, computer, tablets and laptops), mobile phone base stations or tv and radio broadcast transmitters which have to be considered when dealing with RF-EMF exposure. Thus, number or duration of mobile phone calls as an exposure proxy does not represent the whole RF-EMF exposure adequately; therefore other ways have to be found to estimate more exactly RF-EMF exposure.

The biggest challenge however consists in differentiating between effects due to RF-EMF radiation or due to non-radiation related effects, which are mediated by regularly using mobile phones and other wireless devices. For example, frequent mobile phone use may result in better cognitive performance since the regular use of mobile phones could serve as a psychomotor training. The Australian study (Abramson et al. 2009) found some evidence for this hypothesis. The number of mobile phone calls was associated with faster and less accurate response on a number of cognitive tasks. However, they speculated that these behaviors may not be the consequence of RF-EMF radiation emitted from mobile phones since similar associations were observed in relation to the number of text messages, which does not or only marginally produce RF-EMF exposure.

In this thesis I will present own data revealing obstacles when dealing with RF-EMF research and try to provide solutions to the identified gaps in this field of research.

2 Methods and Objectives

2.1 The HERMES (Health Effects Related to Mobile phonE use in adolescentS) study

This thesis is part of the HERMES (**H**ealth **E**ffects **R**elated to **M**obile phon**E** use in adolescent**S**) study. An overview of the study is given in Figure 2. The HERMES study is a prospective cohort study conducted in Central Switzerland with 439 study participants aged 12 to 17 years. During a school visit the adolescents filled in a questionnaire with questions, amongst others, on health symptoms, use of mobile phones and other wireless devices, socio-demographics and other relevant covariables. Two cognitive tests to assess memory performance and concentration capacity using a standardized, computerized cognitive testing system were performed. Additionally a questionnaire for the parents was distributed. The questionnaire for the parents included questions, amongst others, on the behavior of their children, on socio-economic factors, on wireless technology at home and on child development. This procedure was repeated one year later with the same study participants (participation rate: 96.8%). From 234 study participants objectively recorded mobile phone use data for the time period up to six months prior to the baseline investigation until follow-up was received.

A subgroup of 95 study participants took part in personal measurements. The adolescents carried a portable measurement device (exposimeter), and kept a diary on a timeactivity diary application installed on a mobile phone in flight-mode for about three consecutive days. Far-field exposure from fixed site transmitters (radio and TV broadcast transmitters and mobile phone base stations) at home and in school was modelled using a geospatial propagation model.

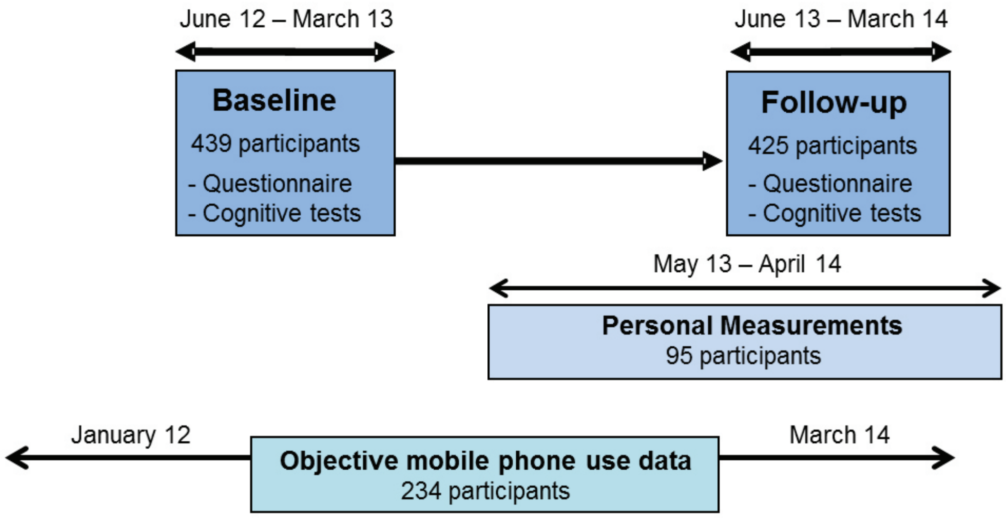

Figure 2: An overview of the HERMES study.

We aimed to evaluate how adolescents' perceived health, cognitive function (memory performance and concentration capacity) and behavior are affected by the use of mobile phones and other wireless devices (cordless phones and computer, tablet and laptop connected to WLAN) including radiofrequency electromagnetic field exposure (Figure 3). This was achieved by using questionnaire data, objectively recorded mobile phone traffic data, cognitive tests, data from personal measurements and a separately developed geospatial propagation model. A brain and whole body RF-EMF dose measure was developed by combining questionnaire data with objectively recorded mobile phone use data, personal measurements and propagation model outputs. To investigate the impact of RF-EMF exposure on health symptoms, cognitive function and behavior in adolescents, the RF-EMF dose measures were applied.

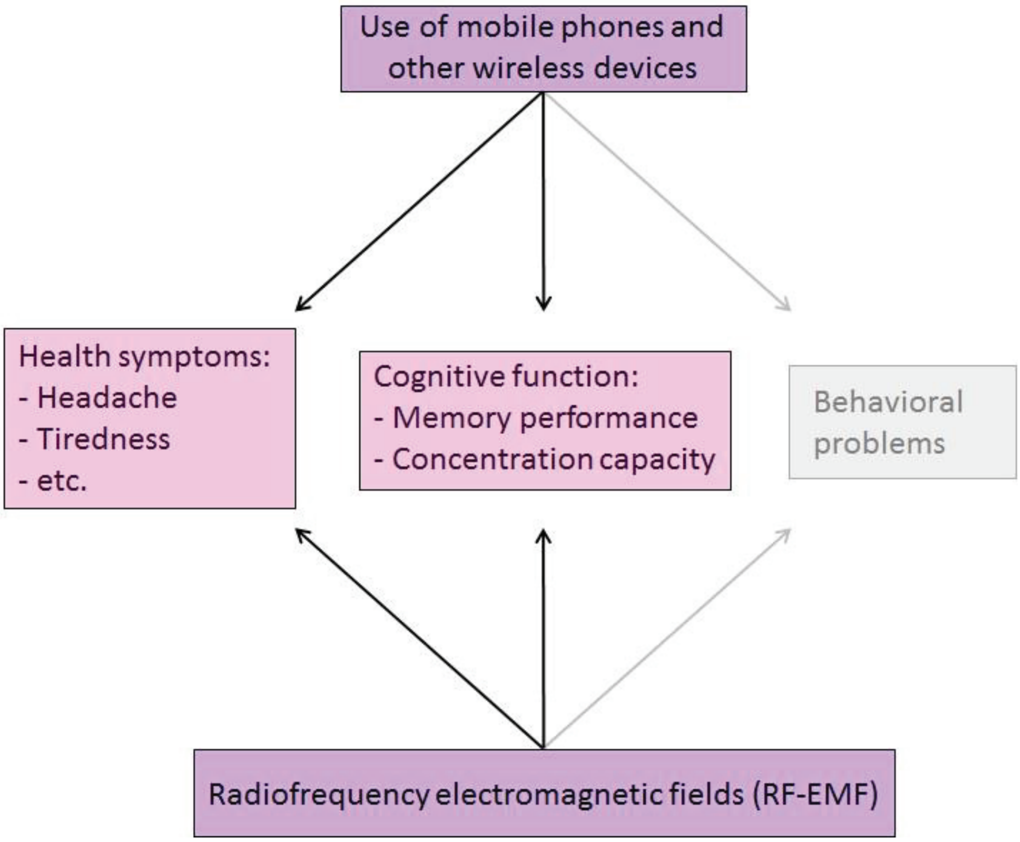

Figure 3: An overview of the aims of the HERMES study. The part of behavioral problems is part of the thesis of Katharina Roser (2015).

2.2 Objectives

Objective 1: To study health symptoms and cognitive function (memory performance and concentration capacity) in relation to mobile phone use during night.

In a cross-sectional study we aimed to investigate whether being awakened during night by an incoming text message or call is associated with negative consequences for health or cognitive function by using both self-reported and objectively operator recorded mobile phone use data. Data on health symptoms were collected by using a questionnaire whereas cognitive tests on memory performance and concentration capacity were performed during a school visit.
The results are illustrated in Article 1.

Objective 2: To apply the newly developped RF-EMF dose measures on the study participants to investigate whether memory performance or health are affected by RF-EMF from wireless devices or by the wireless device use itself due to non-radiation related factors in that context.

Development of the RF-EMF dose measures:
By combining data from questionnaires, objectively recorded mobile phone use data, personal measurements and a separately developed geospatial propagation model, a RF-EMF dose of the brain and the whole body of the participating adolescents was calculated. Various factors affecting near- and far-field RF-EMF exposure were included in the RF-EMF dose measures.
The results of the RF-EMF dose calculations are described in Article 2.

Application of the RF-EMF dose measures on study participants:
Memory performance: The adolescents performed a verbal and figural memory test using a standardized, computerized cognitive testing system at basline and after one year. The use of mobile phones and other wireless devices was assessed using a questionnaire and objectively operator recorded mobile phone use data was obtained for a subgroup of the study participants.
By applying the RF-EMF dose measures to the HERMES cohort study, we aimed to investigate whether memory performance over one year is affected by RF-EMF from wireless devices or by the wireless device use itself due to non-radiation related factors in that context.
The results are illustrated in Article 3.

Health symptoms: Health and the use of mobile phones and other wireless devices were assessed using a questionnaire and and objectively operator recorded mobile phone use data was obtained for a subgroup of the study participants.
By applying the RF-EMF dose measures to the HERMES cohort study, we aimed to investigate whether the health of adolescents is affected by RF-EMF from wireless devices or by the wireless device use itself due to non-radiation related factors in that context.
The results are illustrated in Article 4.

Objective 3: To investigate whether adolescents‘ perceived health is affected by RF-EMF exposure from fixed site transmitters using a geospatial propagation model.

Adolescents‘ perceived health was assessed using a questionnaire and far-field exposure from fixed site transmitters was modelled using a geospatial propagation model based on a comprehensive database of fixed site transmitters, three-dimensional topography and a three-dimensional building model of the study area.
The results are illustrated in Article 5.

3 Mobile phone use during night

3.1 Article 1: Symptoms and cognitive Functions in adolescents in relation to mobile phone use during night

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RESEARCH ARTICLE

Symptoms and Cognitive Functions in Adolescents in Relation to Mobile Phone Use during Night

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Data Availability Statement: The data contain personal and sensitive information, which are needed for confounding adjustment of the regression models. Persons may be easily identifiable from a combination of these variables. This could be a serious problems for the study participants, e.g. when searching for a job. We are willing to share the data on request. In this case we reduce identifying information to a minimum (e.g. rounding of age in months). Any interested researcher will be able to obtain a deidentified dataset upon request. Requests to access data can be sent to Martin Roosli: martin.roosli@unibas.ch

Abstract

Many adolescents tend to leave their mobile phones turned on during night, accepting that they may be awakened by an incoming text message or call. Using self-reported and objective operator recorded mobile phone use data, we thus aimed to analyze how being awakened during night by mobile phone affects adolescents' perceived health and cognitive functions. In this cross-sectional study, 439 adolescents completed questionnaires about their mobile phone use during night, health related quality of life and possible confounding factors. Standardized computerized cognitive tests were performed to assess memory and concentration capacity. Objective operator recorded mobile phone use data was further collected for 233 study participants. Data were analyzed by multivariable regression models adjusted for relevant confounders including amount of mobile phone use. For adolescents reporting to be awakened by a mobile phone during night at least once a month the odds ratio for daytime tiredness and rapid exhaustibility were 1.86 (95% CI: 1.02–3.39) and 2.28 (95% CI: 0.97–5.34), respectively. Similar results were found when analyzing objective operator recorded mobile phone use data (tiredness: 1.63, 95% CI: 0.94–2.82 and rapid exhaustibility: 2.32, 95% CI: 1.01–5.36). The cognitive tests on memory and concentration capacity were not related to mobile phone use during night. Overall, being awakened during night by mobile phone was associated with an increase in health symptom reports such as tiredness, rapid exhaustibility, headache and physical ill-being, but not with memory and concentration capacity. Prevention strategies should focus on helping adolescents set limits for their accessibility by mobile phone, especially during night.

Introduction

Within the last 15 years the use of mobile phones has increased remarkably in adults as well as in adolescents according to the International Telecommunication Union [1]. Many adolescents tend to leave their mobile phones turned on during night and accept that they may be awakened by an incoming text message or call. A survey conducted in 2003 in Belgium showed that 27% of 13 year olds and 43% of 16 year olds reported being disturbed in their sleep by

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incoming text messages, leading to an unhealthy sleep pattern [2]. A follow-up investigation one year later in the same study collective revealed substantially increased levels of tiredness for study participants who used the mobile phone more frequently during night [3]. A cross-sectional study from Munezewa et al.[4] showed that mobile phone use after lights out is associated with short sleep duration, poor sleep quality, daytime sleepiness and insomnia symptoms. Thomée et al.[5] found, in a cross-sectional analysis of data from 4,156 young Swedish adults, that being awakened by mobile phone at night was associated with current stress, sleep disturbances and symptoms of depression.

To our knowledge, no study has investigated mobile phone use during night in relation to effects on cognitive functions. However, an epidemiological study investigated if regular mobile phone use is associated with impaired cognitive functions. Abramson et al.[6] observed that mobile phone use in 317 seventh grade students from Australia was associated with faster and less accurate response on a number of cognitive tasks but speculated that these behaviours may have been learned through frequent use of a mobile phone. In a follow-up investigation one year later, in 236 of these students, changes in response times rather than in accuracy were observed, which were mainly attributed to statistical artefacts [7]. Since amount of mobile phone use in general may be related to the use during night, the observed associations on cognitive functions may be the consequence of night-time use. On the other hand, it is not clear whether the observed patterns with health outcomes are confounded by some other factors related to mobile phone use during night. A limitation of all previous studies is that they were restricted to self-reported mobile phone use data, which has been shown to be inaccurate [8–10]. Rank correlation coefficients between self-reported and objectively recorded mobile phone use varied between 0.1 and 0.9 [8–10] with a tendency for adolescents to overestimate their duration of mobile phone use but being more accurate on the frequency of mobile phone use.

In the framework of the HERMES (Health Effects Related to Mobile phonE use in adolescentS) study we aimed to evaluate how adolescents' perceived health and cognitive functions are affected by various aspects of mobile phone use including electromagnetic field exposure. In this paper, we focus on the question whether being awakened during night by an incoming text message or call is associated with negative consequences by using both self-reported mobile phone use data and objective operator recorded mobile phone use data.

Methods

Ethics Statement

Ethical approval for the conduct of the study was received from the ethical committee of Lucerne, Switzerland (Dienststelle Gesundheit, Ethikkommission des Kantons Luzern, Schweiz) on May 9th, 2012 (Ref. Nr. EK: 12025). The ethical approval was based on the information sheet of the study, the study protocol and summary and questionnaires for the involved parents and adolescents. Written informed consent was obtained from the adolescents and their parents for the participation in the study and for providing the mobile phone operator data.

Study population

439 students (participation rate: 36.8%) aged 12 to 17 years and attending 7th, 8th or 9th grade in 24 schools (participation rate: 19.1%) from rural and urban areas in Central Switzerland participated in the HERMES study. During a school visit between June 2012 and February 2013 the adolescents filled in a questionnaire and performed two cognitive tests using a standardized, computerized cognitive testing system. Additionally a questionnaire for the parents was distributed. The questionnaire for the parents included questions, amongst others, on the

behaviour of their children, on socio-economic factors, on wireless technology at home and on child development. Parents were asked to fill out the questionnaire and send it back directly.

Mobile phone use

The study participants were asked whether they turned off their mobile phone during night and how often they were being awakened by their own or by their roommate's mobile phone. Among those who reported being awakened by mobile phone, they were asked whether they text or call back (referred to as being responsive) during night. For the analysis with the self-reported mobile phone use data, four categories were created. The reference category included those 27 study participants not owning a mobile phone and those reporting to turn off their mobile phone during night ("Mobile phone turned off / no mobile phone"). The other categories referred to those who reported not turning off their mobile phones. The second category included those not awakened by mobile phone during night ("Not being awakened"); the third category included those who reported being awakened by mobile phone at least once a month ("Being awakened (≥1x per month)"); and the forth category is a subgroup of those being awakened who additionally reported to be responsive when being awakened during night ("Being awakened and responsive").

Informed consent to obtain objective mobile phone use data from the mobile phone operators was given by 233 out of 439 study participants and their parents. Data were obtained for up to 6 months before date of investigation. For each participant the number of nights with incoming calls and text messages were calculated by defining night-time use from 11pm to 6am on week days and 12midnight to 8am for Friday and Saturday nights. The mobile phone operators record the time of an incoming text message or call only when the mobile phone is turned on. If the mobile phone is turned off during night, the time of an incoming text message is recorded as soon as the mobile phone is turned on. Thus, when text messages or calls were recorded during night, the mobile phone was turned on.

For the analysis with the objective operator recorded mobile phone use data two categories were created. The 27 study participants not owning a mobile phone were added to the reference group together with those having incoming calls and text messages less than once per month ("No mobile phone / not being awakened (<1x per month)"). An additional analysis was done, omitting study participants not owning a mobile phone.

Health outcomes

In the written questionnaire headache was assessed using the six-item Headache Impact Test [11]. A summary score of all six items can range from 36 to 78. A summary score of 49 or less is considered as "headache has no impact on your life," 50 to 55 is considered as "headache has some impact on your life," 56 to 59 as "headache has substantial impact on your life" and 60 or more as "headache has a very severe impact on your life." A binary variable was created by using 56 as the cut-off value. Tiredness, lack of energy, lack of concentration and rapid exhaustibility (referred to as exhaustibility) were assessed using a four-point Likert scale with categories "never," "rare," "moderate" and "severe." Binary variables were created by combining answer categories "never" with "rare" and "moderate" with "severe". Physical well-being was assessed using the dimension "Physical Well-being" from the Kidscreen-52 questionnaire. This dimension includes five questions exploring the level of adolescent's physical activity, energy and fitness [12,13]. A binary variable was created by using the mean minus half a standard deviation as the cut-off, which is suggested as the guiding principle according to the official Kidscreen questionnaire handbook.

Cognitive tests

Cognitive functions were assessed with a standardized, computerized cognitive test battery (FAKT-II, *Frankfurter Adaptiver Konzentrationsleistungs-Test-II* [14] and a subtest of the IST, *Intelligenz-Struktur-Test 2000R* [15]). Concentration capacity which includes the power of concentration, the accuracy of concentration and the homogeneity of concentration was measured with the FAKT-II. By means of discrimination tasks, the study participant has to discriminate as accurately and as quickly as possible between target and non-target items by pressing "0" for non-target items and "1" for target items. Items with either two or three points in either a circle or a square appeared. Target items have either two points in a square or three points in a circle. Other combinations act as non-target items. Before starting the 6-minute test, the study participants performed a trial-run.

Power of concentration is a measure of the working rate. It measures the number of displayed items per 10 seconds. The higher the power of concentration, the faster the study participant worked. Accuracy of concentration is a measure of the relative correctness. It measures the percentage of non-false items that have been processed. The higher the accuracy of concentration, the more precise the study participant worked. Homogeneity of concentration is a measure of the uniformity of the working rate. It measures the variance of the time an item is displayed. The higher the homogeneity of concentration, the more uniform the study participant worked. These three measures were used for statistical analyses.

Verbal and figural memory was measured with the subtest of the IST. In the verbal memory task, word groups have to be memorized in one minute time. After one minute the study participants give an account of the word groups that have been memorized. In total 10 points can be achieved by remembering the correct word groups. In the figural memory task, pairwise symbols have to be memorized in one minute time. After one minute, one part of the pairwise symbol is shown and the matching part has to be found. A total of 13 points can be achieved. For both the verbal and figural tests, 2 minutes are given to complete the test. For the "overall memory" score, the figural and verbal memory scores are summed. Therefore a total of 23 points can be achieved. For the statistical analyses of verbal and figural memory as well as memory overall the continuous test score values were used as outcome. The cognitive tests, conducted during school time, were administered by two study managers.

Covariates

The written questionnaires for the study participants included questions about age, sex, class level, nationality, school level, physical activity, alcohol consumption and frequency of mobile phone calls. The questionnaires for the parents included questions, among others, on socio-economic factors.

Statistical Analysis

The association between mobile phone use during night and symptoms was analyzed by logistic regression and risk estimates are expressed as odds ratios. The association with cognitive functions was analyzed with linear regression models and thus model coefficients refer to the increase in test score.

A first model (adjusted 1) was adjusted for age, sex, class level (7^{th}, 8^{th} or 9^{th} grade), nationality, school level (college preparatory high school or high school), physical activity, alcohol consumption and education of parents. Since total amount of mobile phone use is associated with night-time use, a second model (adjusted 2) was calculated with additional adjustment; we used self-reported frequency of mobile phone calls per day in the analysis with self-reported data, and recorded duration of mobile phone calls per day in the analysis with operator

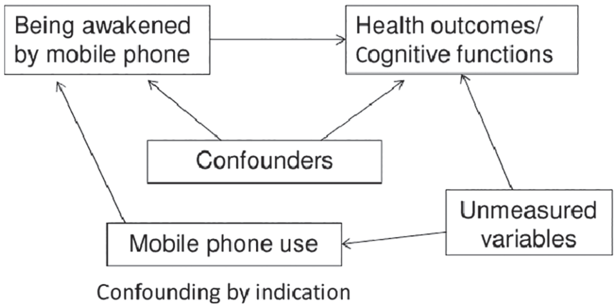

Fig 1. Confounding by indication.

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recorded data. This model addresses potential confounding by indication, which refers to (unmeasured) variables related to mobile phone use and to our outcomes as depicted in Fig 1. The effect of being awakened by mobile phone on the risk of being physically ill/ impaired cognitive functions will be confounded if being awakened by mobile phone is more likely in individuals with higher mobile phone use. Mobile phone use is a risk factor for our outcomes because mobile phone use has a direct causal effect on our outcomes, since both mobile phone use and our outcomes are caused by unmeasured variables (e.g. personality). We suspect confounding by indication because numerous studies observed cross-sectional associations between amount of mobile phone use and symptoms such as fatigue [16–18], depressed mood [5], and headache [17,19]. We hypothesize that such associations may be, at least partly, not directly caused by mobile phone use itself but by unmeasured factors related to mobile phone use such as personality. In epidemiological terms this means that there is a backdoor path between the exposure and the outcomes through the unmeasured variables. This backdoor path could be eliminated by conditioning (adjusting) on the unmeasured variables. Because one cannot adjust for these unmeasured variables, the backdoor path can also be blocked by conditioning (adjusting) on mobile phone use [20]. The results from the analyses with mobile phone adjustment (adjusted 2) thus represent the effect mediated by unmeasured variables (e.g. sleep disturbances) due to nocturnal mobile phone use, whereas for the results of the adjusted 1 model other factors related to mobile phone use in general may also play a role.

Linear regression imputation (14 missing values for alcohol consumption) or imputation of a common category (77 missing values for educational level of the parents) was used to impute missing values in the confounder variables. Statistical analyses were carried out using STATA version 12.1 (StataCorp, College Station, USA).

Results

In total, 439 study participants took part at the baseline investigation. Of those, objective operator data for 233 study participants was obtained. Table 1 shows the distribution of key socio-demographic characteristics in the whole sample (N = 439) and in the subgroup of study participants for which we obtained objective operator recorded data (N = 233).

In total 412 (93.9%) study participants owned a mobile phone. Median age was 13.9 years (range 12–17 years). One study participant did not answer questions about nocturnal mobile phone use and was therefore excluded from analyses with self-reported data. Objective operator recorded mobile phone use data were obtained from this particular study participant and therefore this participant was included in the analyses with operator recorded mobile phone use data.

Table 1. Distribution over socio-demographic characteristics from the whole sample (N = 439) and from the subgroup of study participants with operator recorded data (N = 233).

	N = 439	Prop(%)	N = 233	Prop(%)
Age (years)				
12–13	44	10.0	28	12.0
>13–14	200	45.6	105	45.1
>14–15	142	32.3	80	34.3
>15	53	12.1	20	8.6
Sex				
Female	265	60.4	150	64.4
Male	174	39.6	83	35.6
Class level				
7th grade	105	23.9	52	22.3
8th grade	293	66.8	172	73.8
9th grade	41	9.3	9	3.9
School level				
College preparatory high school	99	22.5	66	28.3
High School	340	77.5	167	71.7
Nationality				
Swiss	348	79.3	189	81.1
Swiss and other	62	14.1	31	13.3
Other	29	6.6	13	5.6
Physically active				
Yes	379	86.3	202	86.7
Number of days with alcohol consumption				
None	304	69.2	156	67.0
One or less than one per month	99	22.6	55	23.6
More than one per month	36	8.2	22	9.4
Highest education of parents				
No education	3	0.7	-	-
Mandatory school / High school	9	2.0	4	1.7
Training school	233	53.1	118	50.6
College preparatory high school	29	6.6	14	6.0
College of higher education	130	29.6	78	33.5
University	35	8.0	19	8.2
Frequency [x/d] of mobile phone calls (self-reported; N = 439)				
never; 0 x/d	27	6.1	-	-
>0 to ≤0.5 x/d	216	49.2	-	-
>0.5 to ≤1 x/d	71	16.2	-	-
>1 to ≤5 x/d	115	26.2	-	-
>5 x/d	10	2.3	-	-
Duration [min/d] of operator recorded mobile phone calls (N = 233)				
≤1 min/day	-	-	151	64.8
>1 to ≤2 min/day	-	-	36	15.4
>2 to ≤5 min/day	-	-	26	11.2
>5 to ≤10 min/day	-	-	12	5.2
>10 min/day	-	-	8	3.4

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From 438 study participants, 126 (28.7%) either had no mobile phone or indicated to switch off their mobile phone during night and reported not being awakened by any other mobile phone. Of study participants who did not switch off their mobile phone at night 216 (49.3%) indicated not being awakened by a mobile phone, while 96 (21.9%) indicated being awakened at night by a mobile phone at least once a month. Of the 96 study participants who are awakened at night by a mobile phone, 61 (67.8%) reported to respond to incoming text messages or calls during night. Of the 233 study participants from which operator recorded data were obtained 110 (42.3%) received an incoming text message or call during night at least once a month.

The Spearman correlation of self-reported frequency of being awakened and the corresponding operator data derived frequency was 0.30. Self-reported frequency of being awakened was also correlated with self-reported frequency of mobile phone calls per day: 0.32. Operator recorded frequency of being awakened was correlated with objective recorded mobile phone use: 0.52. Spearman correlation of self-reported call duration and operator recorded call duration per day was 0.55. The same correlation was found for frequency of calls between self-reported and operator recorded data.

Symptoms

Table 2 shows the association between self-reported mobile phone use during night and health symptoms. After adjusting for age, sex, class level, nationality, school level, physical activity, alcohol and education of parents (adjusted 1), increased OR for all symptoms except for lack of concentration and lack of energy were seen with significant effects for: tiredness (OR:2.06, 95% CI:1.16–3.66), exhaustibility (OR:2.94, 95% CI:1.30–6.63), headache (OR:2.71, 95% CI:1.30–5.63) and physical ill-being (OR:2.93, 95% CI:1.54–5.57) for those reporting being awakened by mobile phone during night at least once a month. After additional adjustment for the frequency of mobile phone calls (adjusted 2) the OR decreased somewhat but the result pattern remained similar.

For the subgroup of people reporting to respond to a text message or call at night, OR (adjusted 1) were even larger for all symptoms with significant effects for: tiredness (OR:3.33, 95% CI:1.67–6.66), exhaustibility (OR:2.79, 95% CI:1.13–6.91), headache (OR:3.08, 95% CI:1.37–6.95) and physical ill-being (OR:4.25, 95% CI:2.05–8.79). After adjustment for the frequency of mobile phone calls (adjusted 2) OR decreased somewhat and only the OR of tiredness and physical ill-being remained significant.

Fig 2 shows the exposure-response frequency of the association between self-reported mobile phone use during night and symptoms. For tiredness, lack of concentration, lack of energy and headache the OR increased with increasing number of reported awakenings per week. For exhaustibility and physical ill-being such an exposure-response pattern was not found. Tiredness showed a significant test of trend.

Table 3 shows results of the objective operator recorded mobile phone use during night. Increased OR (adjusted 1) for all symptoms were seen for participants who were awakened at least once a month by text message or call with significant results for headache (OR: 2.30, 95% CI:1.12–4.73). Additionally adjusting for mobile phone use rather resulted in an increase of the OR than in a decrease as seen for self-reported mobile phone use. In a sensitivity analysis study participants, who did not own a mobile phone, were omitted to possibly obtain a more homogenous reference group. Omitting study participants who did not own a mobile phone yielded higher OR for tiredness (OR: 1.78, 95% CI:1.01–3.14), lack of concentration (OR: 1.39, 95% CI:0.66–2.94), exhaustibility (OR: 2.72, 95% CI:1.08–6.89), lack of energy (OR: 2.18, 95% CI:0.92–5.15) and headache (OR: 3.03, 95% CI:1.33–6.91).

Table 2. Association between self-reported mobile phone use during night and symptoms.

Symptom	n with / without symptoms	crude OR (95% CI)	adjusted 1* OR (95% CI)	adjusted 2** OR (95% CI)
Tiredness *(N = 438)*				
Phone turned off / no phone	50/76	1	1	1
Not being awakened	96/120	1.22 (0.78–1.90)	1.23 (0.78–1.95)	1.18 (0.74–1.88)
Being awakened (≥1x per month)	56/40	**2.13 (1.24–3.65)**	**2.06 (1.16–3.66)**	**1.86 (1.02–3.39)**
Being awakened and responsive[t]	42/19	**3.36 (1.76–6.43)**	**3.33 (1.67–6.66)**	**3.04 (1.48–6.25)**
Lack of concentration *(N = 438)*				
Phone turned off / no phone	22/104	1	1	1
Not being awakened	39/177	1.04 (0.59–1.85)	1.00 (0.55–1.81)	0.92 (0.50–1.69)
Being awakened (≥1x per month)	23/73	1.49 (0.77–2.87)	1.35 (0.67–2.71)	1.14 (0.55–2.38)
Being awakened and responsive[t]	16/45	1.68 (0.81–3.50)	1.57 (0.71–3.46)	1.30 (0.56–3.00)
Exhaustibility *(N = 434)*				
Phone turned off / no phone	12/114	1	1	1
Not being awakened	26/188	1.31 (0.64–2.71)	1.34 (0.64–2.82)	1.18 (0.55–2.52)
Being awakened (≥1x per month)	22/72	**2.90 (1.35–6.22)**	**2.94 (1.30–6.63)**	2.28 (0.97–5.34)
Being awakened and responsive[t]	14/45	**2.96 (1.27–6.88)**	**2.79 (1.13–6.91)**	2.05 (0.79–5.33)
Lack of energy *(N = 438)*				
Phone turned off / no phone	20/106	1	1	1
Not being awakened	29/187	0.82 (0.44–1.52)	0.87 (0.46–1.64)	0.78 (0.41–1.49)
Being awakened (≥1x per month)	23/73	1.67 (0.86–3.26)	1.85 (0.90–3.77)	1.45 (0.68–3.09)
Being awakened and responsive[t]	16/45	1.88 (0.90–3.97)	2.22 (0.99–4.99)	1.67 (0.71–3.96)
Headache *(N = 433)*				
Phone turned off / no phone	16/110	1	1	1
Not being awakened	36/177	1.40 (0.74–2.64)	1.38 (0.71–2.66)	1.14 (0.58–2.24)
Being awakened (≥1x per month)	28/66	**2.92 (1.47–5.79)**	**2.71 (1.30–5.63)**	1.86 (0.86–4.05)
Being awakened and responsive[t]	20/39	**3.53 (1.66–7.48)**	**3.08 (1.37–6.95)**	2.00 (0.84–4.75)
Physical ill-being *(N = 437)*				
Phone turned off / no phone	27/99	1	1	1
Not being awakened	78/138	**2.07 (1.25–3.44)**	**2.21 (1.29–3.79)**	**2.04 (1.18–3.53)**
Being awakened (≥1x per month)	42/53	**2.91 (1.61–5.23)**	**2.93 (1.54–5.57)**	**2.44 (1.25–4.77)**
Being awakened and responsive[t]	32/28	**4.19 (2.16–8.12)**	**4.25 (2.05–8.79)**	**3.52 (1.65–7.52)**

[t] subgroup of the "Being awakened" group.

*adjusted for age, sex, class level, nationality, school level, physical activity, alcohol, education of parents.

**adjusted for frequency of mobile phone calls in addition to adjusted 1.

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Cognitive functions

Descriptive statistics for the cognitive tests are given in Table 4.

The analysis between self-reported mobile phone use during night and cognitive functions are shown in Fig 3. Power of concentration (number of displayed items per 10 seconds), as well as Accuracy of concentration (%) and Homogeneity of concentration (variance of the time an item is displayed) were not associated with self-reported mobile phone use during night.

The spearman correlations of self-reported lack of concentration and Power of concentration, Accuracy of concentration and Homogeneity of concentration measured with the cognitive tests were 0.11, 0.10 and 0.12, respectively. Furthermore no association was found when analyzing verbal, figural and overall memory with self-reported mobile phone use during

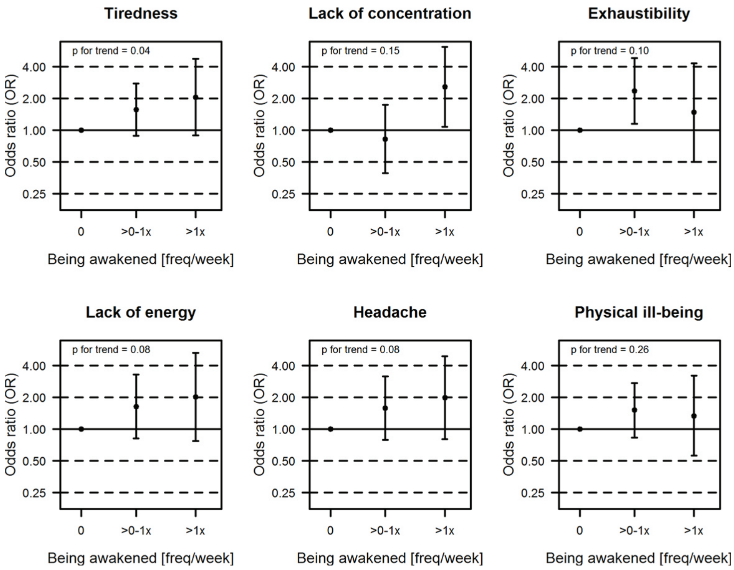

Fig 2. Exposure- response frequency of the association between being awakened during night and symptoms (self-reported; adjusted 2). **adjusted for age, sex, class level, nationality, school level, physical activity, alcohol, education of parents, frequency of mobile phone calls.

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night. These results were confirmed by analyzing objective operator recorded mobile phone use during night (Table 5).

Discussion

The aim of this study was to investigate how the mobile phone use during night affects adolescents' perceived health and cognitive functions. Our results demonstrate that mobile phone use during night is common among adolescents. Increased symptom reports were shown when adolescents are being awakened by mobile phones during night at least once a month. These findings were confirmed by analyzing objective operator recorded mobile phone use data although with wider confidence intervals due to a smaller sample size thus, except for exhaustibility and headache, not reaching statistical significance. Memory and concentration capacity were not associated with nocturnal mobile phone use.

Mobile phone use during night is likely to reduce sleep quality and sleep quantity. Several studies have shown a strong relationship between too short and poor sleep and health consequences such as fatigue [21], headache [22], subjective psychological well-being [23,24], respiratory disorders [25] or cardiovascular diseases [26,27]. The exact underlying mechanisms are not known, but may be mediated by inflammatory responses [28] or by neurophysiological mechanisms [29].

Interruption of sleep may be the underlying mechanism for the observed increase in symptoms in our study when the study participants were being awakened by mobile phone at least once a month. Even higher OR for health outcomes were found when study participants were responsive after being awakened by mobile phone. One could hypothesize that being responsive during night might cause overexcitement and thus negatively affect further sleep, leading to even less sleep compared to those only being awakened. The fact that some OR were slightly increased, even statistically significant for physical ill-being, when the study participants reported to leave their mobile phones turned on (but not report being awakened), could be due to expectation. Only the expectation of getting a call or a text message may lead to poor sleep

Table 3. Association between operator recorded mobile phone use during night and symptoms for the sample of 233 study participants for which operator data were obtained, together with the 27 study participants who do not own a mobile phone.

Symptom	n with /without symptoms	crude OR (95% CI)	adjusted 1* OR (95% CI)	adjusted 2** OR (95% CI)
Tiredness *(N = 260)*				
No phone / not being awakened (<1x per month)	65/85	1	1	1
Being awakened (≥1x per month)	60/50	1.57 (0.96–2.57)	1.53 (0.91–2.60)	1.63 (0.94–2.82)
Lack of concentration *(N = 260)*				
No phone / not being awakened (<1x per month)	25/125	1	1	1
Being awakened (≥1x per month)	22/88	1.25 (0.66–2.36)	1.28 (0.65–2.54)	1.32 (0.65–2.67)
Exhaustibility *(N = 260)*				
No phone / not being awakened (<1x per month)	13/137	1	1	1
Being awakened (≥1x per month)	18/92	2.06 (0.96–4.41)	2.05 (0.91–4.60)	**2.32 (1.01–5.36)**
Lack of energy *(N = 260)*				
No phone / not being awakened (<1x per month)	19/131	1	1	1
Being awakened (≥1x per month)	17/93	1.26 (0.62–2.55)	1.28 (0.61–2.70)	1.55 (0.72–3.38)
Headache *(N = 257)*				
No phone / not being awakened (<1x per month)	21/128	1	1	1
Being awakened (≥1x per month)	28/80	**2.13 (1.14–4.01)**	**2.30 (1.12–4.73)**	**2.17 (1.03–4.56)**
Physical ill-being *(N = 259)*				
No phone / not being awakened (<1x per month)	43/107	1	1	1
Being awakened (≥1x per month)	42/67	1.56 (0.92–2.63)	1.55 (0.86–2.77)	1.67 (0.91–3.06)

*adjusted for age, sex, class level, nationality, school level, physical activity, alcohol, education of parents.

**adjusted for duration of mobile phone calls in addition to adjusted 1.

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and thus to an increase in symptoms. It can also be that some adolescents who kept the mobile phone on during night did not report being occasionally awakened by their mobile phone. However, if that would be the case, we would expect to get some significant results also for other symptoms. The exposure-response pattern of the association between self-reported

Table 4. Descriptive statistics for the tests of the cognitive functions.

	n[1]	mean	sd	min	median	max
Power of concentration (Number of items per 10 sec)	349	8.00	2.76	1.66	7.96	17.10
Accuracy of concentration (%)	349	79.35	5.52	67.30	78.60	98.70
Homogeneity of concentration (Variance of time)	349	25.59	16.48	4.70	22.80	100
Verbal memory (test score)	416	5.02	2.76	0	5	10
Figural memory (test score)	419	8.06	2.76	0	8	13
Memory overall (test score)	416	13.09	4.44	2	13	23

[1] due to technical problems of the computerized testing system, data was not available for the whole sample.

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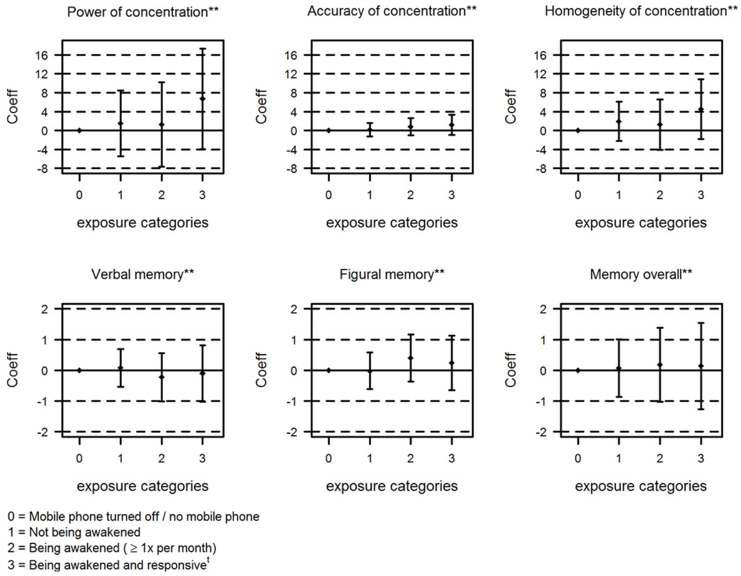

Fig 3. Association between self-reported mobile phone use during night and cognitive functions.
[t] subgroup of the "Being awakened" group. **adjusted for age, sex, class level, nationality, school level, physical activity, alcohol, education of parents, frequency of mobile phone calls.

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mobile phone use during night and health outcomes showed that frequency in addition to being awakened also plays an important role.

Caution is needed in interpreting the directions of the associations. We hypothesize that mobile phone use during night might affect sleep which in turn might lead to more symptoms. An alternative hypothesis would be reverse causality in the sense that study participants with sleep disturbances and more health symptoms use the mobile phone during night more often than their peers who have no sleep disturbances.

Sleep plays an important role concerning health outcomes, but also in learning processes and memory consolidation [30]. Sleep contributes to memory consolidation before and after learning [31]. Furthermore, sleep is not only important for memory consolidation on long-term; it is also important on short-term [32]. Consistently reduced task-related activation in verbal short-term memory tasks were shown in sleep deprived individuals [33,34]. The same applies to concentration and attention tasks [35,36]. A characteristic of a sleep-deprived state is the failing to respond in a time restricted manner to a stimulus [37,38].

Nevertheless, we did not find indications that memory and concentration capacity is affected by nocturnal mobile phone use. One explanation, suggested in a meta-analysis from Pilcher et al.[39], could be that the effects of sleep deprivation have greater influences on feelings of fatigue and other related mood conditions than on cognitive performance. Other explanations could be that these two cognitive tests are not sensitive enough or the sample size was too small. It could also be that a kind of selection bias is present, meaning that adolescents with a high memory and concentration capacity prefer to use mobile phones at night.

Interestingly, the results of the cognitive concentration test and the self-reported lack of concentration are fairly consistent. Self-reported lack of concentration was the symptom that increased the least when being awakened at least once a month with self-reported and objective recorded mobile phone use during night. However, the correlations between self-reported lack of concentration and cognitive test outcomes were small.

Table 5. Association between operator recorded mobile phone use during night and cognitive functions for the sample of 233 study participants for which operator data were obtained, together with the 27 study participants who do not own a mobile phone.

Cognitive Function	n	crude Coeff [1] (95% CI)	adjusted 1* Coeff [1] (95% CI)	adjusted 2** Coeff [1] (95% CI)
Power of concentration *(N = 210)*				
No phone / not being awakened (<1x per month)	118	0	0	0
Being awakened (≥1x per month)	92	0.01 (-0.75–0.76)	-0.07 (-0.81–0.68)	0.04 (-0.73–0.81)
Accuracy of concentration *(N = 210)*				
No phone / not being awakened (<1x per month)	118	0	0	0
Being awakened (≥1x per month)	92	0.25 (-1.33–1.83)	0.24 (-1.37–1.84)	0.25 (-1.41–1.91)
Homogeneity of concentration *(N = 210)*				
No phone / not being awakened (<1x per month)	118	0	0	0
Being awakened (≥1x per month)	92	0.11 (-4.66–4.88)	-0.62 (-5.37–4.12)	-0.14 (-5.03–4.76)
Verbal memory *(N = 251)*				
No phone / not being awakened (<1x per month)	145	0	0	0
Being awakened (≥1x per month)	106	0.23 (-0.47–0.93)	0.16 (-0.54–0.87)	0.30 (-0.43–1.03)
Figural memory *(N = 252)*				
No phone / not being awakened (<1x per month)	145	0	0	0
Being awakened (≥1x per month)	107	0.60 (-0.04–1.24)	0.36 (-0.24–0.97)	0.39 (-0.25–1.02)
Memory overall *(N = 251)*				
No phone / not being awakened (<1x per month)	145	0	0	0
Being awakened (≥1x per month)	106	0.83 (-0.24–1.91)	0.54 (-0.47–1.55)	0.70 (-0.35–1.75)

*adjusted for age, sex, class level, nationality, school level, physical activity, alcohol, education of parents.

**adjusted for duration of mobile phone calls in addition to adjusted 1.

[1] refers to change in the test score per exposure category.

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One of the strengths of our study is the consideration of both self-reported and objective operator recorded data on mobile phone use during night. Both have their merits and limitations. Operator recorded data are not subject to reporting bias compared to self-reported data, but there are several issues that have to be considered when using operator recorded data. Received text messages and calls during night were considered in our study. In operator recorded data only calls being answered are recorded, so one can be sure that if an incoming call was recorded, the call was answered. However, we cannot prove that study participants were already asleep when the call was answered, since we did not have information on sleeping times. Concerning text messages, mobile phone operators can only record text messages that are sent through the Short-Message-Service (SMS). Nowadays adolescents mostly connect to WLAN or use the mobile internet connection on their mobile phone to send messages through internet-based apps e.g. "WhatsApp" instead of using the Short-Message-Service. Text messages using internet-based apps cannot be recorded by mobile phone operators. Thus, somewhat different information is collected with operator recorded data compared to self-reported exposure data and thus correlations between these exposure measures were only moderate in our study. Nevertheless, findings were fairly consistent, which suggests that bias from exposure assessment is unlikely.

We made considerable effort to adjust our analyses for relevant confounding factors. Still, there might be some residual confounding. Strikingly, the symptom risk estimates for models with (adjusted 2) and without (adjusted 1) mobile phone use adjustments were similar for operator recorded exposure data and only a little reduced for self-reported exposure data. This suggests that indeed mobile phone induced sleep disturbances play an important role for the observed associations. And other unmeasured factors related to mobile phone use were not found to substantially modify the observed relations between symptoms and mobile phone use during night when taking them indirectly into account in the adjusted 2 model addressing confounding by indication.

Van den Bulck et al.[2] reported that 27% of 13-year-old adolescents were being awakened by mobile phone at least once per month, which was found to be similar in our study (22% of the study participants). They found that the use of mobile phone during night increased the odds of being tired by 3.3 (95% CI:1.8–6.0) in the follow-up investigation [3]. This result was also similar to the OR we found for study participants reporting being responsive during night (OR: 3.04, 95% CI:1.48–6.25). Punamaki et al.[40] found that intensive mobile phone usage in girls was associated with poor perceived health. They propose the same mediating links as we do.

Conclusion

Among Swiss adolescents, we have observed that nocturnal mobile phone use was associated with an increase in health symptom reports such as tiredness, rapid exhaustibility, headache and physical ill-being, but not with memory and concentration capacity. More studies to investigate these associations are necessary and education in sleep behaviour may be inevitable since the mobile phone is now the most familiar lifestyle factor for adolescents.

Public Health prevention strategies should focus on helping adolescents set limits for their accessibility by mobile phone, especially during night.

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Author Contributions

Conceived and designed the experiments: MR. Performed the experiments: AS KR. Analyzed the data: AS. Contributed reagents/materials/analysis tools: AS KR MR. Wrote the paper: AS. Reviewed and revised the manuscript: KR MR.

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4 RF-EMF dose measure and its application

4.1 Article 2: Development of an RF-EMF exposure surrogate for epidemiologic research

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Article

Development of an RF-EMF Exposure Surrogate for Epidemiologic Research

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Abstract: Exposure assessment is a crucial part in studying potential effects of RF-EMF. Using data from the HERMES study on adolescents, we developed an integrative exposure surrogate combining near-field and far-field RF-EMF exposure in a single brain and whole-body exposure measure. Contributions from far-field sources were modelled by propagation modelling and multivariable regression modelling using personal measurements. Contributions from near-field sources were assessed from both, questionnaires and mobile phone operator records. Mean cumulative brain and whole-body doses were 1559.7 mJ/kg and 339.9 mJ/kg per day, respectively. 98.4% of the brain dose originated from near-field sources, mainly from GSM mobile phone calls (93.1%) and from DECT phone calls (4.8%). Main contributors to the whole-body dose were GSM mobile phone calls (69.0%), use of computer, laptop and tablet connected to WLAN (12.2%) and data traffic on the mobile phone via WLAN (6.5%). The exposure from mobile phone base stations contributed 1.8% to the whole-body dose, while uplink exposure from other people's mobile phones contributed 3.6%. In conclusion, the proposed approach is considered useful to combine near-field and far-field exposure to an integrative exposure surrogate for exposure assessment in epidemiologic studies. However, substantial uncertainties remain about exposure contributions from various near-field and far-field sources.

Keywords: exposure assessment; RF-EMF; mobile phone; adolescents; dose calculation

1. Introduction

Mobile phones and other wireless communication devices using radiofrequency electromagnetic fields (RF-EMF) are an integral part in the everyday life of adolescents. Thus exposure to this radiation is ubiquitous and in studying potential effects of RF-EMF, exposure assessment is a crucial part in this field of research. Since there are a lot of different sources emitting RF-EMF in everyday life, one needs to find a way of combining all of these emissions to one single integrative exposure measure. On one hand there are near-field sources such as mobile phones, computers, laptops and tablets emitting close to the body. On the other hand far-field sources such as fixed site transmitters (mobile phone base stations and broadcast transmitters), Wireless Local Area Network (WLAN) base stations, Digital Enhanced Cordless Telecommunications (DECT) base stations and other mobile phones in the surrounding area contribute to the environmental exposure. So far, little attempts have been made to combine these different types of exposure to one single integrative measure.

In a German study, personal measurements in adolescents and adults have been conducted during 24 h to estimate RF-EMF exposure [1–3]. This approach considered all exposure sources in the environment. However, it is time-consuming and personal measurements may not adequately record exposure from near-field sources because measured values depend highly on the distance between the emitting source and the measurement device, which is not necessarily the same as the distance between the emitting source and the body [4,5]. Other studies focussed on far-field exposures only by using propagation models for fixed site transmitters [6–13]. Frei *et al.* combined modelled RF-EMF exposure from fixed site transmitters at home with personal exposure relevant characteristics and behaviour to estimate personal RF-EMF exposure [14]. In this study, the presence of concrete walls and metal window frames were found to modify RF-EMF exposure from fixed site transmitters. Additional exposure relevant factors included ownership of a mobile phone, ownership of a WLAN at home and having a DECT base station in the bedroom or at the place where the person spent most of their time during the day, time spent at an external workplace and hours per week spent in a train, tram or bus. However, this exposure proxy focussed on far-field sources only and near-field sources were separately considered in their epidemiological analyses on non-specific symptoms of ill health and RF-EMF exposure [15,16]. In the framework of the Interphone study, estimations of RF energy absorbed in the brain from mobile phones were assessed [17]. Lauer *et al.* calculated organ-specific and whole-body RF-EMF proxies taking into account far-field exposure from different sources and near-field exposure from calls on the mobile phone and on the DECT phone using data collected between 2007 and 2009 in Switzerland [18]. However, these data may already be outdated because in the meantime mobile phones have been developed in the direction of multifunctional devices used not only for making calls and sending text messages, but for many additional activities such as browsing the internet, watching videos and gaming. Thus, the exposure predictors are expected to have changed considerably, and a comprehensive overview of relevant factors influencing the RF-EMF exposure emitted by near-field and far-field sources is still missing. The aim of this study was to determine these relevant factors and to develop an integrative exposure assessment method combining near-field and far-field sources for the brain as well as for the whole-body RF-EMF exposure for epidemiologic research. As a result we present cumulative RF-EMF dose for adolescents of a Swiss epidemiologic study called Health Effects Related to Mobile phonE use in adolescentS (HERMES).

2. Methods

2.1. Hermes Study

The HERMES study, a cohort study conducted in Central Switzerland, aimed to prospectively investigate whether the exposure to RF-EMF emitted by mobile phones and other wireless communication devices affects cognitive functions or causes behavioural problems and non-specific health disturbances in adolescents. The investigation took place from June 2012 to March 2013. The study participants filled in a paper-and-pencil questionnaire during school time supervised by two study managers. The questionnaire included detailed questions about their mobile phone use, DECT phone use and computer, laptop and tablet use (in brackets are the corresponding near-field exposure predictors indicated):

- Duration of calls made and received with their own and other mobile phones (GSM and UMTS mobile phone calls);
- Proportion of calls with the mobile phone using a headset (GSM and UMTS mobile phone calls);
- Duration of mobile phone use for data traffic (mobile phone data traffic and mobile phone data traffic WLAN);
- Duration of carrying the mobile phone close to the body (mobile phone close to body);
- Duration of calls made and received with a DECT phone at home (DECT phone calls);
- Duration of computer, laptop and tablet use and WLAN connection of the corresponding devices (computer, laptop and tablet use with WLAN).

Additionally, they were asked about the time spent in trains and buses. Furthermore we distributed paper-and-pencil questionnaires for the parents and asked them to return these directly to the study managers. This questionnaire included questions about DECT phones, WLAN and number of smartphones at home and number of floors and floor location of the residence. In addition, the teacher or head of the school provided us with information about the availability of WLAN in the school and building characteristics of the school building (number of floors and the floor location of the class room the adolescents spent most of their school time). Informed consent was given by the study participants and their parents to obtain objective mobile phone use data from the mobile phone operators. Operator data included records for each call made and received including duration of call and network used when starting the call. The calls were categorised into calls on the Global System for Mobile Communications (GSM) network and on the Universal Mobile Telecommunications System (UMTS) network. There was no differentiation between GSM900 and GSM1800 network in the mobile phone operator data. Average proportions of network use for calls over the recorded time period were used in our analysis.

2.2. Personal Measurements in the Framework of the Hermes Study

A subgroup of the study participants also took part in personal measurements. The adolescents carried a portable measurement device, a so-called exposimeter, for three consecutive days. Two versions of the device Expom (referred to as *Expom 1* for the older version and *Expom 3* for the newer version) were used to measure 13 frequency bands ranging from Digital Video Broadcasting—Terrestrial (DVB-T, centre frequency of 620 MHz) to Worldwide Interoperability for Microwave Access (WiMa, 3500 MHz) [19]. Nine out of the 13 measured frequency bands were used in our analysis (Table 1).

Table 1. Frequency range, quantitation limits and reporting limits for the frequency bands of the measurement devices Expom 1 and Expom 3 used for the personal measurements.

Frequency Band	Frequency Range (MHz)	Quantitation Limit (V/m)		Reporting Limit (V/m)
	Expom 1 and Expom 3	Expom 1	Expom 3	Expom 1 and Expom 3
TV	470–790	0.010	0.005	0.0025
Uplink 900 *	880–915	0.015	0.005	0.0025
Downlink 900 *	925–960	0.015	0.005	0.0025
Uplink 1800 *	1710–1785	0.015	0.005	0.0025
Downlink 1800 *	1805–1880	0.005	0.005	0.0025
DECT	1880–1900	0.005	0.005	0.0025
Uplink 1900 *	1920–1980	0.003	0.003	0.0015
Downlink 2100 *	2110–2170	0.010	0.003	0.0015
WLAN	2400–2485	0.005	0.005	0.0025

* The uplink and downlink bands include all technologies using the particular frequency range. Downlink means the transmission from mobile phone base stations to mobile phone handsets and uplink the transmission from mobile phone handsets to mobile phone base stations.

Additionally, the participants filled in a time-activity diary installed as an application on a smartphone operating in flight mode. These diaries were manually corrected for implausible chronologies of diary entries. Subsequently, summary statistics were calculated after censoring the measurements at the reporting limit and 5 V/m.

2.3. Dose Calculations

We aimed to calculate personal cumulative RF-EMF doses in the brain and the whole-body combining exposure from different sources emitting RF-EMF. The processes of learning and memory are located in the hippocampus, while processes for behaviour and cognitive functions in the prefrontal cortex. The hippocampus and the prefrontal cortex consist mainly of gray matter. Therefore, specific absorption rates (SARs) for *brain gray matter* were used for the brain exposure. Additionally, the same calculations were performed for *brain white matter* and compared with the brain exposure obtained for brain gray matter since the white matter is important for these processes as well.

The personal dose in terms of the time-averaged specific absorption rate (SAR) can be calculated as follows:

$$\mathrm{dose} = \sum_{\mathrm{i}} \mathrm{dose_i} = \sum_{\mathrm{i}} \mathrm{SAR_i} * \mathrm{time_i} \quad (1)$$

with $dose_i$ (in mJ/kg) and SAR_i (in mW/kg) the dose and SAR originating from the exposure in a certain frequency band or due to a certain use of a specific wireless communcation device, and $time_i$ the duration of this exposure. Thus, the proposed integrative exposure surrogate consists of a near-field component combining the exposure from the use of wireless communication devices and a far-field component aggregating the exposure from environmental sources. Therefore, we calculated the total dose as follows:

$$\text{dose} = \text{near----field dose} + \text{far-field dose} \tag{2}$$

2.3.1. Near-Field Dose

For the near-field component, we considered *a priori* the following exposure predictors relevant:

$$\begin{aligned}\text{near-field dose} \\ &= \text{dose}_{\text{GSM mobile phone calls}} + \text{dose}_{\text{UMTS mobile phone calls}} \\ &+ \text{dose}_{\text{DECT phone calls}} + \text{dose}_{\text{mobile phone data traffic}} \\ &+ \text{dose}_{\text{mobile phone close to body}} + \text{dose}_{\text{mobile phone data traffic WLAN}} \\ &+ \text{dose}_{\text{computer,laptop and tablet use with WLAN}}\end{aligned} \tag{3}$$

The particular dose parts of the near-field component of the exposure surrogate (Equation (3)) can be calculated as follows:

$$\text{near-field dose}_i = \text{SAR}_i(\text{literature}) \times \text{time}_i(\text{HERMES questionnaire, operator data}) \tag{4}$$

where the SAR_i were derived from the literature [18,20–25] and the exposure durations $time_i$ were asked in the HERMES questionnaire. For participants with missing operator data, the proportion of network used for calls (GSM and UMTS) was estimated by regression modelling using the available mobile phone operator data from a subgroup of the study participants.

Derivation of the SARs

For the derivation of the SARs for the exposure circumstances in Equation (3) we combined the SARs provided from Lauer *et al.* for calls on the mobile phone and on the DECT phone [18] with the measured uplink output power from Persson *et al.* [24], Gati *et al.* [21] and Huang *et al.* [23]. Additionally, we took into account the SAR ranges presented in the SEAWIND Final Summary Report (referred to as *SEAWIND report*) [20].

For calls with a mobile phone Lauer *et al.* provide a brain (the *brain gray matter* values were used, referred to as *brain*) SAR of 3.198 mW/kg and a whole-body SAR of 0.411 mW/kg for GSM900/GSM1800 calls based on output powers derived from Vrijheid *et al.* for GSM900 and GSM1800 [25] (Table 2). For UMTS calls Lauer *et al.* calculated a brain SAR of 0.023 mW/kg and a whole-body SAR of 0.003 mW/kg using output power values from Gati *et al.* [21] and assuming half of the calls in buildings and the other half outdoors.

On average the SAR decreased by a factor of 1000 by having the device approximately 20 cm away from the body compared to a device touching the body [20]. Therefore, we used a brain SAR of 3.198×10^{-3} mW/kg for GSM900/GSM1800 calls with headset and a brain SAR of 0.023×10^{-3} mW/kg for UMTS calls with headset. For the whole-body exposure we used the same SAR for calls with and without headset referring to a similar distance to the body when having the mobile phone close to the ear or in front of the body while using a headset.

Table 2. Near-field *brain* and *whole-body* SARs, corresponding derivation and references for the near-field predictors.

Near-Field Predictor	Brain SAR		Whole-Body SAR		References
	(mW/kg)	Derivation	(mW/kg)	Derivation	
GSM [1] mobile phone calls without headset	3.198	−	0.411	−	[18]
GSM [1] mobile phone calls with headset	3.198×10^{-3}	3.198 × 0.001	0.411	0.411 × 1	[18,20]
UMTS mobile phone calls without headset	0.023	−	0.003	−	[18]
UMTS mobile phone calls with headset	0.023×10^{-3}	0.023 × 0.001	0.003	0.003 × 1	[18,20]
DECT phone calls without eco mode	0.373	−	0.051	−	[18]
DECT phone calls with eco mode	0.0373	0.373 × 0.1	0.0051	0.051 × 0.1	[18,20]
mobile phone data traffic with mobile internet connection	0.092×10^{-3}	0.023 × 4 × 0.001	0.012	0.003 × 4 × 1	[18,20–24]
mobile phone close to body (passive mobile phone data traffic)	0.092×10^{-3}	0.023 × 4 × 0.001	0.012	0.003 × 4 × 1	[18,20–24]
mobile phone data traffic with WLAN	0.092×10^{-3}	0.023 × 4 × 0.001	0.012	0.003 × 4 × 1	[18,20–24]
computer, laptop and tablet use with WLAN	0.092×10^{-3}	0.023 × 4 × 0.001	0.012	0.003 × 4 × 1	[18,20–24]

[1] For calls with the mobile phone on the GSM network the mean of the SARs for the GSM900 and the GSM1800 network was used because there was no differentiation between GSM900 and GSM1800 network in the mobile phone operator data.

For DECT phone calls Lauer *et al.* derived an average output power from the general transmission power of a DECT phone [18], resulting in a brain SAR of 0.373 mW/kg and a whole-body SAR of 0.051 mW/kg. The SEAWIND report showed a decrease in the SAR by a factor of 10 for calls with an eco mode DECT phone compared to a DECT phone without eco mode [20], therefore we used a brain SAR of 0.0373 mW/kg and a whole-body SAR of 0.0051 mW/kg for calls with a DECT phone provided with eco mode.

For the output power of mobile phones during data transmission we took the following available knowledge into account: Persson *et al.* measured on average an increased output power for data connections compared to voice connections in the UMTS network in the range of a factor of 3.25 to 6.8, depending on rural or urban environment and the bit rates used for the data transmission [24]. In the framework of the LEXNET project an output power increased by about a factor of 4 for data traffic service compared to voice service in the 3G network of Orange in France was found [23]. Gati *et al.* found a mean output power increased by about 6 dB on average for data traffic mode compared to voice mode [21]. Therefore, we used a by a factor of 4 increased output power of the mobile phone for data traffic compared to calls on the UMTS network. To take into account the different positions of the mobile phone during data traffic compared to those during calls (holding the mobile phone in the hand instead of close to the ear) we used the ranges delivered in the SEAWIND report for different distances between the device and the respective tissue [20]. The SAR decreased on average by a factor of 1000 by having the device approximately 20 cm away from the body compared to a device touching the body. Hadjem *et al.* found that the exposure for a mobile phone in watching-like position at 10 cm distance is about ten times below the exposure in voice position. At 40 cm distance it appeared that the exposure was about 1000 times lower [22]. These findings are comparable with the SAR ranges presented in the SEAWIND report for UMTS voice and UMTS data [20]. These considerations led us to use a brain SAR of 0.092×10^{-3} mW/kg for data traffic on the mobile phone via mobile internet connection. For the whole-body SAR we assumed that the mobile phone is held approximately at the same distance from the body for data traffic as for voice calls resulting in a whole-body SAR of 0.012 mW/kg for data traffic on the mobile phone via mobile internet connection.

Considering an approximately equal exposure for transmission of a fixed size data packet using UMTS or WLAN (SEAWIND report, page 3 [20]) we decided to use the same SAR for data traffic via WLAN as for data traffic via mobile internet connection for both the brain and the whole-body SAR.

For using a computer, laptop or tablet connected to the internet via WLAN we used the same SAR as for data traffic on the mobile phone using WLAN assuming approximately the same distance between the device and the brain and the body, respectively.

2.3.2. Far-Field Dose

The far-field component consisted of the following parts:

$$\begin{aligned}\text{far-field dose} = {} & \text{dose}_{\text{radio}} + \text{dose}_{\text{TV}} + \text{dose}_{\text{downlink 900}} + \text{dose}_{\text{downlink 1800}} \\ & + \text{dose}_{\text{downlink 2100}} + \text{dose}_{\text{WLAN}} + \text{dose}_{\text{DECT}} + \text{dose}_{\text{uplink}}\end{aligned} \quad (5)$$

where downlink means the transmission from mobile phone base stations to mobile phone handsets and uplink the transmission from mobile phone handsets to mobile phone base stations.

Far-field exposure from radio and TV broadcast transmitters and mobile phone base stations at home and in school were considered a priori relevant and were modelled using a geospatial propagation model [9,10]. Additionally, behaviours and characteristics relevant for the remaining far-field exposure parts (WLAN, DECT and uplink; Equation (5)) were estimated from the personal measurements. Far-field dose parts were obtained by multiplying the estimated power flux density with the normalized organ and frequency specific SAR derived from the literature [18] and the exposure duration obtained from the HERMES questionnaire or from the diary filled in during the personal measurements:

$$\begin{aligned}\text{far-field dose}_{\text{i}} = {} & \text{SAR}_{\text{i}}(\text{literature, modelling, personal measurements}) \\ & \times \text{time}_{\text{i}}(\text{HERMES questionnaire, personal measurements})\end{aligned} \quad (6)$$

Geospatial Propagation Model

Far-field exposure from fixed site transmitters was modelled using a geospatial propagation model based on a comprehensive database of transmitters, three-dimensional topography and a three-dimensional building model of the study area [9,10]. The coordinates of the home and the school addresses of the study participants were provided from the Swiss Federal Statistical Office. The number of floors of the building and the floor location of the residence and class room for calculating the height of the residence and class room were asked in the parents' and school questionnaire, respectively [9,14]. On average, a damping factor of 4.6 dB was used for outdoor-to-indoor modelling to take into account wall attenuation [9].

2.3.3. Multivariable Regression Models

Behaviours resulting in far-field exposure from WLAN base stations, DECT base stations and uplink of other mobile phones in the surroundings were identified by means of multivariable regression models using non-parametric bootstrap to estimate the coefficients. In these models, personal measurements were used as dependent variables. The explanatory variables, such as time spent in rooms or buildings with WLAN or DECT base station, number of smartphones in the household, or time spent in public transport were derived from the HERMES questionnaire. Regression models were also used to evaluate whether building characteristics modified indoor personal exposure from fixed site transmitters as was previously observed [14].

Combining Near-Field and Far-Field Dose

Using the equations above, we calculated daily brain and whole-body RF-EMF dose for each HERMES study participant. For data visualisation we have additionally chosen three HERMES study participants: a non-user, a normal user and a heavy-user. The non-user is a study participant not owning a mobile phone and not using another mobile phone (12 out of 439 study participants reported not to use a mobile phone at all). The normal user is an average mobile phone call (median = 6.4 min/day) and data traffic user (median data traffic via mobile internet connection = 2.27 min/day, median data traffic via WLAN = 19.0 min/day). The heavy-user represents maximal duration of mobile phone calls (267.1 min/day) and average mobile phone data traffic use. Note that all three users are average HERMES users in terms of calls on the DECT phone at home and computer, laptop and tablet use with WLAN (duration of DECT phone calls and us of devices with WLAN close to the median of the study population, median duration of DECT phone calls = 4.8 min/day, median use of devices with WLAN = 30 min/day).

2.4. Comparison of Dose Calculations with Personal Measurements

For the 95 participants with personal measurements we compared the dose with the personal measurements. For brain and whole-body dose three exposure categories were defined: brain or whole-body dose <50th percentile (*low*), 50th–90th percentile (*medium*) and >90th percentile (*high*).

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Lucerne, Switzerland on 9 May, 2012 (Project identification code: EK 12025).

3. Results

Four hundred and thirty nine (439) adolescents with a mean age of 14.0 years (range: 12.1–17.0 years) took part in the HERMES study. Objectively recorded operator data was available for a subgroup of

233 study participants. After data cleaning of the personal measurements and diary cleaning, 95 out of 121 collected sets of measurements and diaries could be used in our analysis.

3.1. Near-Field Dose

3.1.1. Near-Field Predictors

The adolescents of the HERMES study indicated in the questionnaire average mobile phone call duration of 17.2 min/day, of which 9.5 min were calls on the GSM network and 7.7 min calls on the UMTS network according to the recorded/predicted proportion of network use derived from the operator data (Table 3). They reported to use the DECT phone at home on for calls lasting 9.0 min per day. They used their mobile phone on average 11.5 min/day for data traffic on the mobile phone using a mobile internet connection and 30.6 min/day for data traffic using a WLAN connection. Additionally, they indicated to wear their mobile phone for 4.4 h close to the body. Lastly, they reported to use computers, laptops and tablets connected to the internet via WLAN for almost an hour per day (57.6 min).

3.1.2. Near-Field Dose

The highest dose rate (dose per 1 min) was found for calls on the mobile phone on the GSM network (without headset) with 191.88 mJ/kg/min and 24.66 mJ/kg/min followed by calls on the DECT phone (without eco mode) with 22.38 mJ/kg/min and 3.06 mJ/kg/min for brain and whole-body, respectively (Table 3). Considering all predictors, the brain near-field dose consisted mainly of the exposure from GSM mobile phone calls, on average 1451.78 mJ/kg/day (94.6%), followed by a dose of 74.10 mJ/kg/day (4.8%) from DECT phone calls (Table 3 and Figure 1). UMTS mobile phone calls counted for 8.04 mJ/kg/day (0.5%). Concerning the whole-body near-field dose, the largest part was induced by GSM mobile phone calls with a dose of 234.47 mJ/kg/day (73.3%). DECT phone calls contributed with a dose of 10.13 mJ/kg/day (3.2%). The dose contribution from mobile phone data traffic was 8.29 mJ/kg/day (2.6%) for data traffic via mobile internet connection and 22.03 mJ/kg/day (6.9%) for data traffic via WLAN connection. Using a computer, laptop and tablet connected to WLAN played a considerable role with a mean dose of 41.46 mJ/kg/day (13.0%).

Table 3. SAR, mean exposure duration (with standard deviation), dose rate (dose per 1 min), and mean (with corresponding percentage of the total near-field dose), minimum, median and maximum of the daily cumulative dose for the *brain* and *whole-body* exposure for the near-field predictors.

Near-Field Predictor	Brain SAR (mW/kg)	Whole-Body SAR (mW/kg)	Exposure Duration (min/day)	Brain Dose Rate (mJ/kg/min)	Whole-Body Dose Rate (mJ/kg/min)	Brain Dose (mJ/kg/day)				Whole-Body Dose (mJ/kg/day)			
	Value	Value	Mean (SD)	Value	Value	Mean (%)	Min	Median	Max	Mean (%)	Min	Median	Max
GSM [1] mobile phone calls without headset	3.198	0.411	7.6 (13.0)	191.88	24.66	–	–	–	–	–	–	–	–
GSM [1] mobile phone calls with headset	0.003198	0.411	1.9 (7.6)	0.19	24.66	–	–	–	–	–	–	–	–
GSM [1] mobile phone calls headset considered [2]	–	–	9.5 (16.7)	–	–	1451.78 (94.6%)	0.00	601.90	22587.02	234.47 (73.3%)	0.00	85.14	3785.98
UMTS mobile phone calls without headset	0.023	0.003	5.8 (14.8)	1.38	0.18	–	–	–	–	–	–	–	–
UMTS mobile phone calls with headset	0.000023	0.003	1.9 (8.1)	0.001	0.18	–	–	–	–	–	–	–	–
UMTS mobile phone calls headset considered [2]	–	–	7.7 (19.9)	–	–	8.04 (0.5%)	0.00	2.57	217.49	1.39 (0.4%)	0.00	0.37	34.20
DECT phone calls without eco mode	0.373	0.051	–	22.38	3.06	–	–	–	–	–	–	–	–
DECT phone calls with eco mode	0.0373	0.0051	–	2.24	0.31	–	–	–	–	–	–	–	–
DECT phone calls eco mode considered [3]	–	–	9.0 (10.9)	–	–	74.10 (4.8%)	0.00	18.70	1364.86	10.13 (3.2%)	0.00	2.61	190.28
Mobile phone data traffic	0.000092	0.012	11.5 (22.5)	0.01	0.72	0.06 (0.004%)	0.00	0.01	0.54	8.29 (2.6%)	0.00	1.63	70.89
Mobile phone close to the body (passive data traffic) [4]	0.000092	0.012	265.2 (349.5)	0.00006	0.01	0.01 (0.001%)	0.00	0.01	0.08	1.91 (0.6%)	0.00	0.86	10.37
Mobile phone data traffic WLAN	0.000092	0.012	30.6 (35.0)	0.01	0.72	0.17 (0.01%)	0.00	0.10	0.54	22.03 (6.9%)	0.00	13.68	70.89
Computer, laptop and tablet use with WLAN	0.000092	0.012	57.6 (83.3)	0.01	0.72	0.32 (0.02%)	0.00	0.17	3.42	41.46 (13.0%)	0.00	21.60	446.40

[1] For calls with the mobile phone on the GSM network the mean of the SARs for the GSM900 and the GSM1800 network was used because there was no differentiation between GSM900 and GSM1800 network in the mobile phone operator data; [2] Headset considered means that the proportion of headset use was applied to the mobile phone call duration; [3] Eco mode of the DECT phone at home was considered for all calls if the DECT phone at home was equipped with eco mode and for no calls if the DECT phone at home had no eco mode; [4] A transmission of data for 0.01*exposure duration of carrying the mobile phone close to the body was assumed.

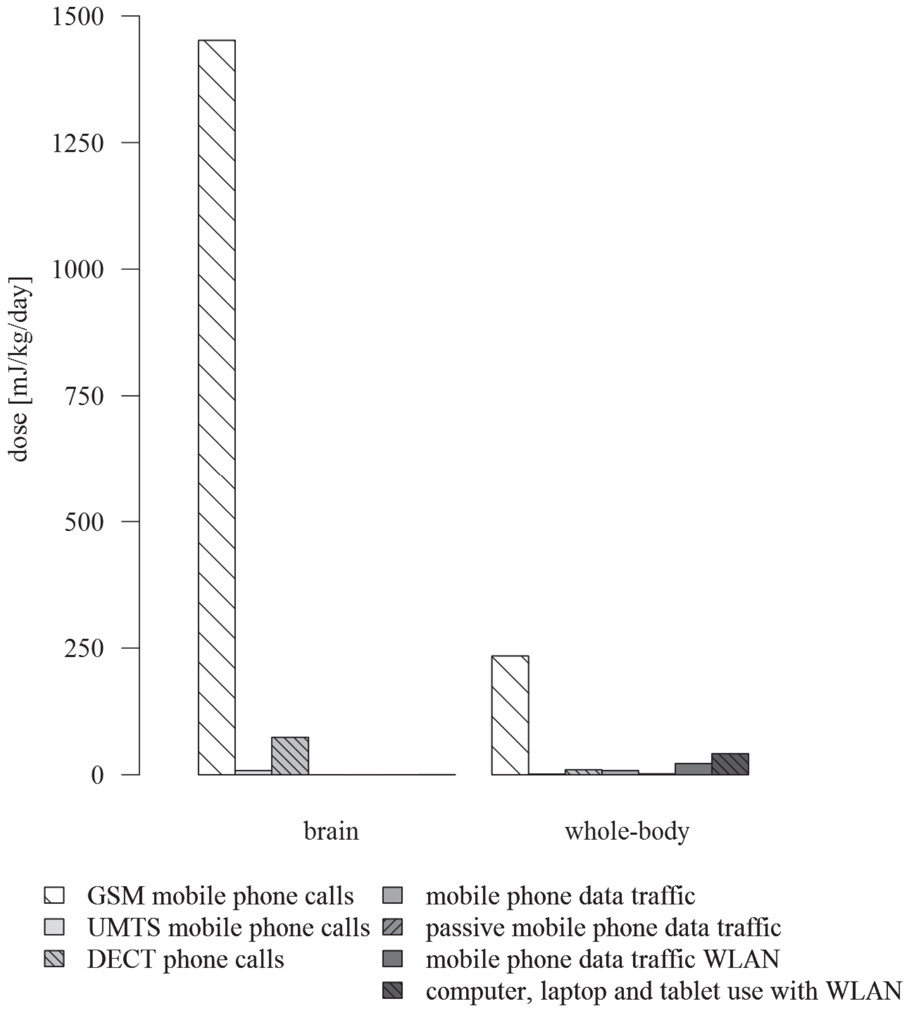

Figure 1. Mean daily cumulative *brain* (left) and *whole-body* (right) dose for the near-field predictors.

3.2. Far-Field Dose

3.2.1. Far-Field Predictors

Mean modelled downlink exposure of the HERMES study participants was 15.8 µW/m² (range: 0.0–476.9 µW/m²) at home and 10.4 µW/m² (0.003–67.1 µW/m²) in school (for details see Supplementary Table S1–Table S4). Mean values for radio broadcasting were 1.7 µW/m² (0.0–40.8 µW/m²) at home and 0.8 µW/m² (0.0–5.1 µW/m²) in school. For TV broadcasting modelled exposure was on average 0.5 µW/m² (0.0–32.1 µW/m²) at home and 0.06 µW/m² (0.0–0.7 µW/m²) in school. In other places (outdoors, in trains, buses and cars, and on locations not further defined in the diary) exposure, obtained from the personal measurements, was on average 46.2 µW/m² for downlink and 5.9 µW/m² for TV. Radio exposure was not measured by the used exposimeters and therefore taken into account only at home and in school. Identification of far-field predictors by multivariable regression models was based on personal measurements for 23.0–121.2 h (measurement duration of 71.2 h on average) from 95 HERMES participants.

When comparing personal measurements with modelling building characteristics, wall and window frame material, window glazing, window and building age, and façade renovation were not found to modify personal radio, TV or downlink indoor exposure at home or in school. Therefore, we did not take into account any building characteristics.

For the DECT far-field exposure no explanatory variable was associated with the measured DECT exposure from the personal measurements. For that reason, we decided to use the DECT measurements without modification using the average DECT exposure at home from the personal measurements which was 1.18 μW/m².

The identified far-field predictors for the WLAN and the uplink far-field exposure together with the derived exposure contribution per day were:

- Availability of WLAN in school: +0.49 μW/m² (WLAN);
- Availability of WLAN at home and not switching off the base station during night: +1.02 μW/m² (WLAN);
- Number of smartphones used at home: +9.39 μW/m² per smartphone (Uplink);
- Time spent in trains: +0.07 μW/m² per minute spent in trains (WLAN), +1.06 μW/m² per minute spent in trains (Uplink);
- Time spent in buses: +0.64 μW/m² per minute spent in buses (Uplink).

For details see Supplementary Material 1.

3.2.2. Far-Field Dose

The cumulative dose was highest for downlink and uplink for both brain and whole-body dose, whereas dose contributions from radio, TV, WLAN and DECT were small compared to the contributions from downlink and uplink (Table 4 and Table 5). The downlink dose was 8.43 mJ/kg per day (33.5%) for the brain and 6.16 mJ/kg per day (30.4%) for the whole-body. The uplink dose was 15.22 mJ/kg per day (60.4%) for the brain and 12.38 mJ/kg per day (61.2%) for the whole-body. It was mainly the exposure at home and other places (outdoors, in trains, buses and cars and locations not further defined in the diaries) that contributed to the downlink exposure (Figure 2). Being at home and, to a smaller extent, spending time in trains and buses contributed to the uplink exposure whereas a considerable part remained unexplained.

Table 4. *Brain* SAR, mean and derivation of the power flux density, *brain* dose rate (dose per 1 min) and mean (with the corresponding percentage of the total brain far-field dose), minimum, median and maximum of the *brain* dose for the far-field exposure.

Band	Description	SAR ((mW/kg)/(mW/m²))	Power Flux Density (mW/m²)		Dose Rate ((mJ/kg)/(mW/m²)/min)	Dose (mJ/kg/day)			
			Mean	Derivation		Mean (%)	Min	Median	Max
Radio [1]	Radio broadcast transmitter	0.001	0.002	modelling	0.09	0.16 (0.6%)	0.00	0.07	3.30
TV	Television broadcast transmitter	0.008	0.001	modelling and personal measurements	0.46	0.79 (3.1%)	0.58	0.58	14.40
Downlink 900	Transmission from base station to mobile phone handset	0.007	–	–	0.41	–	–	–	–
Downlink 1800	Transmission from base station to mobile phone handset	0.003	–	–	0.19	–	–	–	–
Downlink 2100	Transmission from base station to mobile phone handset	0.003	–	–	0.17	–	–	–	–
Downlink	Downlink 900+ Downlink 1800+ Downlink 2100	–	0.019	modelling and personal measurements	–	8.43 (33.5%)	3.76	5.02	124.64
WLAN	Wireless local area network	0.002	0.002	prediction regression model	0.14	0.39 (1.6%)	0.20	0.40	2.37
DECT	Digital enhanced cordless telecommunications	0.003	0.001	personal measurements	0.17	0.19 (0.8%)	0.19	0.19	0.19
Uplink [2]	Transmission from mobile phone handset to base station	0.004	0.041	prediction regression model	0.26	15.22 (60.4%)	2.96	13.54	71.16

[1] Radio = radio FM (Frequency Modulation) + DAB (Digital Audio Broadcasting); Radio was considered only at home and in school (geospatial propagation modelling) because used exposimeters did not measure radio broadcasting; [2] Uplink = Uplink 900+ Uplink 1800+ Uplink 1900; For the far-field uplink exposure from other mobile phones the average of the SARs for the downlink bands downlink 900, downlink 1800 and downlink 2100 was used.

Table 5. *Whole-body* SAR, mean and derivation of the power flux density, *whole-body* dose rate (dose per 1min) and mean (with the corresponding percentage of the total whole-body far-field dose), minimum, median and maximum of the *whole-body* dose for the far-field exposure.

Band	Description	SAR ((mW/kg)/(mW/m²))	Power Flux Density (mW/m²)		Dose Rate ((mJ/kg)/(mW/m²)/min)	Dose (mJ/kg/day)			
			Mean	Derivation		Mean (%)	Min	Median	Max
Radio [1]	Radio broadcast transmitter	0.005	0.002	modelling	0.29	0.54 (2.7%)	0.00	0.22	11.30
TV	Television broadcast transmitter	0.005	0.001	modelling and personal measurements	0.27	0.47 (2.3%)	0.35	0.35	8.61
Downlink 900	Transmission from base station to mobile phone handset	0.004	–	–	0.26	–-	–	–	–
Downlink 1800	Transmission from base station to mobile phone handset	0.003	–	–	0.20	–	–	–	–
Downlink 2100	Transmission from base station to mobile phone handset	0.003	–	–	0.18	–	–	–	–
Downlink	Downlink 900+ Downlink 1800+ Downlink 2100	–	0.019	modelling and personal measurements	–	6.16 (30.4%)	2.46	3.47	86.19
WLAN	Wireless local area network	0.003	0.002	prediction regression model	0.17	0.48 (2.4%)	0.24	0.49	2.90
DECT	Digital enhanced cordless telecommunications	0.003	0.001	personal measurements	0.18	0.20 (1.0%)	0.20	0.20	0.20
Uplink [2]	Transmission from mobile phone handset to base station	0.004	0.041	prediction regression model	0.21	12.38 (61.2%)	2.41	11.01	57.87

[1] Radio = radio FM (Frequency Modulation) + DAB (Digital Audio Broadcasting); Radio was considered only at home and in school (geospatial propagation modelling) because used exposimeters did not measure radio broadcasting; [2] Uplink = Uplink 900+ Uplink 1800+ Uplink 1900; For the far-field uplink exposure from other mobile phones the average of the SARs for the downlink bands downlink 900, downlink 1800 and downlink 2100 was used.

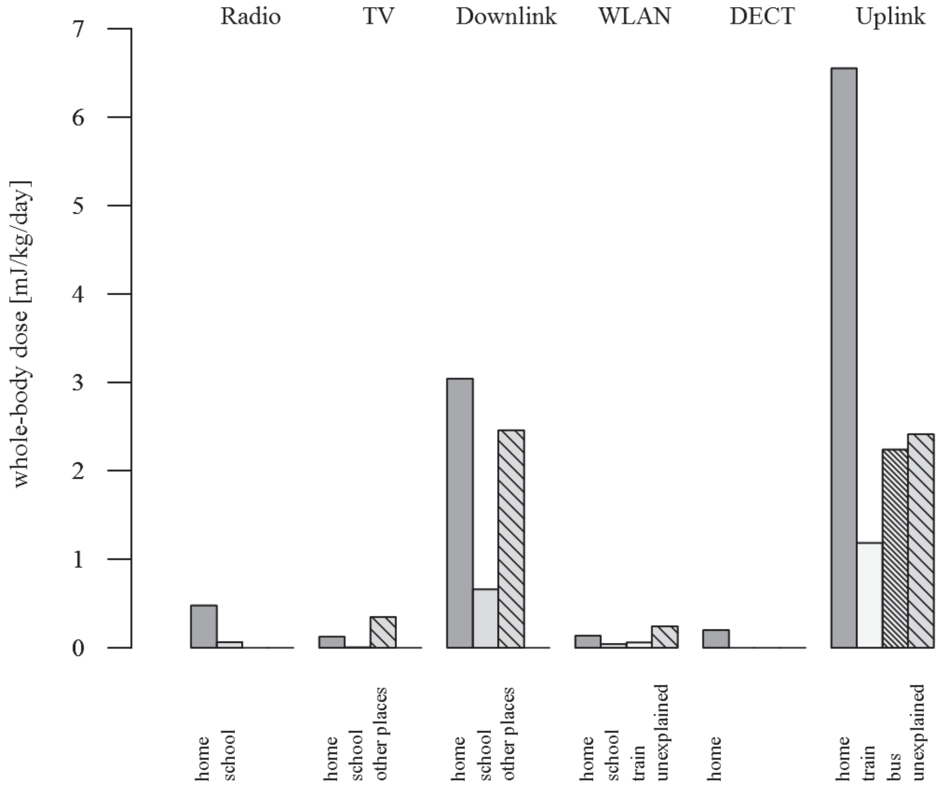

Figure 2. Mean daily cumulative *whole-body* dose for the far-field exposure at different locations; The same pattern was found for the *brain* dose.

3.3. Combining Near-Field and Far-Field Dose

The mean brain dose for the HERMES study participants was 1559.7 mJ/kg per day (range: 13.3–22,607.6 mJ/kg/day) whereas the mean whole-body dose was 339.9 mJ/kg per day (6.5–4064.7 mJ/kg/day). The near-field component counted on average for far the most of the total dose, 98.4% (1534.5 mJ/kg/day) of the total brain dose and 94.0% (319.7 mJ/kg/day) of the total whole-body dose originated from near-field sources. For the three HERMES study participants, a non-user, a normal user and a heavy-user, considerable differences in the cumulative dose and in the proportion of the far-field dose on the total dose were found (Figure 3).

Total brain white matter dose was on average 535.0 mJ/kg per day. This corresponded to 34.3% of the total average brain gray matter dose (1559.7 mJ/kg/day). The proportional contributions of the particular near-field exposure predictors and far-field bands were similar to the brain gray matter dose. The proportion of the near-field dose on the total dose was similar as well (98.4%).

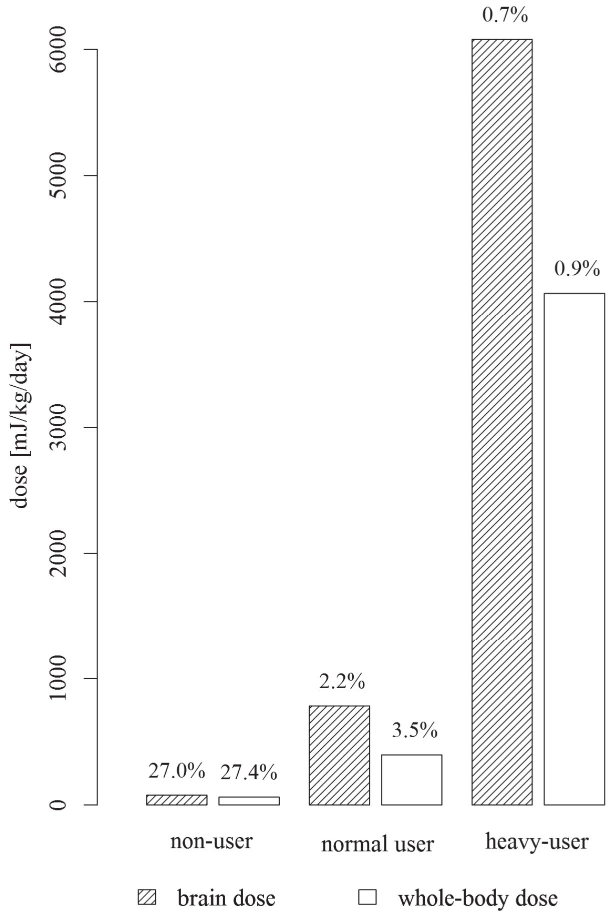

Figure 3. Total brain and whole-body dose for the three HERMES study participants (non-user, normal user, heavy-user); Percentages of the far-field dose on the total dose are indicated above the bars.

3.4. Comparing Dose Calculations and Personal Measurements

In Figure 4 dose predictions are compared with personal measurements. With respect to total dose (first row of Figure 4) there was a slight tendency that the group median of the personal measurements increased with increasing predicted dose. The Spearman correlation between the dose and the mean of the personal measurements was 0.10 (p-value = 0.34) for the brain dose and 0.05 (p-value = 0.63) for the whole-body dose. For the far-field dose the picture was similar, but with a slightly higher correlation of 0.18 (p-value = 0.08) for the brain far-field dose and 0.17 (p-value = 0.09) for the whole-body far-field dose (second row of Figure 4). If taking into account only the downlink dose and the downlink measurements (third row of Figure 4) the mean and the median of the measurements were clearly increased for increasing predicted dose. The Spearman correlation was 0.53 (p-value < 0.0001) for the brain downlink dose and 0.52 (p-value < 0.0001) for the whole-body downlink dose.

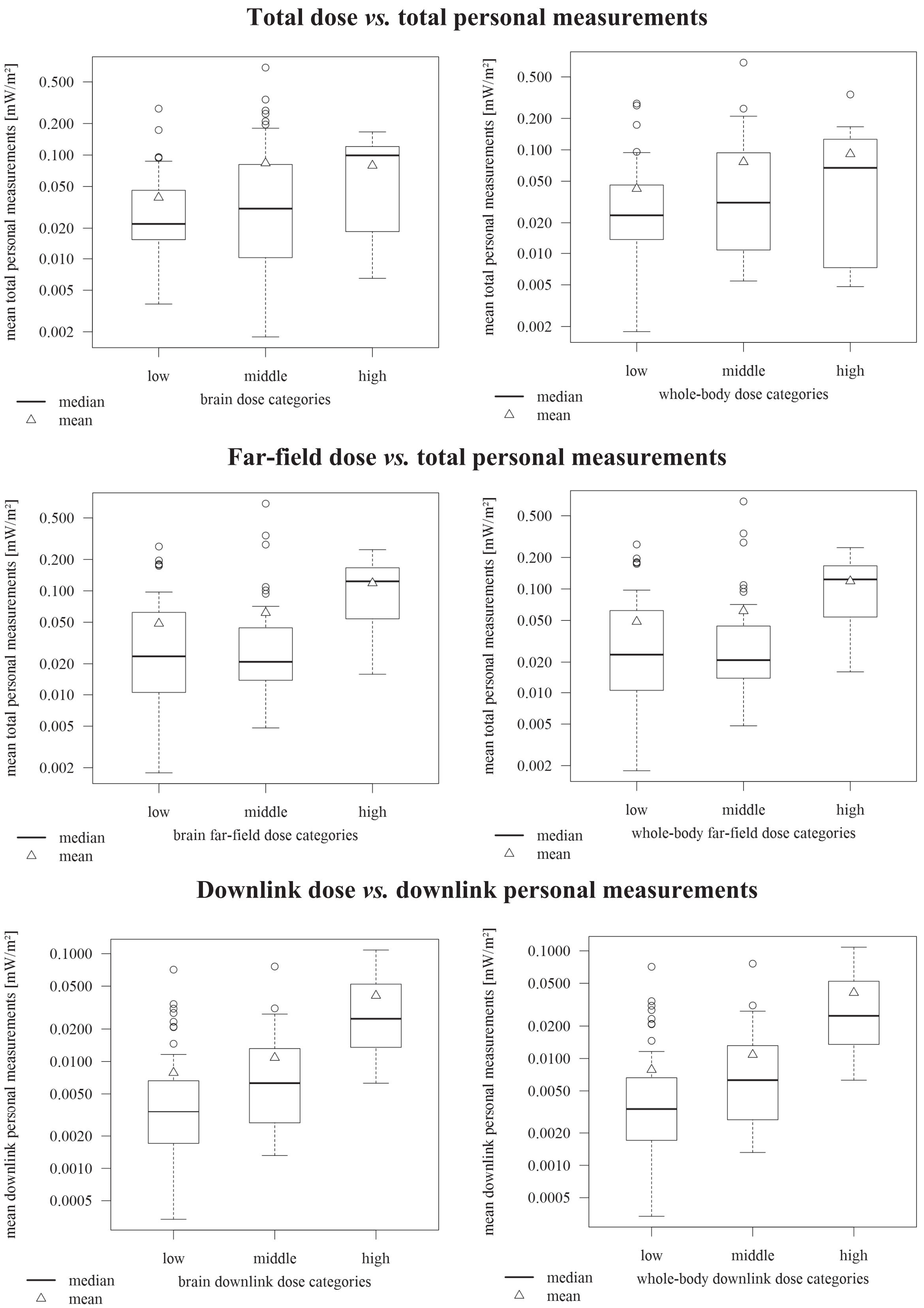

Figure 4. Comparison of predicted dose measures and personal measurements using the three dose categories <50th percentile (low), 50th–90th percentile (medium) and >90th percentile (high); First row: total dose *vs.* total personal measurements; Second row: far-field dose *vs.* total personal measurements; Third row: downlink dose *vs.* downlink personal measurements.

4. Discussion

The aim was to develop an integrative exposure surrogate consisting of a near-field and a far-field component representing together total personal RF-EMF dose. Thus we combined near-field exposure from the use of wireless communication devices and far-field exposure from environmental sources such as fixed site transmitters, WLAN and DECT base stations and other people's mobile phones in the surroundings to one single RF-EMF exposure measure.

4.1. Near-Field Exposure

We found GSM mobile phone calls contribute by far the most to the near-field exposure from the use of wireless communication devices. For the brain exposure, DECT phone calls and to a less extent UMTS mobile phone calls contributed as well. Mobile phone data traffic and computer, laptop and tablet use with WLAN played a minor role. For the whole-body exposure computer, laptop and tablet use with WLAN and mobile phone data traffic via WLAN contributed as well, followed by DECT phone calls and mobile phone data traffic via mobile internet connection. UMTS mobile phone calls played a minor role.

4.2. Far-Field Exposure

Far-field exposures from radio and TV broadcast transmitters and mobile phone base stations were estimated using geospatial propagation modelling. We did not find any influence of building characteristics on the personal measurements taken at home and in school. This is in contrast to our previous study where metal window frames and concrete walls resulted in a significant exposure reduction [14]. However, our finding is in line with a recent study on modelled mobile phone downlink exposure in the city of Amsterdam, Netherlands, where none of the building characteristics could explain additional variance of the modelled values [26]. We found the availability of WLAN at home and not switching off the base station during night and the availability of WLAN in school being relevant exposure predictors. Furthermore, the time spent in trains explained part of the measured WLAN exposure. Because of the increase of WLAN in public spaces and public transport this part of WLAN exposure may become even more important in the future. The number of smartphones being used at home was the strongest predictor for the far-field uplink exposure followed by the time spent in trains and buses. A considerable part of the uplink exposure however remained unexplained. Previous studies have also demonstrated high uplink exposure in public transport [27–29] or investigated the influence of small cells in trains on the exposure of mobile phone users [30]. The relevance of mobile phones in stand-by mode for exposure is still quite unclear. Urbinello *et al.* demonstrated that personal RF-EMF exposure was affected by one's own mobile phone in stand-by mode because of its regular location updates and push functions implemented in applications [29]. This finding may explain why the number of smartphones at home is one of the exposure relevant predictors. And, additionally, this finding led us to include passive mobile phone data traffic for the near-field exposure estimate. Carrying a mobile phone on the body contributed on average 0.56% to the total whole-body exposure of the HERMES participants.

The contribution of the far-field exposure is small compared to the contribution of the near-field exposure (1.6% of the brain dose and 6.0% of the whole-body dose originated from far-field sources). Nevertheless, far-field exposure is relevant: There are public concerns about potential health effects related to mobile phone base stations [31] and exposure from broadcast transmitters and mobile phone base stations is not lifestyle related which complicates the investigation of soft outcomes (e.g., symptoms and behaviour). Furthermore, far-field exposure is long-term and continuous and people are exposed during night as well, which might be a critical time window. Therefore we think it is worth the effort to investigate far-field exposure as well.

4.3. Comparing Dose Calculations and Personal Measurements

In our exposure assessment approach we combined questionnaire data, operator data, modelling and personal measurements from a subsample. This is more efficient than conducting personal measurements in a large sample which is very time- and resource-consuming. Furthermore, near-field exposure from the use of wireless communication devices is not recorded adequately by personal measurements because the measured values depend highly on the distance between the emitting device and the exposimeter, which is not necessarily the same as the distance between the emitting device and the body [4,5]. Only the latter is relevant for exposure. This may also explain why we found only a small correlation between predicted brain and whole-body exposure and personal measurements (Figure 4). For both exposure proxies, the brain dose and the whole-body dose, GSM mobile phone calls are most relevant, but the resulting exposure is not measured accurately with exposimeters during personal measurements [4,5]. However, the predicted far-field dose was also only weakly correlated with personal measurements. This may have several reasons. First, radio broadcasting is not measured by the exposimeters used but modelled at home and in school and thus considered for the dose. Nevertheless, this contribution is small and cannot explain the discrepancy. Second, the prediction models for the WLAN and uplink far-field exposure have limited explanatory power and for DECT no exposure predictor could be identified at all. Thus, there is more work needed to figure out what predictors are able to predict these exposures in a more accurate way. Strikingly, the downlink dose and the personal downlink exposure measurements correlated well. Thus, modelled exposure at home and in school may well be used to predict downlink exposure.

Obviously, the dose calculations are subject to a large uncertainty. We relied our calculations on self-reported amount of mobile phone use, which is typically overestimated by adolescents [32,33]. In our study, overestimation was on average by a factor of 9.3 according to a comparison with operator recorded duration of mobile phone calls. Subsequent dose estimations for our study sample with operator recorded mobile phone data yielded on average a brain gray matter dose of 139.3 mJ/kg per day and a whole-body dose of 24.9 mJ/kg per day for mobile phone calls (brain dose of 1459.8 mJ/kg/day and whole-body dose of 235.9 mJ/kg/day for self-reported duration of mobile phone calls). For the normal user, the proportion of the far-field dose on the total dose was 9.4% for the brain dose and 4.3% for the whole-body dose if taking into account operator recorded duration of mobile phone calls (2.2% and 3.5% for the brain and the whole-body dose, respectively for self-reported duration of mobile phone calls, Figure 3).

We have obtained SAR values from the literature, however, such data are still rare and have a large uncertainty range. Unfortunately, systematic analyses of this uncertainty are not yet published and could thus not be considered in our study. Most of the uncertainty is due to the unknown position of the device in relation to the body. Ideally, this should be measured permanently for each study participant. However, this is impossible and one has thus to rely on assumptions about typical positions. A further source of uncertainty is the emitted output power of mobile phones, in particular during data transmission and in stand-by mode. Depending on the type of data transmission (e.g., watching videos and playing games while connected to the internet, using social networks and reading news), a mobile phone may mainly act as receiver or transmitter. We did not find any data about proportion of time the mobile phone is transmitting data when set in stand-by mode, and which factors are relevant for these emissions. Additional uncertainty remains regarding SARs for newer devices such as tablets. Due to lack of data, we did not take into account exposure from use of the mobile phone as mobile hotspot. Inherent uncertainties are related to the geospatial propagation modelling and predictions derived from the personal measurements. Also the assessment of the proportion of calls made on the GSM and UMTS network comes with uncertainties.

5. Conclusions

Despite all these uncertainties and limitations, the proposed approach is considered useful to combine near-field and far-field exposure to one single integrative exposure surrogate either for the whole-body or for specific organs. However, more work is needed to deepen the understanding of far-field exposure predictors on one hand and near-field exposure from rapidly developing devices such as smartphones and tablets on the other hand. If this approach is refined, the integrative exposure surrogate can be adapted to any population of epidemiologic studies if modelled RF-EMF exposure from fixed site transmitters for the study area, operator data including type of network and specific questionnaire data are available.

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Author Contributions

Martin Röösli conceived and designed the study; Anna Schoeni and Katharina Roser conducted the study; Alfred Bürgi was responsible for the geo-spatial propagation model; Katharina Roser analyzed the data; Katharina Roser wrote the paper.

Conflicts of Interest

The authors declare no conflict of interest. The founding sponsors had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, and in the decision to publish the results.

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Development of an RF-EMF Exposure Surrogate for Epidemiologic Research

Table S1. WLAN prediction model: predicted far-field WLAN exposure contribution from a multivariable regression model using bootstrap (1000 replications), n = 95.

Mean WLAN Personal Measurements (µW/m²)	Exposure Contribution (µW/m²)	95% Confidence Interval	*p*-Value
WLAN in school	0.49	(−1.29, 2.26)	0.589
WLAN at home and not switched off during night	1.02	(−0.80, 2.83)	0.272
Time spent in trains (min/day)	0.07	(−0.06, 0.19)	0.290
Unexplained by the model	1.00	(−0.51, 2.52)	0.195

Table S2. Uplink prediction model: predicted far-field uplink exposure contribution from a multivariable regression model using bootstrap (1000 replications), n = 95.

Mean Uplink Personal Measurements (µW/m²)	Exposure Contribution (µW/m²)	95% Confidence Interval	*p*-Value
Number of smartphones at home	9.39	(−6.33, 25.12)	0.242
Time spent in trains (min/day)	1.06	(0.24, 1.87)	0.011
Time spent in buses (min/day)	0.64	(−0.02, 1.30)	0.057
Unexplained by the model	7.89	(−18.40, 34.18)	0.556

Table S3. Mean exposure duration (per day) of the different locations for the calculation of the far-field dose.

Location	Mean Exposure Duration (per day)
Home day [1]	8 h 21 min
Home night [1]	7 h 21 min
Home	15 h 41 min
School	4 h 43 min
Outside	1 h 41 min
Train	0 h 6 min
Bus	0 h 9 min
Car	0 h 13 min
Unspecified location [2]	1 h 27 min

[1] Home day and night: Home day means the time being at home in the time period 6:00 until 22:00; Home night means the time being at home in the time period 22:00 until 6:00; [2] Unspecified location means diary entries recorded as miscellaneous or other activity or location than the prespecified activities and locations in the time-activity diary.

Table S4. Measured, modelled or predicted mean power flux densities (µW/m²) at the different locations for the calculation of the far-field dose.

Band	Description	Power Flux Density (µW/m²)									
		Home Day [2]	Home Night [2]	Home	School	Outside	Train	Bus	Car	Unspecified Location [3]	Unexplained [4]
Radio [1]	Radio broadcast transmitter	1.73	1.73	–	0.77	–	–	–	–	–	–
TV	Television broadcast transmitter	0.48	0.48	–	0.06	4.14	7.25	24.70	4.38	6.16	–
Downlink 900	Transmission from base station to mobile phone handset	6.52	4.32	–	4.98	35.80	64.30	31.60	16.60	27.60	–
Downlink 1800	Transmission from base station to mobile phone handset	5.15	3.97	–	3.56	5.18	8.49	7.80	5.09	9.89	–
Downlink 2100	Transmission from base station to mobile phone handset	5.81	4.15	–	1.90	6.88	15.20	16.30	3.21	6.09	–
WLAN	Wireless local area network	–	–	0.56	0.18	–	0.24	–	–	–	1.00
DECT	Digital enhanced cordless telecommunications	–	–	1.18	–	–	-	–	–	–	–
Uplink [5]	Transmission from mobile phone handset to base station	–	–	21.48	–	–	3.88	7.33	–	–	7.89

For RF-EMF a power flux density of 1 µW/m² = 0.001 mW/m² corresponds to an electric field strength of 0.019 V/m; [1] Radio = radio FM (Frequency Modulation) + DAB (Digital Audio Broadcasting); Radio was considered only at home and in school (geospatial propagation modelling) because used exposimeters did not measure radio broadcasting; [2] Home day and night: Home day means the time being at home in the time period 6:00 until 22:00; Home night means the time being at home in the time period 22:00 until 6:00; [3] Unspecified location means diary entries recorded as miscellaneous or other activity or location than the prespecified activities and locations in the time-activity diary; [4] Unexplained means the part of the predicted WLAN and uplink power flux density not explained through the relevant far-field predictors found in the multivariable regression model used to predict WLAN and uplink exposure, respectively; [5] Uplink = Uplink 900 + Uplink 1800 + Uplink 1900.

4.2 Article 3: Memory performance, wireless communication and exposure to radiofrequency electromagnetic fields: a prospective cohort study in adolescents

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Memory performance, wireless communication and exposure to radiofrequency electromagnetic fields: A prospective cohort study in adolescents

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ABSTRACT

Background: The aim of this study is to investigate whether memory performance in adolescents is affected by radiofrequency electromagnetic fields (RF-EMF) from wireless device use or by the wireless device use itself due to non-radiation related factors in that context.

Methods: We conducted a prospective cohort study with 439 adolescents. Verbal and figural memory tasks at baseline and after one year were completed using a standardized, computerized cognitive test battery. Use of wireless devices was inquired by questionnaire and operator recorded mobile phone use data was obtained for a subgroup of 234 adolescents.

RF-EMF dose measures considering various factors affecting RF-EMF exposure were computed for the brain and the whole body.

Data were analysed using a longitudinal approach, to investigate whether cumulative exposure over one year was related to changes in memory performance. All analyses were adjusted for relevant confounders.

Results: The kappa coefficients between cumulative mobile phone call duration and RF-EMF brain and whole body dose were 0.62 and 0.67, respectively for the whole sample and 0.48 and 0.28, respectively for the sample with operator data. In linear exposure–response models an interquartile increase in cumulative operator recorded mobile phone call duration was associated with a decrease in figural memory performance score by −0.15 (95% CI: −0.33, 0.03) units. For cumulative RF-EMF brain and whole body dose corresponding decreases in figural memory scores were −0.26 (95% CI: −0.42, −0.10) and −0.40 (95% CI: −0.79, −0.01), respectively. No exposure-response associations were observed for sending text messages and duration of gaming, which produces tiny RF-EMF emissions.

Conclusions: A change in memory performance over one year was negatively associated with cumulative duration of wireless phone use and more strongly with RF-EMF dose. This may indicate that RF-EMF exposure affects memory performance.

1. Introduction

The use of mobile phones has increased remarkably during the last few years especially in children and adolescents. In 2012, 95% of 12 to 19 years old Swiss adolescents owned a mobile phone (Willemse et al., 2012) and two years later, the proportion had increased to 98% (Willemse et al., 2014). This increase has been accompanied by a growing public concern that radiofrequency electromagnetic fields (RF-EMF) emitted by mobile phones and other sources involved in wireless technology have negative impacts on cognitive functions such as memory. In particular, young people have become the focus of increased attention since memory is important in the context of learning. Memory is involved in storing and retrieving information, and is basically considered as the record left by a learning process (Mc Gill University, 2015).

Studies that investigated a possible effect of RF-EMF exposure on memory tasks in children or adolescents are limited to four experimental studies on acute effects and one epidemiological study. All of these studies focused on reaction time and accuracy of memory. In a double blind randomized crossover trial of thirty-two 10–14 years old adolescents Haarala et al. (2005) revealed no significant effects in the accuracy of any working memory task during a 50 minute exposure to a GSM 900 mobile phone. Using the same exposure conditions Preece et al. (2005) found trends toward higher accuracy in memory tasks in 18 adolescents (10–12 years) participating in a three way crossover experiment. However, none of the results reached statistical significance. Movvahedi et al. (2014) showed that after a mobile phone talk period of 10 min,

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short term memory score in a visual reaction time test increased compared to sham condition in 60 elementary school children. In contrast, in a double-blind crossover study of forty-one 13–15 year old adolescents UMTS (3rd generation Universal Mobile Telecommunications System) but not GSM (2nd generation Global System for Mobile Communications) exposure was associated with an 8.4% accuracy decrement in a working memory task (N-back task) compared to sham condition (Leung et al., 2011). The reaction time, however, was not affected. One limitation in all of these studies was the small sample size and the short exposure duration addressing acute effects only. From a public health point of view potential effects of chronic exposure are more relevant, which needs to be investigated with epidemiological studies. So far there has only been one community-based epidemiological study investigating effects of mobile phone use on adolescents' memory. Abramson et al. (2009) showed in a cross-sectional analysis of 317 seventh grade students from Australia that mobile phone use was associated with faster and less accurate response on a number of tasks involving the memory. Since similar associations were found in relation to the number of SMS (short text messages), which produces negligible RF-EMF exposure, they speculated that these behaviours may have been learned through the frequent use of a mobile phone and may not be the consequence of mobile phone radiation. In a follow-up investigation one year later, in 236 of these students, an increase in mobile phone use was associated with a reduction in response time in one out of three tests involving the memory (Thomas et al., 2010). This study relied on self-reported mobile phone use only, which has been shown to be inaccurate. Adolescents tend to substantially overestimate their amount of mobile phone use (Aydin et al., 2011; Inyang et al., 2009).

Regular mobile phone use may affect adolescents in various ways. Thus, the main challenge for research consists in differentiating between RF-EMF radiation effects and other non-RF-EMF related effects from mobile phone use. For instance, frequent texting or gaming on a mobile phone may facilitate cognitive processes (Abramson et al., 2009). It was also observed, that calling and sending texts during night was associated with poor perceived health symptoms such as tiredness, rapid exhaustibility, headache and physical ill-being (Schoeni et al., 2015; Van den Bulck, 2007). Other studies showed that frequent mobile phone use was associated with anxiety (Jenaro et al., 2007), unhealthy lifestyle (Ezoe et al., 2009), depression (Yen et al., 2009) and psychological distress (Beranuy et al., 2009). Thus, to address RF-EMF effects of wireless communication devices, the development of a RF-EMF dose measure, which incorporates all exposure relevant factors, is inevitable. One major factor determining RF-EMF exposure is the type of network used to make a mobile phone call. Calls on the UMTS network cause on average 100–500 times less exposure than calls on the GSM network (Gati et al., 2009). This implies that cumulative RF-EMF exposure is not just a function of the duration of mobile phone use. In Switzerland both types of network are used and with the help of objectively recorded mobile phone use data provided by mobile phone operators and personal RF-EMF measurements, an integrative RF-EMF dose measure for the brain and whole body suitable for epidemiological research was calculated (Roser et al., 2015).

By applying this RF-EMF dose measure to the prospective HERMES (Health Effects Related to Mobile phonE use in adolescentS) cohort study, we thus aimed to investigate whether memory performance is affected by cumulative RF-EMF emitted from wireless communication devices.

2. Methods

2.1. Study population

For the present study, adolescents from 7th, 8th and 9th grade in schools from rural and urban areas in Central Switzerland were recruited. The baseline investigation took place between June 2012 and February 2013. During a school visit the adolescents filled in a questionnaire and performed a memory test using a standardized, computerized cognitive testing system (Liepmann et al., 2006). Additionally parental questionnaires were distributed, which included questions, among others, on the behaviour of their children, on socio-economic factors, on wireless technology at home and on child development. Parents were asked to fill out the questionnaire and send it back directly. This procedure was repeated one year later with the same study participants and the same study managers.

A subgroup of 95 study participants participated in personal measurements. The adolescents carried a portable measurement device, a so-called exposimeter, and kept a diary on a time-activity diary application installed on a smartphone in flight-mode for about three consecutive days. The study was approved by the ethical committee of Lucerne, Switzerland (Dienststelle Gesundheit, Ethikkommission des Kantons Luzern, Schweiz) on May 9th, 2012 (Ref. Nr. EK: 12025).

2.2. Memory

Memory performance was assessed with a standardized, computerized cognitive test battery (IST, *Intelligenz-Struktur-Test 2000R* (Liepmann et al., 2006)). Verbal and figural memory was measured with the subtest of the IST. In the verbal memory task, word groups have to be memorized in one minute time. After 1 min the study participants give an account of the word groups that have been memorized. In total 10 points can be achieved by remembering the correct word groups. In the figural memory task, pairwise symbols have to be memorized in one minute time. After 1 min one part of the pairwise symbols is shown and the matching part has to be found. A total of 13 points can be achieved. For both the verbal and figural tests, 2 min is given to complete the test. Memory performance is considered as the right number of remembered word groups or symbols, respectively. For the statistical analyses of verbal and figural memory the continuous test score values were used as outcome. Every test was conducted once at baseline and once at follow-up investigation.

2.3. Exposure data

In this study we considered objectively recorded data on mobile phone use collected from the Swiss mobile phone operators as well as self-reported data on wireless communication devices usage obtained from a written questionnaire referring to the 6 months period prior to each examination. In terms of RF-EMF related exposure measures we inquired about call duration with own or any other mobile phone (referred to as duration mobile phone calls), call duration with cordless (fixed line) phone and duration of data traffic on the mobile phone, e.g. for surfing and streaming. The duration of gaming on computers and TV and number of all kind of text messages (SMS, WhatsApp etc.) are not, or only marginally relevant for RF-EMF exposure and were thus inquired to be used as negative exposure control variables in the analyses.

Informed consent to obtain objectively recorded mobile phone use data from the mobile phone operators was given by 234 out of 439 study participants and their parents. This included duration of each call and on which network (GSM or UMTS) it started, number of SMS (text messages) sent per day and amount of volume of data traffic (MB/day). Data were obtained for up to 18 months, 6 months before baseline until follow-up investigation.

2.4. RF-EMF dose measures

To be able to calculate a RF-EMF dose of the brain and the whole body of the participating adolescents, an integrative RF-EMF exposure surrogate including various factors affecting near-field and far-field RF-EMF exposure was developed, which is described in detail in Roser et al. (2015). The near-field component combines the exposure from the use of wireless devices (mobile phones, cordless phones, computer/ laptop/tablet connected to wireless internet (WLAN)). For mobile phone calls we also considered the type of network that was used for each call, either directly obtained from the operator data or estimated for self-reported data by mixed linear regression models with school as cluster variable calibrated on the operator data using the following predictors: type of mobile phone operator, use of mobile internet on mobile phone (yes/no) and modelled UMTS exposure levels at home. The far-field component aggregates the exposure from environmental sources, which were derived from propagation modelling for radio and TV broadcast transmitters as well as for mobile phone base stations (Bürgi et al., 2010; Bürgi et al., 2008). Exposure from cordless phone base stations, WLAN access points and other people's mobile phones were estimated by linear regression models calibrated on the personal measurement data available from 95 study participants (Roser et al., 2015).

For each of these exposure situations, specific absorption rates (SAR) for the brain and the whole body were obtained from the literature (Gati et al., 2009; Hadjem et al., 2010; Huang et al., 2014; Lauer et al., 2013; Persson et al., 2012; SEAWIND, 2013; Vrijheid et al., 2009). To obtain a brain and whole body dose for each study participant the obtained SAR values were multiplied by the average exposure duration per day for each exposure situation and summed up to one single brain and whole body dose. This calculation was done twice: first, for the whole sample using self-reported duration for mobile phone calls; and second, for the subsample with operator recorded data mobile phone call duration was derived from the mobile phone operator records. As a result we got a brain and whole body dose measure based on self-reported mobile phone call duration for the whole cohort (dose for the whole sample) and a brain and whole body dose measure based on objectively recorded mobile phone call duration (dose for the sample with operator data) for the subgroup of study participants with operator recorded mobile phone data. All other RF-EMF dose factors were the same for both calculations.

2.5. Cumulative data

To obtain the cumulative objective exposure variables (volume of data traffic, mobile phone call duration and number of SMS sent), data from the whole period between baseline and follow-up investigation were summed up and divided by the time between baseline and follow-up investigation. For all self-reported exposure variables and dose measures a mean between baseline and follow-up data was calculated. For the dose measures of the operator data sample, cumulative objective mobile phone call duration was considered. For easier conception, all cumulative dose and usage measures are expressed as averages per day (between baseline and follow-up).

2.6. Covariates

In the written questionnaires of the study participants, questions about age, sex, nationality, school level, numbers of days with physical activity, numbers of days with alcohol consumption and height were answered. The questionnaires of the parents included questions, among others, on socio-economic factors.

2.7. Statistical analysis

The aim of the longitudinal analysis was to investigate possible associations between changes in the figural and verbal memory performance score (follow-up minus baseline) with respect to cumulative media usage (referred to as usage related factors) or cumulative RF-EMF dose. The primary analysis was based on three exposure categories for all variables: exposure or dose below median (reference), 50th to 75th percentile and the top 25th percentile. In the secondary analysis, linear exposure–response associations were investigated using all exposure variables continuously and effect estimates were expressed per interquartile change in order to be able to compare between different variables.

Further, we conducted a laterality analysis for the brain dose in relation to the verbal and figural memory performance to account for the different brain hemispheres that are involved in these two tasks (Beason-Held et al., 2005; Strandberg et al., 2011). Because most of the study participants were right side user, we stratified the collective into right side users vs. left side users and users with no side preference.

All models were adjusted for age at follow-up, sex, nationality, school level (college preparatory high school or high school) at follow-up, physical activity at follow-up, alcohol consumption at follow-up, change in height between baseline and follow-up, duration between baseline and follow-up in months and education of the parents.

In a sensitivity analyses we repeated all analyses on objective data by including also participants that reported not to own a mobile phone either at baseline or at follow-up. Obviously, these participants could not provide operator data but their objectively recorded mobile phone use could be reliably assumed to be zero.

Linear regression imputation (10 missing values at follow-up for alcohol consumption; 7 missing values at baseline and 6 missing values at follow-up for information on height) or imputation of a common category (1 missing value at follow-up for frequency of physical activity; 60 missing values for educational level of the parents) was used to impute missing values in the confounder variables. Statistical analyses were carried out using STATA version 12.1 (StataCorp, College Station, USA). Figures were made with the software R using version R for Windows 3.0.1.

3. Results

439 students (participation rate: 36.8%) aged 12 to 17 years from 24 schools (participation rate: 19.1%) from rural and urban areas in Central Switzerland participated in the baseline investigation of the HERMES study. 412 (93.9%) study participants owned a mobile phone at baseline. In the follow-up investigation one year later, 425 study participants (participation rate: 96.8%) took part. Of those, 416 (97.9%) study participants owned a mobile phone.

Objectively operator recorded data for 234 study participants were obtained between baseline and follow-up investigation. The follow-up investigation was on average 12.5 months after baseline. The characteristics of the study participants and the results of the memory tests are listed in Table 1. The Supplementary Fig. S1 shows the distribution of the change in the verbal and figural memory tests between baseline and follow-up.

3.1. RF-EMF dose and usage related exposure

Table 2 shows the summary statistics of all exposure and dose measures. The large difference between mean operator recorded and mean self-reported mobile phone call duration is striking (16.0 vs. 1.9 min/ day). Self-reported mobile phone call duration in study participants with operator recorded mobile phone use data was 15.3 min/day, and still 13.3 min/day when subtracting calls that have been reported to be made on other people's mobile phones. Thus, self-reported call duration is 7 times higher than what is recorded by their operator. The large difference between operator recorded and self-reported text messages reflects the fact that adolescents send most of their text messages through internet-based apps instead of using the Short-Message-Service (SMS). Only latter messages are recorded by the operators.

Table 3 shows the kappa coefficients of all cumulative exposure surrogates and dose measures. A substantial correlation can be found between self-reported mobile phone call duration and brain dose of the whole sample (0.62). In line with the high discrepancy between self-reported and objectively recorded mobile phone call duration a somewhat lower agreement was found between objectively recorded mobile

Table 1
Characteristics and scores of the memory tests of the study participants at baseline and follow-up.

	Baseline	Follow-up
	N = 439	N = 425
	n (proportion)	n (proportion)
Male sex, n (%)	174 (39.6)	171 (40.2)
School level		
College preparatory high school	99 (22.5)	109 (25.6)
High school	340 (77.5)	316 (74.4)
Nationality		
Swiss	348 (79.3)	341 (80.2)
Swiss and other	62 (14.1)	59 (13.9)
Other	29 (6.6)	25 (5.9)
Physically active		
1–3 times per month or less	68 (15.5)	57 (13.4)
Once per week	91 (20.7)	90 (21.2)
2–3 times per week	156 (35.5)	170 (40.0)
4–6 times per week	85 (19.4)	74 (17.4)
Daily	39 (8.9)	34 (8.0)
Number of days with alcohol consumption		
None	304 (69.2)	223 (52.5)
One or less than one per month	99 (22.6)	105 (24.7)
2–4 times per month	33 (7.5)	78 (18.3)
2–3 times per week	3 (0.7)	19 (4.5)
Highest education of parents		
No education	3 (0.7)	2 (0.5)
Mandatory school/high school	14 (3.2)	14 (3.3)
Training school	221 (50.3)	215 (50.6)
College preparatory high school	33 (7.5)	32 (7.5)
College of higher education	132 (30.1)	127 (29.9)
University	36 (8.2)	35 (8.2)
	Baseline	Follow-up
	N = 439	N = 425
	Mean (SD)	Mean (SD)
Age	14.0 (0.85)	15.0 (0.79)
Height [cm]	163.7 (8.4)	167.3 (8.5)
Score verbal memory[a]	5.02 (2.76)	6.22 (2.72)
Score figural memory[a]	8.06 (2.76)	8.13 (3.26)

[a] Due to technical problems of the computerized testing system, data was not available for the whole sample.

phone call duration and brain dose of the sample with operator data (0.48). Also whole body RF-EMF dose was correlated with mobile phone call duration (whole sample: 0.67 and sample with operator data: 0.28). Kappa coefficients between whole-body and brain dose was 0.69 for the whole sample and 0.28 for the sample with operator data.

3.2. Associations between memory performance and usage related factors or RF-EMF doses

Table 4 and Table 5 show the results of the categorical analyses. Except a significant decrease of figural memory score for the medium exposure group of operator recorded numbers of SMS, none of the usage related exposure measures was significantly associated with changes in verbal and figural memory outcomes. There was no consistency in terms of directions of associations (sign of the coefficients) (Table 4). In contrast, various dose measures tended to be associated with figural memory performances (Table 5). Compared to the low exposure group (below median), significant decreases were observed in the high exposure group for brain dose (−1.16; 95% CI: −1.99, −0.34) and whole body dose (−0.86; 95% CI: −1.67, −0.05) of the whole sample and for the brain dose of the sample with operator data (−1.62; 95% CI: −2.63, −0.61).

Fig. 1 shows the results of the linear exposure response modelling (for numbers see Supplementary Table S1). The result pattern was similar to the categorical analyses with stronger associations for dose measures than for usage related exposure variables or negative control variables (see Supplementary Fig. S2 for results of negative control variables). In a sensitivity analysis including non-mobile phone users (n = 6) in the objective data analysis similar results were found (data not shown).

Fig. 2 shows the results of the laterality analyses. Stratified analyses according to preferred side of mobile phone use revealed for the analyses of the figural memory test in the whole sample a stronger effect estimate for the brain dose of right side mobile phone users compared to the group of left side and no preference side users (change per interquartile range: −0.52 (95% CI: −0.82, −0.22) vs. 0.27 (95% CI: −0.35, 0.89)); although such a pattern was not seen for the sample with operator data. For the verbal memory test the pattern tended to be reverse with somewhat stronger effect estimates for the left side users and those without a side preference compared to the right side users.

4. Discussion

In longitudinal analyses changes in figural memory performance score over one year tended to be decreased in relation to various RF-

Table 2
Descriptive statistics of all cumulative exposure and dose measures.

	Mean	SD	25%	Median	75%	Max
Usage						
Self-reported (whole sample)						
Duration data traffic on mobile phone [min/day]	48.2	33.2	22.5	43.9	74.3	107.8
Duration cordless phone calls [min/day]	7.3	7.6	2.5	4.8	9.4	53.2
Duration mobile phone calls [min/day]	16.0	25.7	3.0	7.6	18.6	293.9
Objective (sample with operator data)						
Volume data traffic on mobile phone [MB/day]	9.0	19.0	0.01	0.9	10.9	140.2
Duration mobile phone calls [min/day]	1.9	3.6	0.2	0.6	1.8	28.6
Negative control variables						
Self-reported (whole sample)						
Duration gaming [min/day]	45.2	54.7	6.4	23.6	65.0	257.9
Texts sent [x/day]	30.9	20.8	12.0	31.5	48.8	76.4
Objective (sample with operator data)						
SMS sent [x/day]	1.7	2.3	0.5	0.9	1.8	16.1
Dose						
Whole sample[a]						
Brain [mJ/kg/day]	1421	1979	275	710	1854	16233
Whole body [mJ/kg/day]	322	431	120	205	380	6044
Sample with operator data[b]						
Brain [mJ/kg/day]	235	432	60	102	236	4787
Whole body [mJ/kg/day]	125	87	73	107	157	756

[a] Calculation based on self-reported mobile phone call duration.
[b] Calculation based on objectively recorded mobile phone call duration.

Table 3
Kappa coefficients of usage related factors and the RF-EMF doses for the three exposure categories.

	Dose: whole sample [mJ/kg/day]		Dose: sample with operator data [mJ/kg/day]	
	Brain	Whole body	Brain	Whole body
Usage				
Self-reported (whole sample)				
Duration data traffic on mobile phone [min/day]	0.15[a]	0.21[a]	0.08[a]	0.28[a]
Duration cordless phone calls [min/day]	0.25[a]	0.22[a]	0.21[a]	0.11[a]
Duration mobile phone calls [min/day]	0.62[a]	0.67[a]	0.32	0.32
Objective (sample with operator data)				
Volume data traffic on mobile phone [MB/day]	0.01	0.13	0.10	0.20
Duration mobile phone calls [min/day]	0.20	0.25	0.48[a]	0.28[a]
Negative control variables				
Self-reported (whole sample)				
Duration gaming [min/day]	−0.02	0.10	0.04	0.15
Texts sent [x/day]	0.13	0.19	0.15	0.24
Objective (sample with operator data)				
SMS sent [x/day2]	0.08	0.05	0.15	0.21

[a] These usage variables have been used for the corresponding dose calculation.

EMF dose measures but less so with respect to wireless phone and media usage measures, which are scarcely related to RF-EMF exposure. This may indicate that indeed RF-EMF may impair the memory performance in adolescents.

A particular strength of this study is the longitudinal design. To the best of our knowledge this is the first longitudinal study on memory performance in adolescents using not only mobile phone call duration as an exposure proxy, but calculating RF-EMF dose measures derived from objectively recorded operator data and propagation modelling. Compared to a cross-sectional design where changes over time cannot be assessed and where reverse causality is of concern, longitudinal studies allow for more robust conclusions.

We put substantial emphasize on a comprehensive exposure assessment method considering most relevant RF-EMF sources and exposure relevant behaviours (Roser et al., 2015). The integrative RF-EMF dose measures for the brain and the whole body combined from questionnaire data, objectively recorded mobile phone use data, propagation modelling and personal measurements are unique and have not been applied before. Relevant exposure factors have been identified and were used to calculate the dose measures. Most relevant contributors for the brain dose are calls on the GSM network (on average 93.3% for the whole sample based on self-reported data and 58.7% for the sample with operator data using operator recorded information) followed by calls with the cordless phones (4.2% and 21.0%, respectively). For the whole body dose, calls on the GSM network (on average 66.9% for the whole sample and 19.5% for the sample with operator data), the use of computer/laptop/tablet connected to WLAN (12.0% and 29.1%, respectively) and data traffic on mobile phones over WLAN (8.1% and

Table 4
Results of the usage measures of the categorical analyses: medium and high exposure groups compared to low exposure (≤median). Significant estimates ($p < 0.05$) in bold.

	n	Medium exposure (>50% to ≤75%)		High exposure (>75%)	
		Crude (95% CI)	Adjusted[a] (95% CI)	Crude (95% CI)	Adjusted[a] (95% CI)
Usage related to EMF exposure					
Verbal memory					
Self-reported (whole sample)					
Duration data traffic on mobile phone [min/day]	375	0.02 (−0.71, 0.75)	0.06 (−0.68, 0.81)	0.32 (−0.40, 1.05)	0.40 (−0.37, 1.17)
Duration cordless phone calls [min/day]	375	−0.06 (−0.81, 0.70)	0.01 (−0.76, 0.77)	−0.12 (−0.84, 0.60)	−0.08 (−0.82, 0.66)
Duration mobile phone calls [min/day]	375	−0.16 (−0.88, 0.56)	−0.14 (−0.87, 0.60)	0.10 (−0.64, 0.84)	0.13 (−0.68, 0.93)
Objective (sample with operator data)					
Volume data traffic on mobile phone [MB/day]	210	0.30 (−0.65, 1.26)	0.40 (−0.56, 1.37)	0.62 (−0.41, 1.64)	0.64 (−0.40, 1.67)
Duration mobile phone calls [min/day]	210	0.47 (−0.49, 1.43)	0.46 (−0.54, 1.47)	0.99 (−0.01, 1.99)	0.96 (−0.13, 2.06)
Figural memory					
Self-reported (whole sample)					
Duration data traffic on mobile phone [min/day]	381	0.18 (−0.58, 0.93)	0.30 (−0.47, 1.08)	0.26 (−0.51, 1.02)	0.42 (−0.39, 1.23)
Duration cordless phone calls [min/day]	381	0.31 (−0.47, 1.10)	0.29 (−0.51, 1.08)	−0.55 (−1.30, 0.19)	−0.54 (−1.31, 0.22)
Duration mobile phone calls [min/day]	381	−0.21 (−0.96, 0.54)	−0.18 (−0.94, 0.59)	−0.51 (−1.29, 0.26)	−0.52 (−1.36, 0.31)
Objective (sample with operator data)					
Volume data traffic on mobile phone [MB/day]	212	0.35 (−0.58, 1.27)	0.38 (−0.57, 1.33)	0.25 (−0.74, 1.24)	0.44 (−0.58, 1.46)
Duration mobile phone calls [min/day]	212	−0.74 (−1.66, 0.19)	−0.83 (−1.82, 0.16)	−0.90 (−1.87, 0.07)	−1.02 (−2.10, 0.05)
Usage marginally related to EMF exposure (negative control variables)					
Verbal memory					
Self-reported (whole sample)					
Duration gaming [min/day]	375	0.35 (−0.39, 1.09)	0.42 (−0.37, 1.21)	0.26 (−0.46, 0.98)	0.56 (−0.34, 1.45)
Texts sent [x/day]	375	0.14 (−0.59, 0.87)	0.13 (−0.63, 0.88)	0.36 (−0.37, 1.08)	0.47 (−0.30, 1.25)
Objective (sample with operator data)					
SMS sent [x/day]	210	0.33 (−0.66, 1.31)	0.25 (−0.74, 1.25)	0.19 (−0.80, 1.18)	0.13 (−0.94, 1.20)
Figural memory					
Self-reported (whole sample)					
Duration gaming [min/day]	381	−0.42 (−1.19, 0.35)	−0.28 (−1.10, 0.55)	−0.40 (−1.16, 0.35)	−0.14 (−1.08, 0.80)
Texts sent [x/day]	381	0.24 (−0.52, 1.01)	0.31 (−0.49, 1.10)	0.26 (−0.50, 1.02)	0.45 (−0.37, 1.27)
Objective (sample with operator data)					
SMS sent [x/day]	212	**−1.22 (−2.15, −0.29)**	**−1.27 (−2.22, −0.31)**	−0.38 (−1.33, 0.57)	−0.30 (−1.34, 0.74)

[a] Adjusted for age, sex, nationality, school level, physical activity, alcohol, education of parents, change in height and time between baseline and follow-up investigation.

Table 5
Results of the dose measures of the categorical analyses: medium and high exposure groups compared to low exposure (≤median). Significant estimates ($p < 0.05$) in bold.

Cumulative dose [mJ/kg/day]	n	Medium exposure (>50% to ≤75%)		High exposure (>75%)	
		Crude (95% CI)	Adjusted[c] (95% CI)	Crude (95% CI)	Adjusted[c] (95% CI)
Verbal memory					
Whole sample[a]					
Brain	375	**−0.79 (−1.51, −0.07)**	−0.74 (−1.48, 0.001)	−0.12 (−0.86, 0.61)	−0.15 (−0.94, 0.65)
Whole body	375	−0.53 (−1.26, 0.21)	−0.40 (−1.16, 0.36)	−0.14 (−0.87, 0.59)	−0.13 (−0.91, 0.65)
Sample with operator data[b]					
Brain	210	0.06 (−0.91, 1.03)	−0.19 (−1.19, 0.81)	0.64 (−0.35, 1.64)	0.44 (−0.61, 1.49)
Whole body	210	0.79 (−0.19, 1.77)	0.75 (−0.25, 1.74)	−0.08 (−1.06, 0.90)	−0.23 (−1.25, 0.80)
Figural memory					
Whole sample[a]					
Brain	381	−0.02 (−0.77, 0.73)	−0.05 (−0.82, 0.72)	**−1.06 (−1.82, −0.29)**	**−1.16 (−1.99, −0.34)**
Whole body	381	−0.38 (−1.14, 0.38)	−0.32 (−1.11, 0.47)	**−0.89 (−1.65, −0.14)**	**−0.86 (−1.67, −0.05)**
Sample with operator data[b]					
Brain	212	−0.29 (−1.21, 0.64)	−0.28 (−1.25, 0.68)	**−1.49 (−2.44, −0.54)**	**−1.62 (−2.63, −0.61)**
Whole body	212	0.06 (−0.89, 1.01)	0.13 (−0.85, 1.12)	−0.87 (−1.82, 0.07)	−0.76 (−1.77, 0.25)

[a] Calculation based on self-reported mobile phone call duration.
[b] Calculation based on objectively recorded mobile phone call duration.
[c] Adjusted for age, sex, nationality, school level, physical activity, alcohol, education of parents, change in height and time between baseline and follow-up investigation.

22.3%, respectively) counted for the most part. Less important for the dose measures were exposure from radio and TV broadcast transmitters (brain dose: 0.1% and 0.4%, respectively; whole body dose: 0.3% and 0.9%, respectively) and mobile phone base stations (brain dose: 0.6% and 3.5%, respectively; whole body dose: 2.0% and 4.8%, respectively).

We calculated effect estimates for various wireless communication devices and media usage patterns comprising none to substantial RF-EMF exposure and compared them with effect estimates of brain and whole body RF-EMF dose measures by calculating regression coefficients per interquartile range. If there was a causal association between RF-EMF exposure and memory, one would expect more pronounced associations for dose measures compared to simple usage surrogates. Strikingly, an indication for such a pattern was found for figural memory performance. In particular, media usage measures which are not, or only

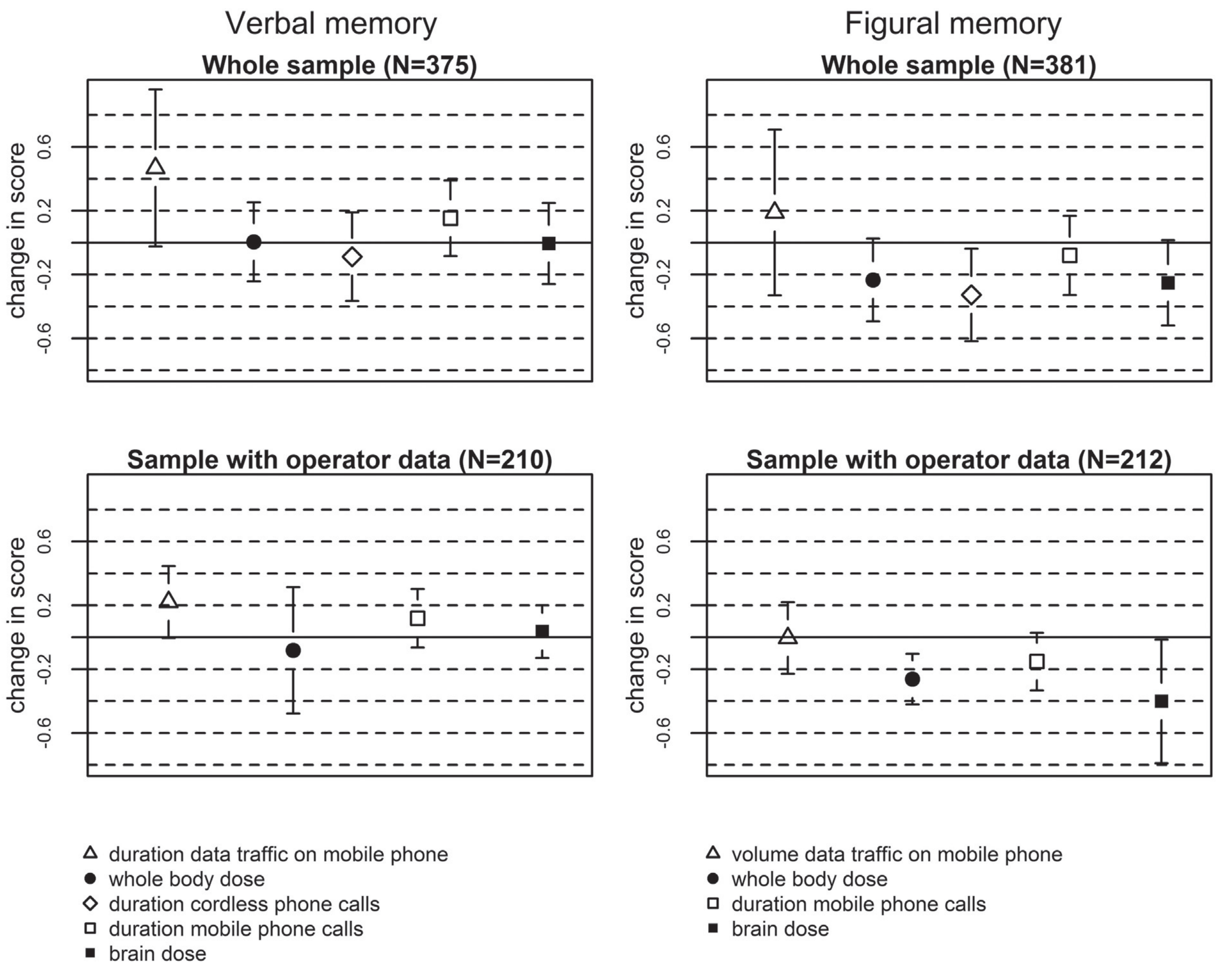

Fig. 1. Results of the linear exposure response modelling: change in score per inter quartile range. All models are adjusted for age, sex, nationality, school level, physical activity, alcohol, education of parents, change in height and time between baseline and follow-up investigation.

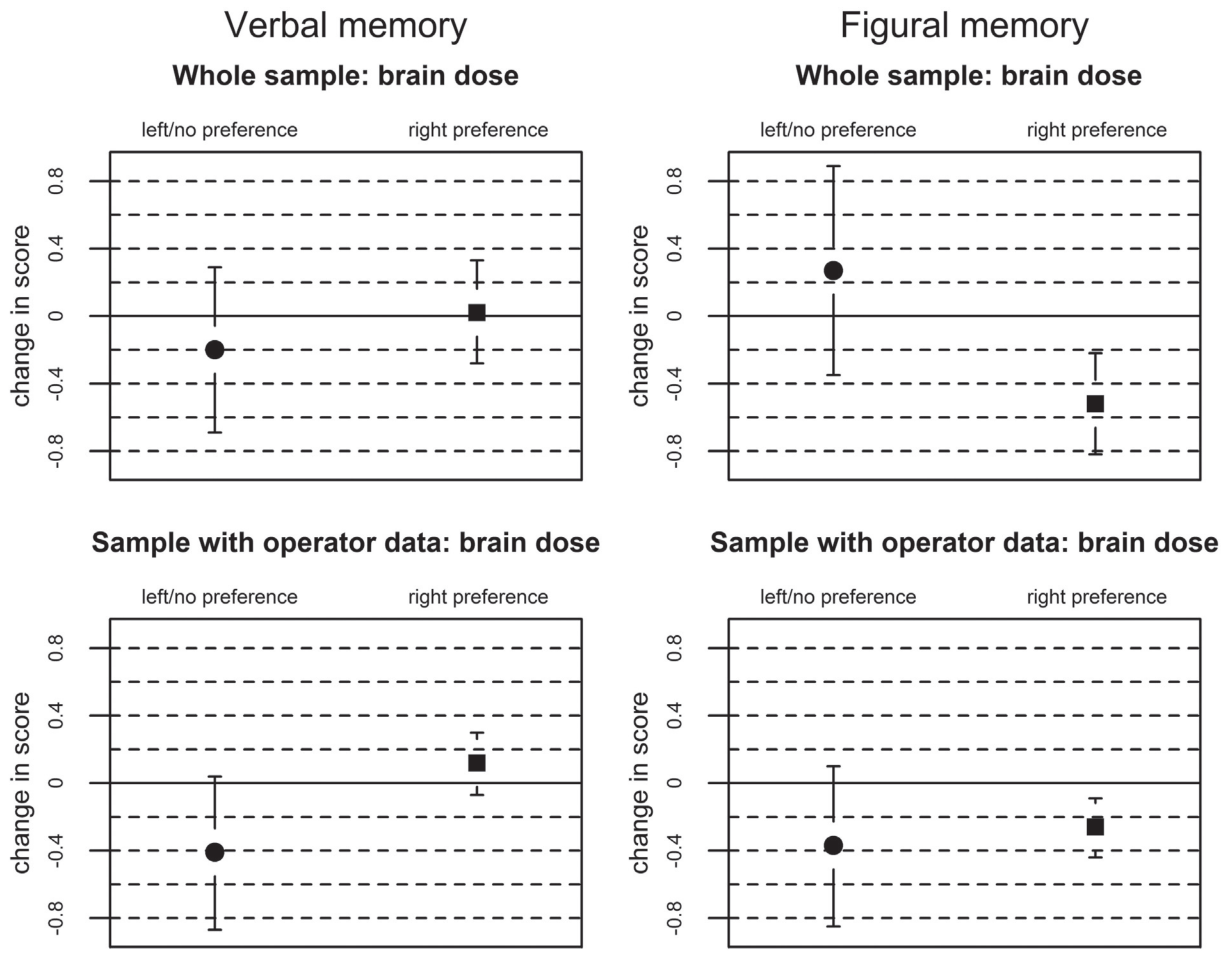

Fig. 2. Results of the laterality analyses (linear exposure response): change in score per inter quartile range. All models are adjusted for age, sex, nationality, school level, physical activity, alcohol, education of parents, change in height and time between baseline and follow-up investigation. Change in score per inter quartile range.

marginally associated with RF-EMF were not associated with figural memory performance (e.g. sending text messages, playing games, and duration/volume of data traffic on the mobile phone). On the other hand, mobile and cordless phone use, which involves RF-EMF exposure, tended to be negatively correlated, although not statistically significant, whereas the dose measures were significantly correlated in many models. The relative high correlation between dose measures and self-reported and objectively recorded mobile phone call duration respectively, limits the possibility to disentangle effects due to RF-EMF exposure or due to other factors associated with mobile phone use. Thus, the confidence intervals of estimates for cordless and mobile phone call duration are overlapping with the effect estimates of RF-EMF dose measures. Nevertheless, the pattern looks quite consistent. Within various dose measures, stronger associations were observed for brain than for whole body dose.

Since we found stronger associations between RF-EMF doses and figural memory but not verbal memory, one could speculate that this might be due to different brain areas involved in the verbal and figural memory tasks. The type of information being processed determines the brain activity during encoding and retrieval and as a consequence brain activity patterns during figural memory tasks differ from those observed during verbal memory tasks. During figural memory processes, encoding elicits bilateral prefrontal activity and retrieval increases the activity in bilateral or right-sided temporal regions and in bilateral prefrontal regions (Beason-Held et al., 2005; Roland and Gulyas, 1995; Wagner et al., 1998). During verbal encoding increases in prefrontal and temporal brain activity in the left hemisphere can be seen (Heun et al., 2000; Iidaka et al., 2000; Reber et al., 2002; Strandberg et al., 2011) and during verbal retrieval the activity in bilateral or right-sided prefrontal regions, bilateral or left-sided temporal regions and the anterior cingulate are increased (Beason-Held et al., 2005; Buckner et al., 1998; Cabeza et al., 1997). Stronger overall effects observed for figural memory processes predominantly involving the right hemisphere compared to the verbal memory tasks mostly involving the left hemisphere is compatible with the fact that 81.2% of the study participants reported at follow-up to mainly use mobile phones on the right side but only 18.8% on the left side or with no laterality preference. Strikingly, our laterality analyses indicated indeed stronger associations for right side users for the figural memory task whereas the reverse pattern was seen for the verbal task. However, the sample size of the laterality analysis was small for the subgroup with left side or no side preference for mobile phone use ($n = 80$).

A limitation of the dose measure calculation is the large uncertainty. It is impossible to directly measure the absorbed RF-EMF dose and a validation of our dose calculations could not be done. Thus, it is difficult to quantify the uncertainty at that time. For example the absorbed radiation by the body depends heavily on the unknown position of the emitting device in relation to the body, which is expected to show a high variability. A further source of uncertainty is the emitted exposure from mobile phones, in particular during data traffic and in stand-by mode (Urbinello and Röösli, 2013) and errors in modelling and personal measurements (Roser et al., 2015). In our study, self-reported mobile phone call duration is highly overestimated as seen in other studies of adolescents, although not to that extent (Aydin et al., 2011; Inyang et al., 2009). For that reason we put a lot of effort to consider objectively recorded mobile phone call duration in our analysis for at least a subgroup of our cohort. However, although objectively recorded, it is also subject to uncertainty. Adolescents sometimes call with others than with their own mobile phone to avoid costs, which is obviously not recorded in their objective mobile phone use data. However, according to the questionnaire, use of other people's phone is not very common and contributes to about 12% of total mobile phone call duration.

Unfortunately, operator recorded cordless phone use cannot be assigned to our study participants living in families, where many people use the same cordless phone. Thus, the dose calculation for the sample with operator data still relies on self-reported cordless phone call duration. No data is available to transfer objectively recorded data traffic volume into absorbed RF-EMF dose and thus we had to rely on self-reported data (duration of data traffic on the mobile phone), for which so-called transfer functions have been published (Gati et al., 2009). Together, cordless phone use and data traffic accounts on average for 21.2% of the brain dose and 56.8% of the whole body dose in the sample with operator data. This is an additional source of uncertainty.

We considered a number of potential confounders and adjusted model estimates were relatively similar to the crude model estimates, which indicates that confounding seems not to have a substantial impact on the results. Nevertheless, we cannot exclude that we have missed a relevant confounder. For instance the outcome measure scores are likely to be affected by carefulness and motivation of the participants. However, this factor is only a confounder in our analyses, if carefulness and motivation is strongly correlated with the RF-EMF dose measures but less so with media usage measures. There is no easy explanation for such a pattern.

Participation rate for enrolment in the cohort was moderate, which may affect the representativeness of the cohort for the source population. However, almost everybody who participated in the baseline investigation also took part in the follow-up investigation, resulting in a participation rate of 96.8%. Thus, potential bias in the effect estimates from lost to follow-up is negligible.

To the best of our knowledge the only previous longitudinal epidemiological study on cognitive functions in children observed changes in response time in a simple reaction and a working memory task for those participants with an increase in the number of mobile phone voice calls after one year, whereas accuracy of the responses was not affected (Thomas et al., 2010). This study relied on self-reported exposure data only, and neither objective data nor RF-EMF dose measures were considered. The authors attributed their findings to statistical artefacts because they were mainly seen in adolescents who had fewer voice calls at baseline. Such an explanation does not fit to our results, since the calculation of the cumulative exposure and dose between baseline and follow-up is not vulnerable to this kind of statistical artefact.

4.1. Conclusion

The observed striking pattern with more consistent associations for RF-EMF dose measures compared to usage measures and no indications of associations for negative control exposure variables may indicate that RF-EMF exposure affects the figural memory of adolescents. However, given the complex correlation structure for various exposure measures and the uncertainty in the RF-EMF dose calculation, the observed associations need to be interpreted with caution.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.envint.2015.09.025.

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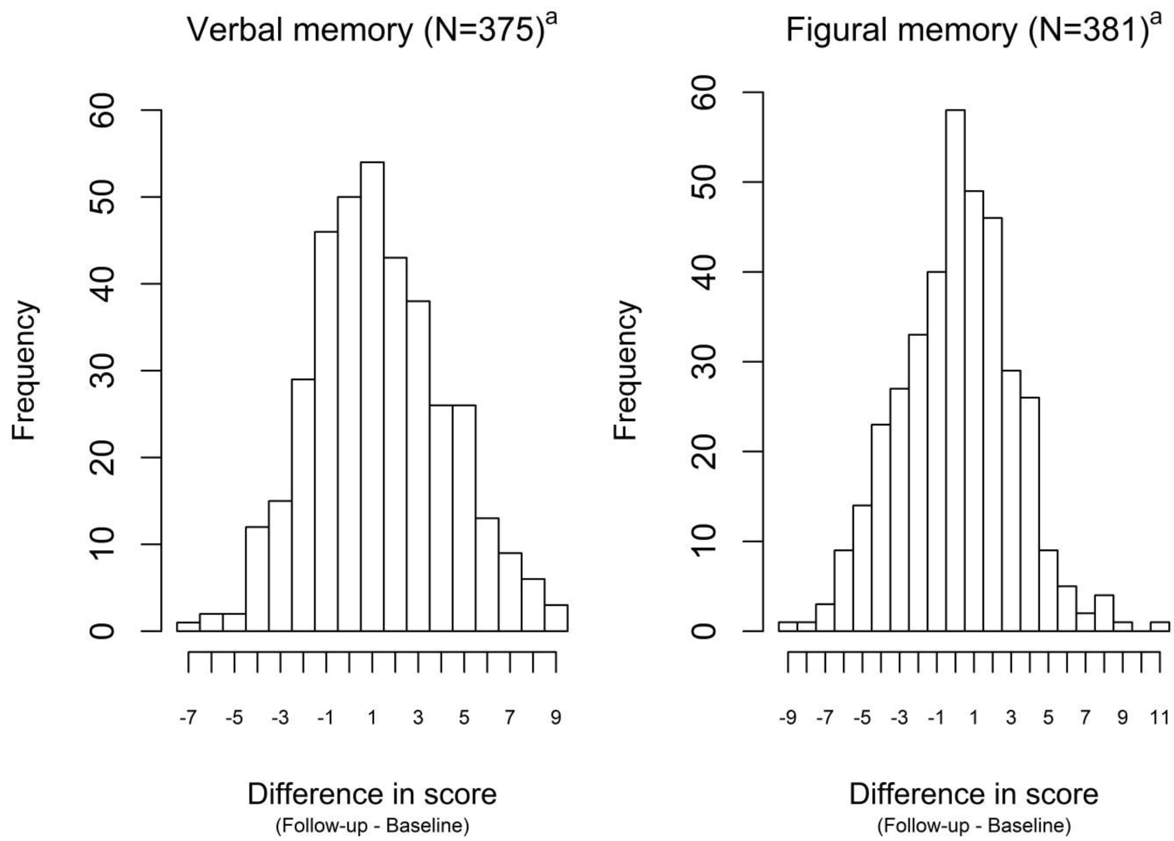

[a] due to technical problems of the computerized testing system, data was not available for the whole sample

Figure S1. The distribution of the change in the verbal and figural memory tests between baseline and follow-up.

Table S1. Results of the linear exposure response modelling: Change in score per inter quartile range.

	n	crude (95% CI)	adjusted [c] (95% CI)
Usage related to EMF exposure			
Verbal Memory			
self-reported (whole sample)			
duration data traffic on the mobile phone [min/d]	375	0.37 (-0.10, 0.84)	0.47 (-0.02, 0.96)
duration cordless phone calls [min/d]	375	-0.08 (-0.35, 0.19)	-0.09 (-0.37, 0.19)
duration mobile phone calls [min/d]	375	0.14 (-0.08, 0.35)	0.15 (-0.08, 0.39)
objective (sample with operator data)			
volume data traffic on the mobile phone [MB/d]	210	0.21 (-0.01, 0.43)	0.22 (-0.004, 0.45)
duration mobile phone calls [min/d]	210	0.14 (-0.03, 0.31)	0.12 (-0.06, 0.30)
Figural Memory			
self-reported (whole sample)			
duration data traffic on the mobile phone [min/d]	381	0.09 (-0.40, 0.58)	0.19 (-0.33, 0.71)
duration cordless phone calls [min/d]	381	**-0.34 (-0.61, -0.06)**	**-0.33 (-0.62, -0.04)**
duration mobile phone calls [min/d]	381	-0.09 (-0.31, 0.14)	-0.08 (-0.33, 0.17)
objective (sample with operator data)			
volume data traffic on the mobile phone [MB/d]	212	-0.03 (-0.25, 0.18)	-0.01 (-0.23, 0.22)
duration mobile phone calls [min/d]	212	-0.14 (-0.31, 0.02)	-0.15 (-0.33, 0.03)
Usage marginally related to EMF exposure (negative control variables)			
Verbal Memory			
self-reported (whole sample)			
duration gaming [min/d]	375	-0.03 (-0.35, 0.28)	0.01 (-0.37, 0.39)
texts sent [x/d]	375	0.24 (-0.29, 0.77)	0.34 (-0.24, 0.91)
objective (sample with operator data)			
SMS sent [x/d]	210	0.18 (-0.06, 0.43)	0.18 (-0.08, 0.44)
Figural Memory			
self-reported (whole sample)			
duration gaming [min/d]	381	-0.17 (-0.50, 0.16)	-0.03 (-0.43, 0.37)
texts sent [x/d]	381	0.05 (-0.51, 0.61)	0.21 (-0.40, 0.82)
objective (sample with operator data)			
SMS sent [x/d]	212	0.03 (-0.21, 0.27)	0.07 (-0.19, 0.33)
Cumulative Dose [mJ/kg/d]			
Verbal Memory			
whole sample [a]			
brain	375	0.01 (-0.23, 0.24)	-0.01 (-0.26, 0.25)
whole body	375	0.01 (-0.23, 0.24)	0.004 (-0.24, 0.25)
sample with operator data [b]			
brain	210	0.06 (-0.10, 0.22)	0.04 (-0.13, 0.20)
whole body	210	-0.01 (-0.39, 0.37)	-0.08 (-0.48, 0.31)
Figural Memory			
whole sample [a]			
brain	381	-0.24 (-0.49, 0.01)	-0.25 (-0.52, 0.01)
whole body	381	-0.23 (-0.48, 0.01)	-0.23 (-0.49, 0.02)
sample with operator data [b]			
brain	212	**-0.25 (-0.40, -0.10)**	**-0.26 (-0.42, -0.10)**
whole body	212	**-0.41 (-0.78, -0.05)**	**-0.40 (-0.79, -0.01)**

[a] calculation based on self-reported mobile phone call duration.
[b] calculation based on objectively recorded mobile phone call duration.
[c] adjusted for age, sex, nationality, school level, physical activity, alcohol, education of parents, change in height and time between baseline and follow-up investigation.

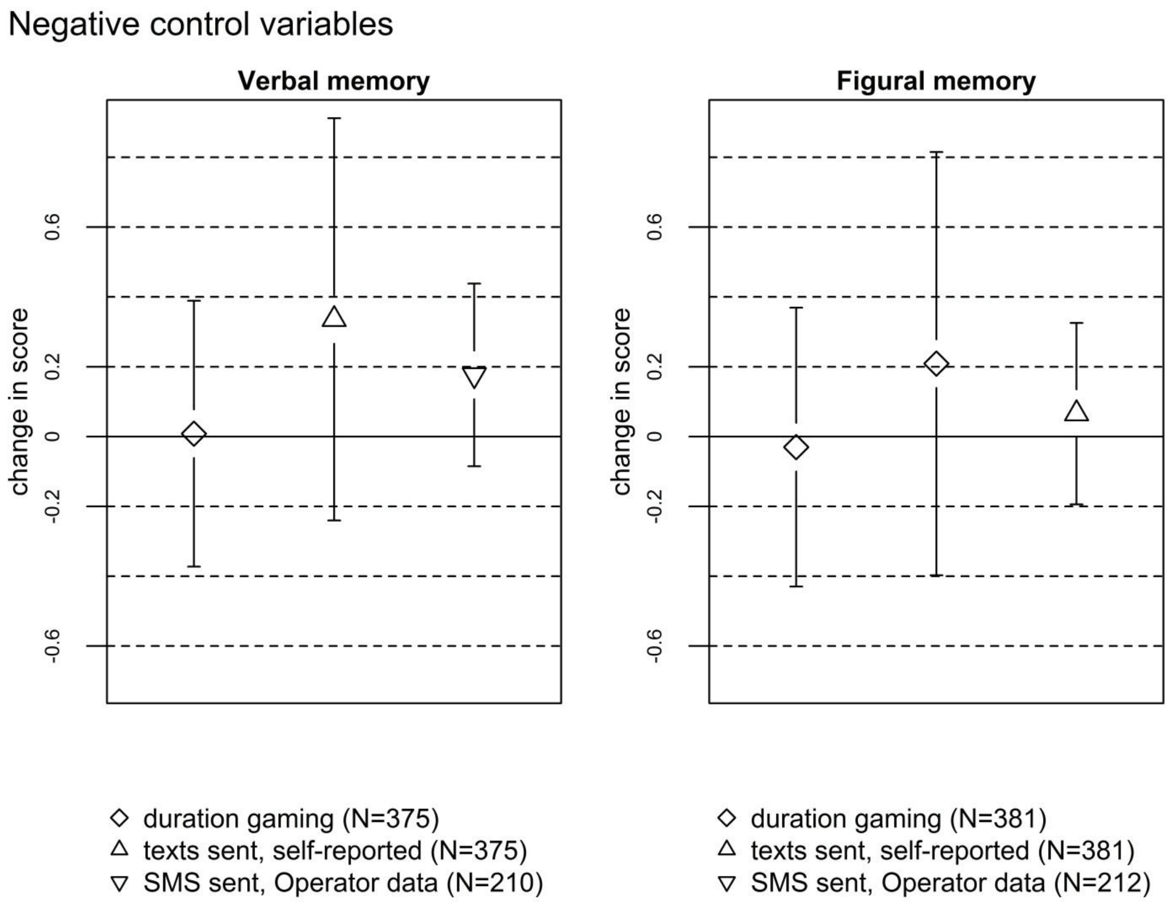

Figure S2. Results of negative control variables of the linear exposure response modelling: Change in score per inter quartile range. Adjusted for age, sex, nationality, school level, physical activity, alcohol, education of parents, change in height and time between baseline and follow-up investigation.

4.3 Article 4: Symptoms and use of wireless communication devices: a prospective cohort study in Swiss adolescents

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Symptoms and the use of wireless communication devices: A prospective cohort study in Swiss adolescents

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ABSTRACT

Background: We investigated whether radiofrequency electromagnetic fields (RF-EMF) from mobile phones and other wireless devices or by the wireless device use itself due to non-radiation related factors in that context are associated with an increase in health symptom reports of adolescents in Central Switzerland.
Methods: In a prospective cohort study, 439 study participants (participation rate: 36.8%) aged 12–17 years, completed questionnaires about their mobile and cordless phone use, their self-reported symptoms and possible confounding factors at baseline (2012/2013) and one year later (2013/2014). Operator recorded mobile phone data was obtained for a subgroup of 234 adolescents. RF-EMF dose measures considering various factors affecting RF-EMF exposure were computed for the brain and the whole body.

Data were analysed using a mixed-logistic cross-sectional model and a cohort approach, where we investigated whether cumulative dose over one year was related to a new onset of a symptom between baseline and follow-up. All analyses were adjusted for relevant confounders.
Results: Participation rate in the follow-up was 97% (425 participants). In both analyses, cross-sectional and cohort, various symptoms tended to be mostly associated with usage measures that are only marginally related to RF-EMF exposure such as the number of text messages sent per day (e.g. tiredness: OR:1.81; 95%CI:1.20–2.74 for cross-sectional analyses and OR:1.87; 95%CI:1.04–3.38 for cohort analyses). Outcomes were generally less strongly or not associated with mobile phone call duration and RF-EMF dose measures.
Conclusions: Stronger associations between symptoms of ill health and wireless communication device use than for RF-EMF dose measures were observed. Such a result pattern does not support a causal association between RF-EMF exposure and health symptoms of adolescents but rather suggests that other aspects of extensive media use are related to symptoms.

1. Introduction

Use of wireless communication devices by adolescents has substantially increased in the last few years (Waller et al., 2016). This development has raised public concerns regarding adverse health effects especially in young people since the lifetime exposure of adolescents will be longer than that of present-day adults. It has been suggested that children and adolescents may be more susceptible to RF-EMF exposure due to their still developing nervous system (Kheifets et al., 2005).

Several studies have focused on mobile phone use and health symptoms in children and adolescents relying on self-reported number or duration of mobile phone calls and texts as an exposure proxy for RF-EMF. In a nationwide Taiwanese cross-sectional study, Chiu et al. (2014) found that mobile phone use was associated with a significantly increased odds ratio (OR) for headache and migraine (OR: 1.42, 95% CI: 1.12–1.81) and skin itches (OR: 1.84, 95%CI: 1.47–2.29). In a large Swedish cross-sectional study of 2000 adolescents, self-reported use of mobile phones was related to self-reported health complaints such as tiredness, stress, headache, anxiety, concentration difficulties and sleep disturbances (Soderqvist et al., 2008). Redmayne et al. (2013) found significant cross-sectional associations between adolescents' well-being and their wireless phone use, with most consistent associations for headache. In a cross-sectional Korean study, feeling of discomfort and dry skin were associated with the number of outgoing calls per day and dry skin, fatigue and dizziness were associated with average duration per call (Byun et al., 2013). Ikeda and Nakamura (2014) found associations between mobile phone use and depressed mood or fatigue, respectively in 2785 Japanese high school students. In a representative Finnish sample of 7300 adolescents, high-mobile phone users showed

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more symptoms of depression and sleep disturbances than low-mobile phone users (Koivusilta et al., 2007). Roser et al. (2016a) found that physical well-being was significantly decreased in the 10% of adolescents belonging to the highest category in the shortened 10-item version of the Mobile Phone Problem Use Scale (Foerster et al., 2015).

Most of the existing evidence concerning the exposure of RF-EMF on adverse health effects however comes from cross-sectional studies, where changes over time cannot be assessed and where reverse causality, as well as confounding by lifestyle related factors related to mobile phone use and well-being are of concern. Another limitation in all of these studies was the self-reported mobile phone use, which has been shown to be inaccurate. Adolescents tend to substantially overestimate their amount of mobile phone use (Aydin et al., 2011; Inyang et al., 2009).

Thus, to address RF-EMF long term effects of mobile phone use, the application of a cumulative RF-EMF dose measure, which does not depend on usage only, is necessary, whereas for more transient effects recent exposure is relevant. One major factor determining RF-EMF exposure and not strongly correlated to the duration of mobile phone use is the type of network used. Calls on the UMTS network (3rd generation Universal Mobile Telecommunications System) cause on average 100–500 times less exposure than calls on the GSM network (2nd generation Global System for Mobile Communications) (Gati et al., 2009). In Switzerland both types of network are used and with the help of objectively recorded mobile phone use data provided by mobile phone operators and personal RF-EMF measurements, an integrative RF-EMF dose measure suitable for epidemiological research was calculated (Roser et al., 2015).

By applying this RF-EMF dose measure to the prospective HERMES (Health Effects Related to Mobile phonE use in adolescentS) cohort study, we thus aimed to investigate whether self-reported symptoms are associated with RF-EMF from mobile phones and other wireless devices or by the wireless device use itself due to non-radiation related factors in that context.

2. Material and methods

2.1. Study procedure

For the present study, 126 schools (7th, 8th and 9th grade) from rural and urban areas in Central Switzerland were contacted by an initial phone call with the head of the school. In a subsequent visit in the classes of 24 schools that agreed to participate, 1193 adolescents were informed about the study. Participation was voluntary and had to be preceded by informed consent of the adolescents and a parent. The baseline investigation then took place in school during school time between June 2012 and February 2013. The adolescents filled in a questionnaire with questions on non-specific symptoms of ill health, use of wireless communication devices, socio demographics, and other relevant covariables. This information was complemented by a parental questionnaire with additional items such as wireless technology at home and questions on child development. Parents were asked to fill out the questionnaire and send it back directly. This procedure was repeated one year later by the same study managers with the same study participants.

A subgroup of 95 study participants participated voluntarily in personal measurements. The participants were selected so that they represent a broad range of the HERMES cohort according to basic criteria such as age, gender, school level and urbanization of home and school place. The adolescents carried a portable measurement device, a so-called exposimeter, and kept a time-activity diary application installed on a smartphone in flight-mode for about three consecutive days. This sample has been used to estimate the exposure from cordless phone base stations, WLAN access points and other people's mobile phones, which has been used for the development of the RF-EMF dose measures. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Lucerne, Switzerland on May 9th, 2012 (Ref. Nr. EK: 12025). Written informed consent was obtained from the adolescents and their parents for the participation in the study and for providing the mobile phone operator data.

2.2. Symptoms

In the written questionnaire, headache was assessed using the six-item Headache Impact Test (HIT-6) providing a summary score of all six items ranging from 36 to 78 (Kosinski et al., 2003). According to Kosinski et al. (2003), a summary score of 49 or less is considered as "headache has no impact on your life," 50–55 is considered as "headache has some impact on your life," 56–59 as "headache has substantial impact on your life" and 60 or more as "headache has a very severe impact on your life." A binary variable was created by using 56 as the cut-off value. Tiredness, lack of energy, lack of concentration and rapid exhaustibility (referred to as exhaustibility) were assessed using a four-point Likert scale with categories "never," "rare," "moderate" and "severe." Binary variables were created by combining answer categories "never" with "rare" and "moderate" with "severe". Physical well-being was assessed using the dimension "Physical Well-being" from the Kidscreen-52 questionnaire. This dimension includes five questions exploring the level of adolescents' physical activity, energy and fitness (The KIDSCREEN Group Europe, 2006; Hadjem et al., 2010; Ravens-Sieberer et al., 2005). A binary variable was created by using the mean minus half a standard deviation as the cut-off, which is suggested as the guiding principle according to the official Kidscreen questionnaire handbook. For coherent data presentation, the Kidscreen Well-being scale was inverted and is expressed as ill-being scale.

In most health questions, we referred to the time period 4 weeks prior to the date of examination.

2.3. Exposure data

In the written adolescent questionnaire, all study participants were asked about call duration with their own or any other mobile phone (referred to as duration mobile phone calls), call duration with cordless (fixed line) phone and duration of data traffic on the mobile phone, e.g. for surfing and streaming. The duration of gaming on computers and TV and number of all kind of text messages (SMS, WhatsApp etc.) are not, or only marginally relevant for RF-EMF exposure and were thus asked about to be used as negative exposure control variables in the analyses.

Informed consent to obtain objectively recorded mobile phone use data from the mobile phone operators was given by 234 out of 439 study participants and their parents. This included duration of each call and on which network (GSM or UMTS) it started, number of SMS (text messages) sent per day and volume of data traffic (MB/day). Data were obtained for up to 18 months, from 6 months before baseline until the follow-up investigation.

2.4. RF-EMF dose measures

To be able to calculate a RF-EMF dose to the brain and the whole body of the participating adolescents, an integrative RF-EMF exposure surrogate including various factors affecting near-field and far-field RF-EMF exposure was developed, which is described in detail in Roser et al. (2015). The near-field component combines the exposure from the use of wireless devices (mobile phones, cordless phones, computer/laptop/tablet connected to wireless internet (WLAN)). For mobile phone calls, we also considered the proportion in each network type (network type proportion). Among participants for whom we obtained operator data, network type proportion was calculated directly from objective information. For the other participants, the network type proportion was predicted by mixed linear regression models with mobile phone operator, duration of mobile internet use on the mobile phone, and modelled UMTS exposure levels at home as input variables, and school as a cluster variable. The far-field component aggregates the exposure from environmental sources, which were derived from propagation modelling for radio and TV broadcast transmitters as well as for mobile phone base stations (Bürgi et al., 2010, 2008). Exposure from cordless phone base stations, WLAN access points and other people's mobile phones were estimated by linear regression models calibrated on the personal measurement data available from 95 study participants (Roser et al., 2016c).

Specific absorption rates (SAR) for the brain and the whole body were obtained from the literature (Gati et al., 2009; Huang et al., 2014; Lauer et al., 2013; Persson et al., 2012; Vrijheid et al., 2009b; SEAWIND, 2013; Hadjem et al., 2010) for all exposure relevant situations, which included mobile and cordless phone call durations, duration of use of computer/laptop/tablet connected to WLAN, duration of mobile internet use on the mobile phone, radio and TV broadcast transmitters, other people's mobile phones, WLAN access points, and cordless phone base stations. The brain and whole body dose for each study participant were calculated by summing the products of their SAR values by the average exposure duration per day for each exposure situation. This calculation was done twice: first, using exposure duration of mobile phone calls obtained from the questionnaire for the whole sample (dose for the whole sample); and second, mobile phone call durations from the mobile phone operator records for the subsample with that data (dose for the sample with operator data). Since no data was found that translates operator recorded data traffic by a mobile phone into a SAR value, we had to use self-reported duration of data traffic by mobile phone for the dose calculation in the operator sample. Similarly, DECT phone use is self-reported in both samples.

2.5. Cumulative exposure data

For the objective exposure variables (volume of data traffic, duration of mobile phone calls and number of SMS sent), data from the whole period between baseline and follow-up investigation were summed up and divided by the time between baseline and follow-up investigation, to obtain averages per day for easier interpretation. For every self-reported exposure variable (duration mobile phone calls, call duration with cordless phone, duration of data traffic on the mobile phone, duration of gaming and number of all kind of text messages) and for the dose measures (brain and whole body dose) a mean between baseline and follow-up data was calculated.

2.6. Statistical Analysis

Two main analyses (a and b) were performed to investigate possible associations between self-reported symptoms and non-radiation related factors in the context of mobile phone use or RF-EMF sources in the everyday environment:

a) A mixed-logistic cross-sectional regression analysis of a combined dataset consisting of baseline and follow-up data, accounting for the repeated measures for each individual.
b) A cohort analysis, including all participants without the target symptom at baseline (based on the binary category), to investigate, whether occurrence of the symptom was related to cumulative wireless device use or cumulative RF-EMF dose.

In both analyses (a and b) two different approaches were chosen. In a primary approach, exposure-response associations were investigated using a logistic regression model. All exposure variables were used continuously, using a linear term and odds ratios were expressed per interquartile change in exposure, in order to be able to compare between different exposure surrogates. In a second approach, a logistic regression model based on three exposure categories for all exposure variables was applied: exposure or dose below median (reference), 50th to 75th percentile and the top 25 per cent.

All models were adjusted for age, sex, nationality, school level (college preparatory high school or high school), physical activity, alcohol consumption and education of parents. In the cohort analyses we adjusted for confounders at follow-up. Additionally, all models of the cohort analysis (b) were adjusted for change in body height between baseline and follow-up and the time between baseline and follow-up in months.

Linear regression imputation (14 missing values at baseline and 10 missing values at follow-up for alcohol consumption; 7 missing values at baseline and 6 missing values at follow-up for information on body height) or imputation of a common category (2 missing values at baseline and 1 missing value at follow-up for frequency of physical activity; 60 missing values for educational level of the parents) was used to impute missing values in the confounder variables. Statistical analyses were carried out using STATA version 12.1 (StataCorp, College Station, USA). Figures were made with the software R using version R for Windows 3.0.1.

3. Results

439 students (participation rate: 36.8%) aged 12–17 years from 24 schools (participation rate: 19.1%) from rural and urban areas in Central Switzerland participated in the baseline investigation of the HERMES study. 412 (93.9%) study participants owned a mobile phone at baseline. In the follow-up investigation one year later, 425 study participants (participation rate: 96.8%) took part. 416 (97.9%) study participants owned a mobile phone at follow-up. Between baseline and follow-up, objectively recorded mobile phone use data was available for 234 study participants. The follow-up investigation was on average 12.5 months after baseline. The characteristics of the study participants are listed in Table 1.

3.1. RF-EMF dose and usage related exposure

Table 2 gives an overview of the samples and their variables.

The summary statistics of all exposure and dose measures from the dataset of the cumulative data can be found in Table 3. Mean self-reported mobile phone call duration was 16.0 min/day whereas mean operator recorded mobile phone call duration was 1.9 min/day. Self-reported mobile phone call duration of those we obtained operator recorded data was 15.3 min/d. When subtracting calls that have been reported to be made on other people's mobile phones, it was still 13.3 min/d. Thus, self-reported call duration is 7 times higher than what is recorded by their operator.

Most relevant contributors for the brain dose are calls on the GSM network (on average 93.3% for the whole sample and 58.7% for the sample with operator data) followed by calls with the cordless phones (4.2% and 21.0%, respectively). For the whole body dose, calls on the GSM network (on average 66.9% for the whole sample and 19.5% for the sample with operator data), the use of computer/laptop/tablet connected to WLAN (12.0% and 29.1%, respectively) and data traffic on mobile phones (8.1% and 22.3%, respectively) counted for the most part. Less important for the dose measures were exposure from radio and TV broadcast transmitters (brain dose: 0.1% and 0.4%, respectively; whole body dose: 0.3% and 0.9%, respectively) and mobile phone base stations (brain dose: 0.6% and 3.5%, respectively; whole body dose: 2.0% and 4.8%, respectively).

A substantial correlation was found between the cumulative usage measures and the cumulative RF-EMF doses: a kappa coefficient of 0.62 was found for self-reported mobile phone call duration and brain dose of the whole sample. Also the whole body dose of the whole sample was highly correlated with self-reported mobile phone call duration (0.67). Duration of mobile phone use is shorter according to

Table 1
Characteristics of the study participants at baseline and follow-up.

	Baseline N=439	Follow-up N=425
	Mean (SD)	**Mean (SD)**
Age	14.0 (0.85)	15.0 (0.79)
Body height [cm]	163.7 (8.4)	167.3 (8.5)
	n (proportion)	**n (proportion)**
Male sex, n (%)	174 (39.6)	171 (40.2)
School level		
College preparatory high school	99 (22.5)	109 (25.6)
High School	340 (77.5)	316 (74.4)
Nationality		
Swiss	348 (79.3)	341 (80.2)
Swiss and other	62 (14.1)	59 (13.9)
Other	29 (6.6)	25 (5.9)
Physically active		
1–3 times per month or less	68 (15.5)	57 (13.4)
once per week	91 (20.7)	90 (21.2)
2–3 times per week	156 (35.5)	170 (40.0)
4–6 times per week	85 (19.4)	74 (17.4)
daily	39 (8.9)	34 (8.0)
Number of days with alcohol consumption		
None	304 (69.2)	223 (52.5)
One or less than one per month	99 (22.6)	105 (24.7)
2–4 times per month	33 (7.5)	78 (18.3)
2–3 times per week	3 (0.7)	19 (4.5)
Highest education of parents		
No education	3 (0.7)	2 (0.5)
Mandatory school/High school	14 (3.2)	14 (3.3)
Training school	221 (50.3)	215 (50.6)
College preparatory high school	33 (7.5)	32 (7.5)
College of higher education	132 (30.1)	127 (29.9)
University	36 (8.2)	35 (8.2)

Table 2.
Different samples and their variables.

Whole sample
duration gaming [min/d], self-reported
number of texts sent [x/d], self-reported
duration data traffic on mobile phone [min/d], self-reported
duration cordless phone calls [min/d], self-reported
duration mobile phone calls [min/d], self-reported
brain dose [mJ/kg/d]
whole body dose [mJ/kg/d]
Sample with operator data
volume data traffic on mobile phone [MB/d], operator recorded
duration mobile phone calls [min/d], operator recorded
number of SMS sent [x/d], operator recorded
brain dose [mJ/kg/d]
whole body dose [mJ/kg/d]
Sample of subgroup
used for the development of the RF-EMF dose measures

objective data and thus, the contribution of this exposure condition to the total RF-EMF dose is smaller. As a consequence correlation between objectively recorded mobile phone call duration and brain dose was lower (0.48) than for self-reported data (0.62). The same holds for the correlation between objectively recorded mobile phone call duration and whole body dose (0.28).

The correlation between whole body dose of the sample with operator data and data traffic on the mobile phone and duration gaming was 0.28 and 0.15, respectively.

Table 3
Descriptive statistics of all cumulative exposure and dose measures.

	Mean	sd	Median	Max
Usage measures marginally related to RF-EMF exposure (negative control variables)				
duration gaming [min/d], self-reported	45.2	54.7	23.6	257.9
number of texts sent [x/d], self-reported	30.9	20.8	31.5	76.4
number of SMS sent [x/d], operator recorded	1.7	2.2	0.9	16.1
Usage measures related to RF-EMF exposure				
duration data traffic on mobile phone [min/d], self-reported	48.2	33.2	43.9	107.8
duration cordless phone calls [min/d], self-reported	7.3	7.6	4.8	53.1
duration mobile phone calls [min/d], self-reported	16.0	25.6	7.6	293.9
Objective usage measures related to RF-EMF exposure				
volume data traffic on mobile phone [MB/d], operator recorded	9.0	19.0	0.9	140.2
duration mobile phone calls [min/d], operator recorded	1.9	3.6	0.6	28.6
Dose (whole sample)				
brain [mJ/kg/d]	1421	1979	710	16233
whole body [mJ/kg/d]	322	431	205	6044
Dose (sample with operator data)				
brain [mJ/kg/d]	235	432	102	4787
whole body [mJ/kg/d]	125	87	107	756

3.2. Associations between symptoms and usage related exposures or RF-EMF doses

3.2.1. Mixed-logistic cross-sectional analyses (a)

Fig. 1 and Supplemental Table S1 shows the odds ratios (OR) related to an interquartile increase in self-reported exposure variables and the dose measures of the whole sample estimated by means of a mixed-logistic cross-sectional model of baseline and follow-up data. These analyses with continuous exposure variables showed a tendency towards increased odds ratios for all the symptoms in relation to various self-reported usage measures. Typically strongest associations were observed for duration of data traffic on the mobile phone and number of text messages sent. Associations with RF-EMF dose measures for the whole sample tended to be small but were statistically significant for headache and exhaustibility. An analysis based on three exposure categories with cut-offs at the median and the 75th percentile yielded similar results as with continuous exposure variables (data not shown).

The results of the mixed-logistic cross-sectional analyses of the usage and dose measures from the sample with operator data can be seen in the Supplemental Table S2. Except for a significant increased odds ratio of exhaustibility for the volume of data traffic on the mobile phone and of physical ill-being for number of SMS sent, none of the objective usage related exposure measures were significantly associated with any of the symptoms. In contrast, dose measures from the sample with operator data, especially the whole body dose, were significantly associated with various symptoms. The analysis based on three exposure categories yielded similar results as with continuous exposure variables (data not shown).

3.2.2. Cohort analyses (b)

Fig. 2 and Table 4 show the results of the cohort analyses based on self-reported data and dose measures for the whole sample. The results of the analyses with continuous exposure variables showed a similar

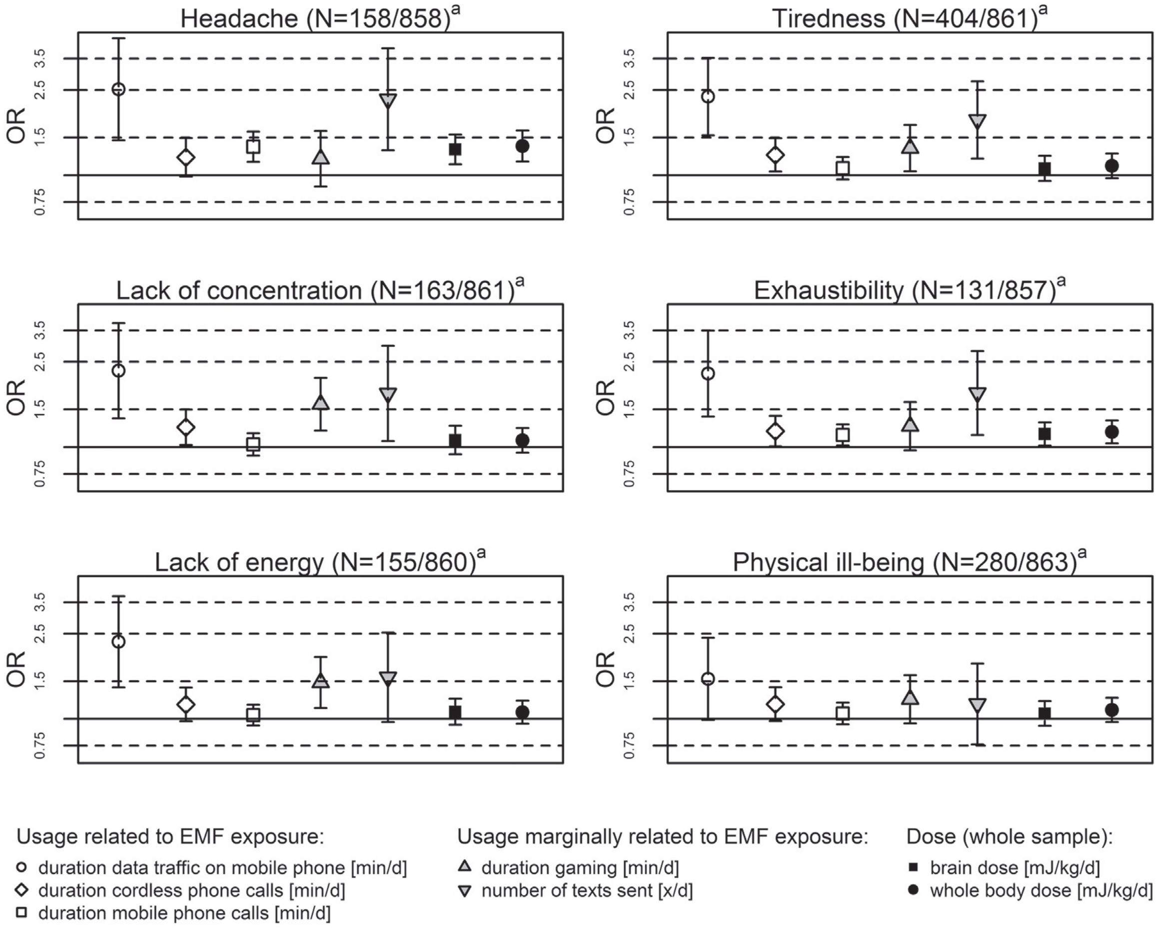

Fig. 1. Results of the mixed-logistic cross-sectional analyses of baseline and follow-up data expressed as OR per interquartile change of the exposure variables. All models are adjusted for age, sex, nationality, school level, physical activity, alcohol and education of parents. [a] number of study participants with symptoms/total number of study participants. All the numbers of these figures are shown in the Supplemental Table S1.

pattern as for the mixed-logistic cross-sectional analyses (a) of baseline and follow-up data, with highest estimates for duration of data traffic on the mobile phone and number of text messages sent per day.

For the subsample with operator data, analyses of the cumulative, objectively recorded mobile phone measures (volume data traffic, duration of mobile phone calls and number of SMS sent) and of dose measures are shown in the Supplemental Table S3. Results were similar to the self-reported data of the whole sample, with significant associations between duration of mobile phone calls and tiredness (OR: 1.37; 95%CI: 1.07–1.75) and lack of concentration (OR: 1.21; 95%CI: 1.03–1.44), respectively. Other significant associations were found for the volume of data traffic on the mobile phone and physical ill-being (OR: 1.42; 95%CI: 1.06–1.90) and for the number of SMS sent per day and lack of concentration (OR: 1.29; 95%CI: 1.04–1.61). Associations with the brain dose of the sample with operator data tended to be small and non-significant. The whole body dose of the sample with operator data, however, was significantly associated with all symptoms except for physical ill-being. We found a similar pattern when the exposures were based on three exposure categories (data not shown).

4. Discussion

In cross-sectional and cohort analyses (a and b) increased health symptom reports were shown in relation to various wireless phone usage measures and whole body RF-EMF dose. Strongest associations were observed for the duration of data traffic on the mobile phone and number of text messages sent per day.

A particular strength of this study is the longitudinal design. Compared to a cross-sectional design, longitudinal studies allow for more robust conclusions. To the best of our knowledge, this is the first cohort study on non-specific symptoms in adolescents, using not only mobile phone call duration as an exposure proxy, but using RF-EMF dose measures derived from self-reported and objectively recorded mobile phone use data and propagation modelling. Our results of the cross-sectional analyses, where we found an increase in self-reported health symptom reports in relation to various self-reported usage measures, are in line with other cross-sectional studies on symptoms, mental health or sleeping problems (Byun et al., 2013; Ikeda and Nakamura, 2014; Koivusilta et al., 2007; Redmayne et al., 2013; Roser et al., 2016a; Schoeni et al., 2015b; Soderqvist et al., 2008).

In our cohort approach of the whole sample, the cross-sectional associations between symptoms and use of wireless communication devices could mostly be confirmed. The cohort analysis is less vulnerable to reverse causality and residual confounding since within person changes are considered. Strikingly, such a pattern was not observed in the only two other longitudinal studies on mobile phone use in adolescents and young adults. In these studies, less pronounced longitudinal associations with mental outcomes (Thomee et al., 2011) or cognitive functions (Thomas et al., 2010) were observed compared to their corresponding cross-sectional analyses. However, they were based on self-reported mobile phone call duration only. No study with operator recorded mobile phone use and symptoms has been conducted in adolescents so far and only one study was identified in adults (Frei et al., 2012). In this study of 1124 adults aged between 30 and 60 years, results of cross-sectional and cohort analyses were similar with a tendency of a negative correlation between symptoms and self-reported

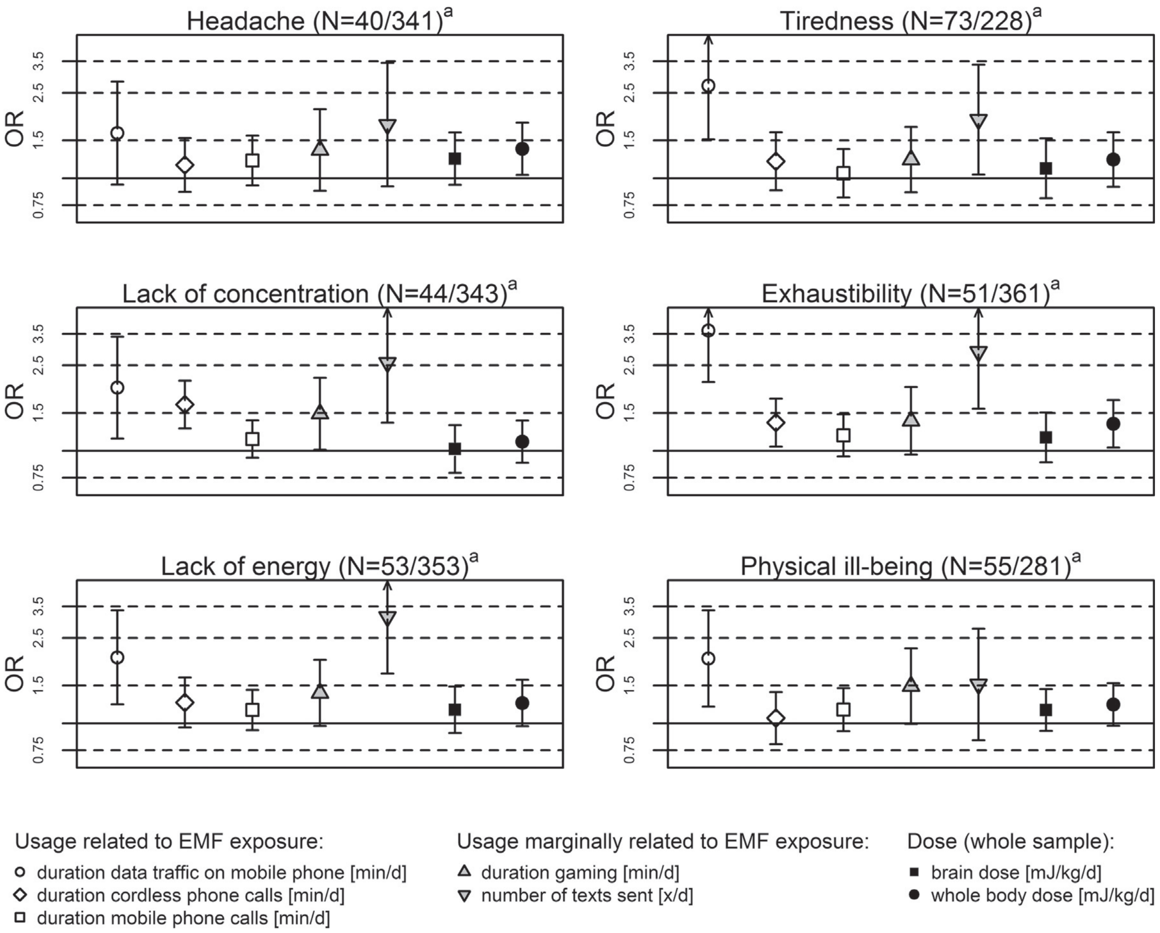

Fig. 2. Results of the cohort analyses expressed as OR per interquartile change of the exposure variables. All models are adjusted for age, sex, nationality, school level, physical activity, alcohol, education of parents, change in body height and time between baseline and follow-up investigation. [a] number of study participants with occurrence of symptoms / total number of study participants. All the numbers of these figures are shown in Table 4.

mobile phone use and no indication of an association for operator recorded mobile phone use, which was available for 451 study participants. This might suggest that not the use of mobile phone per se causes the symptoms but other factors associated with the use of mobile phones, which may be different for adults than adolescents, such as sleep deprivation due to night-time use, muscular tensions or lack of physical activity.

Self-reported mobile phone call duration is only modestly correlated to the actual mobile phone call duration in adolescents and recall and information bias is of concern (Aydin et al., 2011; Inyang et al., 2009; Vrijheid et al., 2009a). As seen in our study, self-reported mobile phone call duration is highly overestimated. Although objectively recorded mobile phone call duration seems to be more accurate, it may not represent the whole truth about mobile phone call duration in adolescents. Adolescents sometimes also make calls with phones other than their own to avoid costs. The use of other mobile phones is obviously not recorded in the objective mobile phone use data. However, according to the questionnaire, use of other people's mobile phone is not very common and contributes to about 12% of total mobile phone call duration. In our analyses, results for operator recorded and self-reported mobile phone usage measures were relatively similar, although effect estimates tended to be somewhat higher for the latter.

We put substantial emphasis on a comprehensive exposure assessment method, including most relevant RF-EMF sources and exposure relevant behaviours (Roser et al., 2015). We calculated effect estimates for various wireless device use variables and compared it with effect estimates of dose measures by calculating regression coefficients per interquartile range, which allows direct comparison. If there was a causal association between RF-EMF exposure and symptoms, one would expect more pronounced associations for RF-EMF dose measures compared to simple usage surrogates, as seen in the same study for memory performance (Schoeni et al., 2015a) but not for behavioural problems and concentration capacity (Roser et al., 2016b). Mostly for the whole body RF-EMF dose, but rarely for the brain dose, we found some significant associations in the cross-sectional, as well as in the cohort analyses. This pattern was particularly evident in the sample with operator data. Although objectively recorded mobile phone use has been used for dose calculation in this group, it has to be emphasized that the associations between whole body dose of the sample with operator data and symptoms are heavily driven by the self-reported duration of data traffic on the mobile phone (contributes over 20% to the whole body dose of the sample with operator data) and the self-reported use of computer/laptop/tablet connected to WLAN (29%). Strikingly, odds ratios for self-reported data traffic on the mobile phone (Table 4) were considerably more pronounced than the odds ratio for whole body dose in the operator sample (Supplemental Table S3). This demonstrates that the significant associations for whole body dose in the operator samples are heavily driven by the strong associations of symptoms with self-reported data traffic but unlikely to be caused by RF-EMF exposure. Also in all other cross-sectional and cohort analyses, associations tended to be less pronounced for RF-EMF than for number of text messages sent or data traffic.

Chance findings cannot be ruled out since we have conducted 168 analyses. If a multiple testing correction were applied, one needs to consider the complex correlation structure between the outcomes and

Table 4
Results of the cohort analyses of the self-reported usage measures and dose measures for the whole sample. All odds ratios refer to an interquartile (IQR) increase in exposure.

	n with occurrence of symptoms/n total	IQR 25%[b]	75%[b]	Odds ratio crude (95% CI)	Odds ratio adjusted (95% CI)[c]
Usage measures marginally related to RF-EMF exposure (negative control variables)					
Headache					
duration gaming [min/d]	40/341	6.4	65.0	1.09 (0.75–1.59)	1.35 (0.88–2.09)
number of texts sent [x/d]	40/341	12.0	48.8	1.36 (0.75–2.46)	1.78 (0.92–3.44)
Tiredness					
duration gaming [min/d]	73/228	6.4	65.0	1.20 (0.90–1.61)	1.22 (0.86–1.73)
number of texts sent [x/d]	73/228	12.0	48.8	1.29 (0.79–2.11)	**1.87 (1.04–3.38)**
Lack of concentration					
duration gaming [min/d]	44/343	6.4	65.0	1.28 (0.94–1.75)	**1.49 (1.01–2.19)**
number of texts sent [x/d]	44/343	12.0	48.8	**2.30 (1.29–4.08)**	**2.57 (1.35–4.89)**
Exhaustibility					
duration gaming [min/d]	51/361	6.4	65.0	1.26 (0.93–1.69)	1.38 (0.96–1.98)
number of texts sent [x/d]	51/361	12.0	48.8	**2.00 (1.17–3.40)**	**2.89 (1.57–5.32)**
Lack of energy					
duration gaming [min/d]	53/353	6.4	65.0	1.26 (0.94–1.69)	1.39 (0.97–1.98)
number of texts sent [x/d]	53/353	12.0	48.8	**2.46 (1.44–4.20)**	**3.13 (1.71–5.75)**
Physical ill-being[a]					
duration gaming [min/d]	55/281	6.4	65.0	1.17 (0.85–1.60)	1.49 (0.99–2.24)
number of texts sent [x/d]	55/281	12.0	48.8	1.49 (0.88–2.53)	1.52 (0.84–2.76)
Usage measures related to RF-EMF exposure					
Headache					
duration data traffic on mobile phone [min/d]	40/341	22.5	74.3	1.38 (0.83–2.31)	1.62 (0.93–2.82)
duration cordless phone calls [min/d]	40/341	2.5	9.4	1.13 (0.86–1.47)	1.15 (0.86–1.54)
duration mobile phone calls [min/d]	40/341	3.0	18.6	1.16 (0.91–1.48)	1.21 (0.93–1.58)
Tiredness					
duration data traffic on mobile phone [min/d]	73/228	22.5	74.3	**1.69 (1.06–2.69)**	**2.70 (1.52–4.80)**
duration cordless phone calls [min/d]	73/228	2.5	9.4	1.14 (0.86–1.51)	1.20 (0.88–1.64)
duration mobile phone calls [min/d]	73/228	3.0	18.6	0.92 (0.73–1.16)	1.06 (0.81–1.37)
Lack of concentration					
duration data traffic on mobile phone [min/d]	44/343	22.5	74.3	**1.91 (1.17–3.14)**	**1.97 (1.14–3.40)**
duration cordless phone calls [min/d]	44/343	2.5	9.4	**1.67 (1.31–2.14)**	**1.64 (1.27–2.12)**
duration mobile phone calls [min/d]	44/343	3.0	18.6	1.17 (0.98–1.40)	1.14 (0.93–1.38)
Exhaustibility					
duration data traffic on mobile phone [min/d]	51/361	22.5	74.3	**2.56 (1.60–4.10)**	**3.63 (2.09–6.31)**
duration cordless phone calls [min/d]	51/361	2.5	9.4	**1.30 (1.02–1.65)**	**1.35 (1.05–1.75)**
duration mobile phone calls [min/d]	51/361	3.0	18.6	1.12 (0.92–1.36)	1.18 (0.94–1.48)
Lack of energy					
duration data traffic on mobile phone [min/d]	53/353	22.5	74.3	**1.87 (1.19–2.96)**	**2.03 (1.23–3.35)**
duration cordless phone calls [min/d]	53/353	2.5	9.4	1.25 (0.97–1.61)	1.25 (0.96–1.63)
duration mobile phone calls [min/d]	53/353	3.0	18.6	1.17 (0.97–1.42)	1.16 (0.93–1.43)
Physical ill-being[a]					
duration data traffic on mobile phone [min/d]	55/281	22.5	74.3	**2.15 (1.35–3.42)**	**2.00 (1.20–3.36)**
duration cordless phone calls [min/d]	55/281	2.5	9.4	1.13 (0.88–1.45)	1.06 (0.80–1.40)
duration mobile phone calls [min/d]	55/281	3.0	18.6	1.16 (0.96–1.40)	1.16 (0.92–1.46)
Cumulative Dose (whole sample)					
Headache					
brain [mJ/kg/d]	40/341	274.7	1853.6	1.20 (0.93–1.56)	1.23 (0.93–1.63)
whole body [mJ/kg/d]	40/341	120.1	380.3	**1.29 (1.004–1.67)**	**1.37 (1.04–1.81)**
Tiredness					
brain [mJ/kg/d]	73/228	274.7	1853.6	0.95 (0.71–1.25)	1.11 (0.81–1.53)
whole body [mJ/kg/d]	73/228	120.1	380.3	1.03 (0.80–1.32)	1.22 (0.91–1.64)
Lack of concentration					
brain [mJ/kg/d]	44/343	274.7	1853.6	1.08 (0.85–1.36)	1.02 (0.79–1.32)
whole body [mJ/kg/d]	44/343	120.1	380.3	1.14 (0.93–1.41)	1.10 (0.88–1.38)
Exhaustibility					

(continued on next page)

Table 4 *(continued)*

	n with occurrence of symptoms/n total	IQR 25%[b]	75%[b]	Odds ratio crude (95% CI)	Odds ratio adjusted (95% CI)[c]
brain [mJ/kg/d]	51/361	274.7	1853.6	1.13 (0.88–1.45)	1.15 (0.88–1.51)
whole body [mJ/kg/d]	51/361	120.1	380.3	**1.26 (1.001–1.58)**	**1.34 (1.04–1.72)**
Lack of energy					
brain [mJ/kg/d]	53/353	274.7	1853.6	1.20 (0.95–1.51)	1.16 (0.90–1.49)
whole body [mJ/kg/d]	53/353	120.1	380.3	**1.26 (1.004–1.58)**	1.24 (0.97–1.59)
Physical ill-being[a]					
brain [mJ/kg/d]	55/281	274.7	1853.6	1.18 (0.96–1.44)	1.15 (0.92–1.44)
whole body [mJ/kg/d]	55/281	120.1	380.3	**1.24 (1.01–1.52)**	1.22 (0.98–1.54)

Odds ratios are expressed per inter quartile change of the exposure variables.

[a] Kidscreen well-being inverted to ill-being for coherent data presentation.

[b] 25th and 75th percentile, respectively. IQR: inter quartile range.

[c] adjusted for age, sex, nationality, school level, physical activity, alcohol, education of parents, change in body height and time between baseline and follow-up investigation.

between the exposure variables. A Bonferroni correction would thus certainly be too conservative but a correction factor of 50 may be realistic. In this case the strongest observed associations ($p < 0.001$) in the cohort analyses would still be significant such as the link between lack of energy and number of texts sent or the association between exhaustibility and duration of data traffic on mobile phone (Table 4). It has to be emphasized, however, that these analyses are not designed as independent tests but with the clear objective to evaluate the pattern of association with respect to the EMF exposure involved to various degrees in the exposure variables. This pattern would not be affected by any kind of multiple adjustment correction.

Uncertainty of the dose measure calculation cannot be quantified at that time. For example the absorbed radiation by the body depends on the unknown position of the emitting device in relation to the body. A further source of uncertainty is the emitted power from mobile phones, in particular during data traffic and in stand-by mode and errors in modelling and personal measurements (Roser et al., 2015).

The analyses in the sample with operator data have also some limitations. First, selection bias may be of concern, since only about 50% of the sample agreed to provide operator data. Second, operator recorded text messages (SMS) are most likely not relevant for the real texting behaviour of our study participants, since according to the questionnaire they use mostly web based applications such as “WhatsApp”. Thus, the strong associations between self-reported number of text messages and symptoms in both the cohort and the cross-sectional analyses are thus likely to be more accurate than the absence of associations seen for most symptoms in relation to operator recorded text messages. Third, it has to be emphasized, that the difference between the dose calculation in the whole sample and in the operator sample is restricted to duration of mobile phone use only (self-reported vs. operator recorded). This has a large impact on the brain dose calculation, where no indications for an association were seen in the operator sample, but not on the whole body dose, where operator recorded mobile phone use contributes only 20.0%. For all these reasons, we decided to use the whole sample analysis as the main analysis.

In summary, our study demonstrates that usage measures, such as the duration of data traffic on the mobile phone, or the number of texts sent per day are more consistently associated with symptoms than cumulative RF-EMF dose within one year or RF-EMF from fixed site transmitters as shown in Schoeni et al. (2016). This suggests that rather media use than RF-EMF exposure is related to non-specific symptoms in adolescents. A possible reason for increased health symptom reports related to wireless communication device use might be sleep deprivation. Mobile phone use in the evening or even during night may compete with sleeping hours which in turn might lead to more symptoms (Schoeni et al., 2015b). It was also shown that blue light emanating from the screens of the mobile phones has an impact on human sleep (Chellappa et al., 2013), and suppresses melatonin secretion (Vartanian et al., 2015). Circadian misalignment as a result of suppressed melatonin secretion caused by chronic artificial light at night may have negative effects on the psychological, cardiovascular and/or metabolic functions (Cho et al., 2015).

An alternative explanation for the observed association is residual confounding or reverse causality, which would mean that adolescents with symptoms (cross-sectional analyses) or more prone to develop symptoms (cohort analyses) are more likely to use wireless communication devices. It is also conceivable that study participants find the constant accessibility and availability via mobile phones to be stressful which might lead to increased symptom reports. Thomee et al. (2011) found that perceived stressfulness of accessibility around the clock was the strongest predictor of mental health outcomes. We have seen in a previous cross-sectional analysis of our data that, independent of amount of mobile phone use, decreased well-being and behavioural problems were particularly pronounced in participants who scored high on the 10-item Problematic Mobile Phone Use Scale (Roser et al., 2016a). This scale was developed in the framework of addiction and measures and covers aspects such as loss of control, withdrawal and negative life consequences (Foerster et al., 2015). This may indicate that aspects of addiction may play a role for the observed associations.

5. Conclusion

In conclusion, this cohort study confirms associations between wireless communication device use and an increase in health symptom reports in adolescents previously seen in cross-sectional studies. The study suggest that other aspects of extensive media use cause symptoms and not RF-EMF, because associations were less pronounced for RF-EMF dose measures compared to various wireless device use variables such as texting or data traffic.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.envres.2017.01.004.

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Table S1. Results of the mixed-logistic cross-sectional analyses of self-reported usage measures and dose measures for the whole sample. All odds ratios refer to an interquartile (IQR) increase in exposure.

	n with symptoms / n total	IQR 25% [b]	75% [b]	Odds ratio crude (95% CI)	Odds ratio adjusted (95% CI) [c]
Usage measures marginally related to RF-EMF exposure (negative control) variables)					
Headache					
duration gaming [min/d]	158/858	0.0	68.6	1.13 (0.86 to 1.48)	1.19 (0.89 to 1.61)
number of texts sent [x/d]	158/858	4.4	51.6	**2.05 (1.27 to 3.29)**	**2.26 (1.31 to 3.90)**
Tiredness					
duration gaming [min/d]	404/861	0.0	68.6	**1.29 (1.02 to 1.61)**	**1.34 (1.04 to 1.72)**
number of texts sent [x/d]	404/861	4.4	51.6	**1.72 (1.19 to 2.49)**	**1.81 (1.20 to 2.74)**
Lack of concentration					
duration gaming [min/d]	163/861	0.0	68.6	**1.60 (1.23 to 2.07)**	**1.58 (1.19 to 2.10)**
number of texts sent [x/d]	163/861	4.4	51.6	**1.63 (1.04 to 2.55)**	**1.78 (1.07 to 2.97)**
Exhaustibility					
duration gaming [min/d]	131/857	0.0	68.6	1.12 (0.89 to 1.42)	1.25 (0.97 to 1.62)
number of texts sent [x/d]	131/857	4.4	51.6	**1.86 (1.24 to 2.80)**	**1.79 (1.14 to 2.80)**
Lack of energy					
duration gaming [min/d]	155/860	0.0	68.6	**1.32 (1.03 to 1.69)**	**1.48 (1.12 to 1.94)**
number of texts sent [x/d]	155/860	4.4	51.6	**1.67 (1.08 to 2.58)**	1.56 (0.97 to 2.53)
Physical ill-being [a]					
duration gaming [min/d]	280/863	0.0	68.6	1.06 (0.83 to 1.35)	1.24 (0.95 to 1.60)
number of texts sent [x/d]	280/863	4.4	51.6	1.17 (0.79 to 1.74)	1.18 (0.76 to 1.81)
Usage measures related to RF-EMF exposure					
Headache					
duration data traffic on mobile phone [min/d]	158/858	5.5	87.8	**2.46 (1.45 to 4.16)**	**2.52 (1.45 to 4.36)**
duration cordless phone calls [min/d]	158/858	2.5	10.5	**1.24 (1.01 to 1.53)**	1.21 (0.99 to 1.49)
duration mobile phone calls [min/d]	158/858	2.0	18.6	**1.37 (1.17 to 1.60)**	**1.36 (1.15 to 1.60)**
Tiredness					
duration data traffic on mobile phone [min/d]	404/861	5.5	87.8	**2.27 (1.52 to 3.39)**	**2.33 (1.54 to 3.52)**
duration cordless phone calls [min/d]	404/861	2.5	10.5	**1.24 (1.03 to 1.48)**	**1.25 (1.04 to 1.49)**
duration mobile phone calls [min/d]	404/861	2.0	18.6	1.09 (0.97 to 1.23)	1.08 (0.96 to 1.22)
Lack of concentration					
duration data traffic on mobile phone [min/d]	163/861	5.5	87.8	**2.22 (1.35 to 3.65)**	**2.27 (1.36 to 3.78)**
duration cordless phone calls [min/d]	163/861	2.5	10.5	**1.25 (1.04 to 1.51)**	**1.24 (1.02 to 1.50)**
duration mobile phone calls [min/d]	163/861	2.0	18.6	1.05 (0.94 to 1.19)	1.03 (0.91 to 1.16)
Exhaustibility					
duration data traffic on mobile phone [min/d]	131/857	5.5	87.8	**2.31 (1.48 to 3.62)**	**2.20 (1.39 to 3.49)**
duration cordless phone calls [min/d]	131/857	2.5	10.5	**1.22 (1.03 to 1.43)**	**1.19 (1.01 to 1.40)**
duration mobile phone calls [min/d]	131/857	2.0	18.6	**1.17 (1.05 to 1.31)**	**1.14 (1.02 to 1.27)**
Lack of energy					
duration data traffic on mobile phone [min/d]	155/860	5.5	87.8	**2.38 (1.47 to 3.84)**	**2.29 (1.40 to 3.74)**
duration cordless phone calls [min/d]	155/860	2.5	10.5	1.16 (0.97 to 1.39)	1.17 (0.98 to 1.40)
duration mobile phone calls [min/d]	155/860	2.0	18.6	1.06 (0.95 to 1.18)	1.04 (0.93 to 1.16)
Physical ill-being [a]					
duration data traffic on mobile phone [min/d]	280/863	5.5	87.8	**1.57 (1.02 to 2.42)**	1.54 (0.99 to 2.39)
duration cordless phone calls [min/d]	280/863	2.5	10.5	**1.24 (1.03 to 1.48)**	1.17 (0.98 to 1.40)
duration mobile phone calls [min/d]	280/863	2.0	18.6	**1.13 (1.003 to 1.28)**	1.06 (0.94 to 1.19)
Cumulative Dose (whole sample)					
Headache					
brain [mJ/kg/d]	158/858	191.6	1658.2	**1.32 (1.13 to 1.55)**	**1.32 (1.12 to 1.55)**
whole body [mJ/kg/d]	158/858	103.6	364.3	**1.38 (1.17 to 1.62)**	**1.37 (1.16 to 1.62)**
Tiredness					
brain [mJ/kg/d]	404/861	191.6	1658.2	1.09 (0.95 to 1.24)	1.08 (0.94 to 1.23)
whole body [mJ/kg/d]	404/861	103.6	364.3	1.12 (0.99 to 1.28)	1.11 (0.97 to 1.26)
Lack of concentration					
brain [mJ/kg/d]	163/861	191.6	1658.2	1.12 (0.96 to 1.30)	1.08 (0.93 to 1.26)
whole body [mJ/kg/d]	163/861	103.6	364.3	1.11 (0.98 to 1.27)	1.08 (0.94 to 1.23)
Exhaustibility					
brain [mJ/kg/d]	131/857	191.6	1658.2	**1.18 (1.04 to 1.33)**	**1.15 (1.02 to 1.30)**
whole body [mJ/kg/d]	131/857	103.6	364.3	**1.21 (1.07 to 1.36)**	**1.18 (1.04 to 1.33)**
Lack of energy					
brain [mJ/kg/d]	155/860	191.6	1658.2	1.10 (0.96 to 1.26)	1.08 (0.94 to 1.24)
whole body [mJ/kg/d]	155/860	103.6	364.3	1.10 (0.97 to 1.24)	1.07 (0.95 to 1.22)
Physical ill-being [a]					
brain [mJ/kg/d]	280/863	191.6	1658.2	**1.14 (1.00 to 1.31)**	1.06 (0.93 to 1.21)
whole body [mJ/kg/d]	280/863	103.6	364.3	**1.19 (1.04 to 1.36)**	1.10 (0.97 to 1.26)

[a] Kidscreen well-being inverted to ill-being for coherent data presentation.
[b] 25th and 75th percentile, respectively. IQR: inter quartile range.
[c] adjusted for age, sex, nationality, school level, physical activity, alcohol and education of parents.

Table S2. Results of the mixed-logistic cross-sectional analyses of the usage and dose measures for the sample with operator data. All odds ratios refer to an interquartile (IQR) increase in exposure.

	n with symptoms / n total	IQR 25% [b]	75% [b]	Odds ratio crude (95% CI)	Odds ratio adjusted (95% CI) [c]
Objective usage measures marginally related to RF-EMF exposure					
Headache					
number of SMS sent [x/d]	79/458	0.4	2.1	**1.12 (1.01 to 1.26)**	1.11 (0.998 to 1.24)
Tiredness					
number of SMS sent [x/d]	224/461	0.4	2.1	1.06 (0.93 to 1.21)	1.07 (0.94 to 1.22)
Lack of concentration					
number of SMS sent [x/d]	85/461	0.4	2.1	0.94 (0.80 to 1.11)	0.97 (0.83 to 1.13)
Exhaustibility					
number of SMS sent [x/d]	69/461	0.4	2.1	0.95 (0.82 to 1.11)	0.95 (0.81 to 1.11)
Lack of energy					
number of SMS sent [x/d]	74/460	0.4	2.1	0.91 (0.75 to 1.09)	0.90 (0.75 to 1.09)
Physical ill-being [a]					
number of SMS sent [x/d]	159/461	0.4	2.1	**1.17 (1.02 to 1.34)**	**1.16 (1.01 to 1.33)**
Objective usage measures related to RF-EMF exposure					
Headache					
volume data traffic on mobile phone [MB/d]	79/458	0.0	8.0	1.05 (0.96 to 1.16)	1.04 (0.95 to 1.14)
duration mobile phone calls [min/d]	79/458	0.2	1.7	1.11 (0.996 to 1.23)	1.10 (0.98 to 1.22)
Tiredness					
volume data traffic on mobile phone [MB/d]	224/461	0.0	8.0	1.00 (0.91 to 1.10)	1.00 (0.91 to 1.10)
duration mobile phone calls [min/d]	224/461	0.2	1.7	1.00 (0.89 to 1.13)	1.00 (0.88 to 1.13)
Lack of concentration					
volume data traffic on mobile phone [MB/d]	85/461	0.0	8.0	1.09 (0.97 to 1.22)	1.07 (0.96 to 1.21)
duration mobile phone calls [min/d]	85/461	0.2	1.7	1.09 (0.95 to 1.26)	1.06 (0.91 to 1.22)
Exhaustibility					
volume data traffic on mobile phone [MB/d]	69/461	0.0	8.0	**1.13 (1.02 to 1.25)**	**1.11 (1.003 to 1.22)**
duration mobile phone calls [min/d]	69/461	0.2	1.7	1.08 (0.96 to 1.21)	1.06 (0.94 to 1.19)
Lack of energy					
volume data traffic on mobile phone [MB/d]	74/460	0.0	8.0	1.06 (0.95 to 1.18)	1.04 (0.93 to 1.16)
duration mobile phone calls [min/d]	74/460	0.2	1.7	1.08 (0.95 to 1.22)	1.05 (0.92 to 1.19)
Physical ill-being [a]					
volume data traffic on mobile phone [MB/d]	159/461	0.0	8.0	1.04 (0.95 to 1.13)	1.03 (0.94 to 1.12)
duration mobile phone calls [min/d]	159/461	0.2	1.7	1.04 (0.93 to 1.16)	1.03 (0.92 to 1.15)
Cumulative Dose (sample with operator data)					
Headache					
brain [mJ/kg/d]	79/458	52.6	234.3	**1.17 (1.01 to 1.36)**	1.14 (0.98 to 1.32)
whole body [mJ/kg/d]	79/458	63.8	164.4	**1.88 (1.34 to 2.65)**	**1.77 (1.25 to 2.51)**
Tiredness					
brain [mJ/kg/d]	224/461	52.6	234.3	1.05 (0.89 to 1.24)	1.05 (0.89 to 1.25)
whole body [mJ/kg/d]	224/461	63.8	164.4	**1.72 (1.18 to 2.52)**	**1.79 (1.20 to 2.66)**
Lack of concentration					
brain [mJ/kg/d]	85/461	52.6	234.3	**1.28 (1.04 to 1.56)**	**1.24 (1.01 to 1.52)**
whole body [mJ/kg/d]	85/461	63.8	164.4	**1.93 (1.19 to 3.11)**	**1.79 (1.10 to 2.93)**
Exhaustibility					
brain [mJ/kg/d]	69/461	52.6	234.3	**1.22 (1.05 to 1.42)**	**1.19 (1.02 to 1.39)**
whole body [mJ/kg/d]	69/461	63.8	164.4	**1.74 (1.20 to 2.51)**	**1.65 (1.12 to 2.43)**
Lack of energy					
brain [mJ/kg/d]	74/460	52.6	234.3	1.17 (0.98 to 1.38)	1.14 (0.96 to 1.36)
whole body [mJ/kg/d]	74/460	63.8	164.4	**1.78 (1.21 to 2.63)**	**1.71 (1.14 to 2.56)**
Physical ill-being [a]					
brain [mJ/kg/d]	159/461	52.6	234.3	1.09 (0.94 to 1.26)	1.04 (0.90 to 1.20)
whole body [mJ/kg/d]	159/461	63.8	164.4	**1.48 (1.08 to 2.04)**	1.33 (0.97 to 1.83)

[a] Kidscreen well-being inverted to ill-being for coherent data presentation.

[b] 25^{th} and 75^{th} percentile, respectively. IQR: inter quartile range.

[c] adjusted for age, sex, nationality, school level, physical activity, alcohol and education of parents.

Table S3. Results of the cohort analyses of the objective usage measures and dose measures for the sample with operator data. All odds ratios refer to an interquartile (IQR) increase in exposure.

	n with occurrence of symptoms / n total	IQR 25% [b]	75% [b]	Odds ratio crude (95% CI)	Odds ratio adjusted (95% CI) [c]
Objective usage measures marginally related to RF-EMF exposure					
Headache					
number of SMS sent [x/d]	24/187	0.5	1.8	1.06 (0.85 to 1.33)	1.03 (0.80 to 1.32)
Tiredness					
number of SMS sent [x/d]	40/122	0.5	1.8	1.11 (0.90 to 1.37)	1.28 (0.97 to 1.70)
Lack of concentration					
number of SMS sent [x/d]	25/190	0.5	1.8	**1.31 (1.08 to 1.59)**	**1.29 (1.04 to 1.61)**
Exhaustibility					
number of SMS sent [x/d]	33/205	0.5	1.8	0.89 (0.67 to 1.18)	0.87 (0.65 to 1.18)
Lack of energy					
number of SMS sent [x/d]	31/202	0.5	1.8	1.05 (0.86 to 1.28)	1.07 (0.84 to 1.34)
Physical ill-being [a]					
number of SMS sent [x/d]	39/153	0.5	1.8	0.98 (0.75 to 1.28)	0.92 (0.66 to 1.28)
Objective usage measures related to RF- EMF exposure					
Headache					
volume data traffic on mobile phone [MB/d]	24/187	0.0	10.9	1.10 (0.92 to 1.32)	1.09 (0.91 to 1.32)
duration mobile phone calls [min/d]	24/187	0.2	1.8	1.05 (0.90 to 1.23)	1.03 (0.86 to 1.23)
Tiredness					
volume data traffic on mobile phone [MB/d]	40/122	0.0	10.9	1.17 (0.92 to 1.50)	1.21 (0.94 to 1.57)
duration mobile phone calls [min/d]	40/122	0.2	1.8	**1.17 (1.01 to 1.36)**	**1.37 (1.07 to 1.75)**
Lack of concentration					
volume data traffic on mobile phone [MB/d]	25/190	0.0	10.9	**1.20 (1.01 to 1.44)**	1.20 (0.99 to 1.44)
duration mobile phone calls [min/d]	25/190	0.2	1.8	**1.21 (1.05 to 1.41)**	**1.21 (1.03 to 1.44)**
Exhaustibility					
volume data traffic on mobile phone [MB/d]	33/205	0.0	10.9	1.17 (0.996 to 1.38)	1.17 (0.99 to 1.38)
duration mobile phone calls [min/d]	33/205	0.2	1.8	1.11 (0.98 to 1.26)	1.11 (0.97 to 1.28)
Lack of energy					
volume data traffic on mobile phone [MB/d]	31/202	0.0	10.9	1.07 (0.90 to 1.28)	1.05 (0.87 to 1.27)
duration mobile phone calls [min/d]	31/202	0.2	1.8	**1.15 (1.02 to 1.31)**	1.11 (0.96 to 1.27)
Physical ill-being [a]					
volume data traffic on mobile phone [MB/d]	39/153	0.0	10.9	**1.48 (1.12 to 1.94)**	**1.42 (1.06 to 1.90)**
duration mobile phone calls [min/d]	39/153	0.2	1.8	1.10 (0.97 to 1.25)	1.07 (0.93 to 1.23)
Cumulative Dose (sample with operator data)					
Headache					
brain [mJ/kg/d]	24/187	59.9	235.7	1.06 (0.94 to 1.20)	1.05 (0.92 to 1.20)
whole body [mJ/kg/d]	24/187	73.3	157.4	**1.41 (1.02 to 1.95)**	**1.44 (1.01 to 2.06)**
Tiredness					
brain [mJ/kg/d]	40/122	59.9	235.7	1.17 (0.98 to 1.40)	1.28 (0.97 to 1.69)
whole body [mJ/kg/d]	40/122	73.3	157.4	**1.55 (1.03 to 2.35)**	**2.04 (1.11 to 3.77)**
Lack of concentration					
brain [mJ/kg/d]	25/190	59.9	235.7	1.15 (0.99 to 1.33)	1.13 (0.98 to 1.31)
whole body [mJ/kg/d]	25/190	73.3	157.4	**1.55 (1.09 to 2.19)**	**1.47 (1.03 to 2.10)**
Exhaustibility					
brain [mJ/kg/d]	33/205	59.9	235.7	1.14 (0.996 to 1.31)	1.13 (0.98 to 1.30)
whole body [mJ/kg/d]	33/205	73.3	157.4	**1.59 (1.13 to 2.23)**	**1.61 (1.10 to 2.34)**
Lack of energy					
brain [mJ/kg/d]	31/202	59.9	235.7	1.12 (0.99 to 1.28)	1.09 (0.95 to 1.24)
whole body [mJ/kg/d]	31/202	73.3	157.4	**1.60 (1.13 to 2.26)**	**1.51 (1.03 to 2.22)**
Physical ill-being [a]					
brain [mJ/kg/d]	39/153	59.9	235.7	1.08 (0.96 to 1.22)	1.04 (0.92 to 1.18)
whole body [mJ/kg/d]	39/153	73.3	157.4	**1.66 (1.14 to 2.41)**	1.48 (0.999 to 2.19)

[a] Kidscreen well-being inverted to ill-being for coherent data presentation.

[b] 25th and 75th percentile, respectively. IQR: inter quartile range.

[c] adjusted for age, sex, nationality, school level, physical activity, alcohol, education of parents, change in body height and time between baseline and follow-up investigation.

5 Far-field exposure and health symptoms

5.1 Article 5: Symptoms in Swiss adolescents in relation to exposure from fixed site transmitters: a prospective cohort study

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Symptoms in Swiss adolescents in relation to exposure from fixed site transmitters: a prospective cohort study

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Abstract

Background: There is public concern regarding potential health effects of radiofrequency electromagnetic fields (RF-EMF) emitted by fixed site transmitters. We therefore investigated whether self-reported general well-being in adolescents is affected by RF-EMF exposure from mobile phone base stations (downlink) and broadcast transmitters (TV and radio).

Methods: In a prospective cohort study, 439 study participants aged 12-17 years, completed questionnaires about their self-reported well-being and possible confounding factors at baseline and one year later. Exposure from fixed site transmitters at home and school was calculated by using a geospatial propagation model.
Data were analysed using a mixed-logistic cross-sectional model of a combined dataset consisting of baseline and follow-up data and a longitudinal approach where we investigated whether exposure at baseline (cohort analysis) or changes in exposure between baseline and follow-up (change analysis) were related to a new onset of a symptom between baseline and follow-up. All analyses were adjusted for relevant confounders.

Results: Mean exposure (median; 75th) for broadcast transmitters, downlink and total exposure at baseline were 1.9 μW/m^2 (1.0 μW/m^2; 2.8 μW/m^2), 14.4 μW/m^2 (3.8 μW/m^2; 11.0 μW/m^2) and 16.3 μW/m^2 (5.8 μW/m^2; 13.4 μW/m^2), respectively. In cross-sectional analyses no associations were observed between any symptom and RF-EMF exposure from fixed site transmitters. In the cohort and change analyses only a few significant associations were observed including an increased OR for tiredness (2.94, 95%CI: 1.43 to 6.05) for participants in the top 25th percentile of total RF-EMF exposure from fixed site transmitters at baseline, in comparison to participants exposed below the median and a decreased OR for exhaustibility (0.50, 95%CI: 0.27 to 0.93) for participants with an exposure increase between baseline and follow-up.

Conclusions: In this cohort study, using a geospatial propagation model, RF-EMF exposure from fixed site transmitters was not consistently associated with self-reported symptoms in Swiss adolescents. The few observed associations have to be interpreted with caution and might represent chance findings.

Keywords: Geospatial propagation model, Adolescents, Symptoms, Fixed site transmitter, RF-EMF

Background

Number of sources emitting radio-frequency electromagnetic fields (RF-EMF) such as base stations, mobile and cordless phones, broadcast transmitters and WLAN have substantially increased in the everyday environment during the last few decades. This increase has been accompanied by a growing public concern that RF-EMF may have an effect on human health; especially on non-specific symptoms like headache or sleep disturbances. The majority of RF-EMF research so far has focused on the exposure from mobile phones whereas the exposure from broadcast transmitters (TV and radio) and base stations has received less attention. This might be due to the relative low induced exposure levels from broadcast transmitters and base stations compared to the

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exposure that is induced by mobile phones and other wireless communication devices operating close to the body.

According to a systematic review [1] where human experimental and epidemiological studies until March 2009 were included, not one single symptom or symptom pattern was consistently related to exposure from mobile phone base stations. In the epidemiological studies, a tendency towards increased symptom reports was observed in studies using subjective exposure surrogates (e.g., self-estimated distance to closest mobile phone base station), while no effects could be shown in studies with objective exposure surrogates. However, studies in children and adolescents were scarce. The only experimental study investigating effects of mobile phone base station exposure on health symptoms that included adolescents was from Riddervold et al. [2]. They observed a larger change in headache score after UMTS exposure than after sham exposure when the data from 40 adults and 40 adolescents were pooled. However, this change was due to a lower headache baseline score before exposure rather than to a higher score after exposure. In an epidemiological study (MobilEe-study), using 24 h personal measurements for assessing RF-EMF exposure no consistent associations between measured exposure and acute symptoms in children and adolescents were seen [3]. Some associations reaching statistical significance were not consistent over two time points (morning and afternoon) and the authors hypothesized that the observed associations are due to chance because of multiple testing. Additionally, they did not only consider exposure from fixed site transmitters because the dosimeter was limited to differentiate between uplink (mobile phone handsets) and downlink bands. In the same study they investigated associations between measured exposure and chronic symptoms [4]. They did not find any association between individual personal RF-EMF exposure and chronic well-being although measured RF-EMF exposure in the highest quartile was associated to overall behavioural problems for adolescents but not for children [5].

We aimed thus to investigate whether self-reported general well-being in Swiss adolescents is affected by RF-EMF exposure from mobile phone base stations and broadcast transmitters using a geospatial propagation model.

Methods

Study population

For the present study, as part of the HERMES (Health Effects Related to Mobile phonE use in adolescentS) study, adolescents from 7th, 8th and 9th grade in schools from rural and urban areas in Central Switzerland were recruited. The baseline investigation took place between June 2012 and February 2013. During a school visit the adolescents filled in a questionnaire with questions on non-specific symptoms of ill health, socio demographics, and other relevant covariables. This information was complemented by a parental questionnaire with additional items such as house characteristics. Parents were asked to fill out the questionnaire and send it back directly. Teachers were asked to fill out a questionnaire with questions on school building characteristics and floor location of the class room. This procedure was repeated one year later with the same study participants and the same study managers.

Ethical approval for the conduct of the study was received from the ethical committee of Lucerne, Switzerland (Dienststelle Gesundheit, Ethikkommission des Kantons Luzern, Schweiz) on May 9th, 2012 (Ref. Nr. EK: 12025).

Well-being

In the written questionnaire headache was assessed using the six-item Headache Impact Test (HIT-6) [6]. A summary score of all six items can range from 36 to 78. A summary score of 49 or less is considered as “headache has no impact on your life,” 50 to 55 is considered as “headache has some impact on your life,” 56 to 59 as “headache has substantial impact on your life” and 60 or more as “headache has a very severe impact on your life.” A binary variable was created by using 56 as the cut-off value. Occurrence of tiredness, lack of energy, lack of concentration and rapid exhaustibility (referred to as exhaustibility) during the four weeks prior to fill in the questionnaire were assessed using a four-point Likert scale with categories “never,” “rare,” “moderate” and “severe.” Binary variables were created by combining answer categories “never” with “rare” and “moderate” with “severe”. Physical well-being was assessed using the dimension “Physical Well-being” from the Kidscreen-52 questionnaire. This dimension includes five questions exploring the level of adolescent’s physical activity, energy and fitness [7, 8]. A binary variable was created by using the mean minus half a standard deviation as the cut-off, which is suggested as the guiding principle according to the official Kidscreen questionnaire handbook. For coherent data presentation, the Kidscreen Well-being was inverted to an ill-being scale by considering a low score as ill-being.

RF-EMF exposure from fixed site transmitters

Far-field exposure from fixed site transmitters (radio and TV broadcast transmitters and mobile phone base stations, where downlink exposure are included) at home and in school were modelled using a geospatial propagation model based on a comprehensive database of fixed site transmitters and on a three-dimensional topography and building model of the study area [9, 10]. The model was initially developed for the NIR-monitoring project of Central Switzerland, the transmitter data were provided by the environmental offices of the cantons involved. The coordinates of the home and school addresses of the study participants were geocoded from the address using the database of the Swiss Federal Statistical Office. The parents' and teachers' questionnaires provided information on the number of floors of the building and the floor location of the residence and of the class room for calculating the height of the residence and of the class room [9, 10]. In order to take into account attenuation by buildings, the following damping factors were applied: 3 dB for outer walls, 5 dB for roofs and 0.6 dB/m in the interior of buildings. The building database that has been used for modelling had no information about very new buildings, therefore a damping factor of 4.6 dB was used when building information was missing [10]. Time weighted average exposure per day for each participant was calculated from the modelled exposure at home (weight: 4/5; 19.2 h) and at school (weight: 1/5; 4.8 h taking into account weekend and holidays). Exposure is expressed in units of the power flux density ($\mu W/m^2$) of the electromagnetic wave.

Statistical analysis

Three main analyses were performed to investigate possible associations between self-reported general well-being and RF-EMF exposure from fixed site transmitters:

a) A mixed-logistic cross-sectional regression analysis of a combined dataset consisting of baseline and follow-up data.
b) A cohort analysis including all participants without the target symptom at baseline to investigate whether new onset of a symptom was related to the exposure level at baseline.
c) A change analysis including all participants without the target symptom at baseline to investigate whether new onset of a symptom was related to an increase in exposure between baseline and follow-up.

The analyses for the mixed logistic cross-sectional regression analyses (a) and the cohort analyses (b) were based on three exposure categories for all variables: exposure below median (reference), 50^{th} to 75^{th} percentile and the top 25^{th} percentile. In the change analyses (c) we compared study participants with an increase in exposure (>0 $\mu W/m^2$) to the remaining study participants who did not experience an exposure increase between baseline and follow-up (reference).

All models were adjusted for age, sex, nationality, school level (college preparatory high school or high school), physical activity, alcohol consumption and education of parents. In the cohort and change analyses we adjusted for confounders at follow-up. Additionally, all models of the cohort and change analyses (b) were adjusted for change in body height between baseline and follow-up.

Linear regression imputation (14 missing values at baseline and 10 missing values at follow-up for alcohol consumption; 7 missing values at baseline and 6 missing values at follow-up for information on body height) or imputation of a common category (2 missing values at baseline and 1 missing value at follow-up for frequency of physical activity; 60 missing values for educational level of the parents) was used to impute missing values in the confounder variables. Statistical analyses were carried out using STATA version 12.1 (StataCorp, College Station, USA). Figures were made with the software R using version R for Windows 3.0.1.

Results

439 students (participation rate: 36.8 %) aged 12 to 17 years from 24 schools (participation rate: 19.1 %) from rural and urban areas in Central Switzerland participated in the baseline investigation of the HERMES study. The follow-up investigation was on average 12.5 months after baseline. Mean (SD) age of the study participants at follow-up was 15.0 years (0.79) and mean (SD) body height at follow-up was 167.3 cm (8.5 cm). More than half of the study participants were female (59.8 %) and 109 (25.7 %) attended a college preparatory high school. The majority (80.2 %) had Swiss nationality, whereas 13.9 % had mixed and 5.9 % foreign nationality.

Most of the study participants are physically active for 2 -3 times per week (40.0 %) and don't drink any alcohol (52.5 %). Highest education of the parents was for 50.6 % the Training school followed by College of higher education (29.9 %).

Mean exposure (median; 75^{th}) for broadcast transmitters, downlink and total exposure at baseline were 1.9 $\mu W/m^2$ (1.0 $\mu W/m^2$; 2.8 $\mu W/m^2$), 14.4 $\mu W/m^2$ (3.8 $\mu W/m^2$; 11.0 $\mu W/m^2$) and 16.3 $\mu W/m^2$ (5.8 $\mu W/m^2$; 13.4 $\mu W/m^2$), respectively. Mean difference (range) between baseline and follow-up exposure for broadcast transmitters, downlink and total exposure were 0.1 $\mu W/m^2$ (-3.2 to 20.8 $\mu W/m^2$), 0.8 $\mu W/m^2$ (-274.1 to 220.9 $\mu W/m^2$) and 0.9 $\mu W/m^2$ (-277.4 to 220.9 $\mu W/m^2$), respectively. Figure 1 shows the distribution of the exposure variables at baseline with its

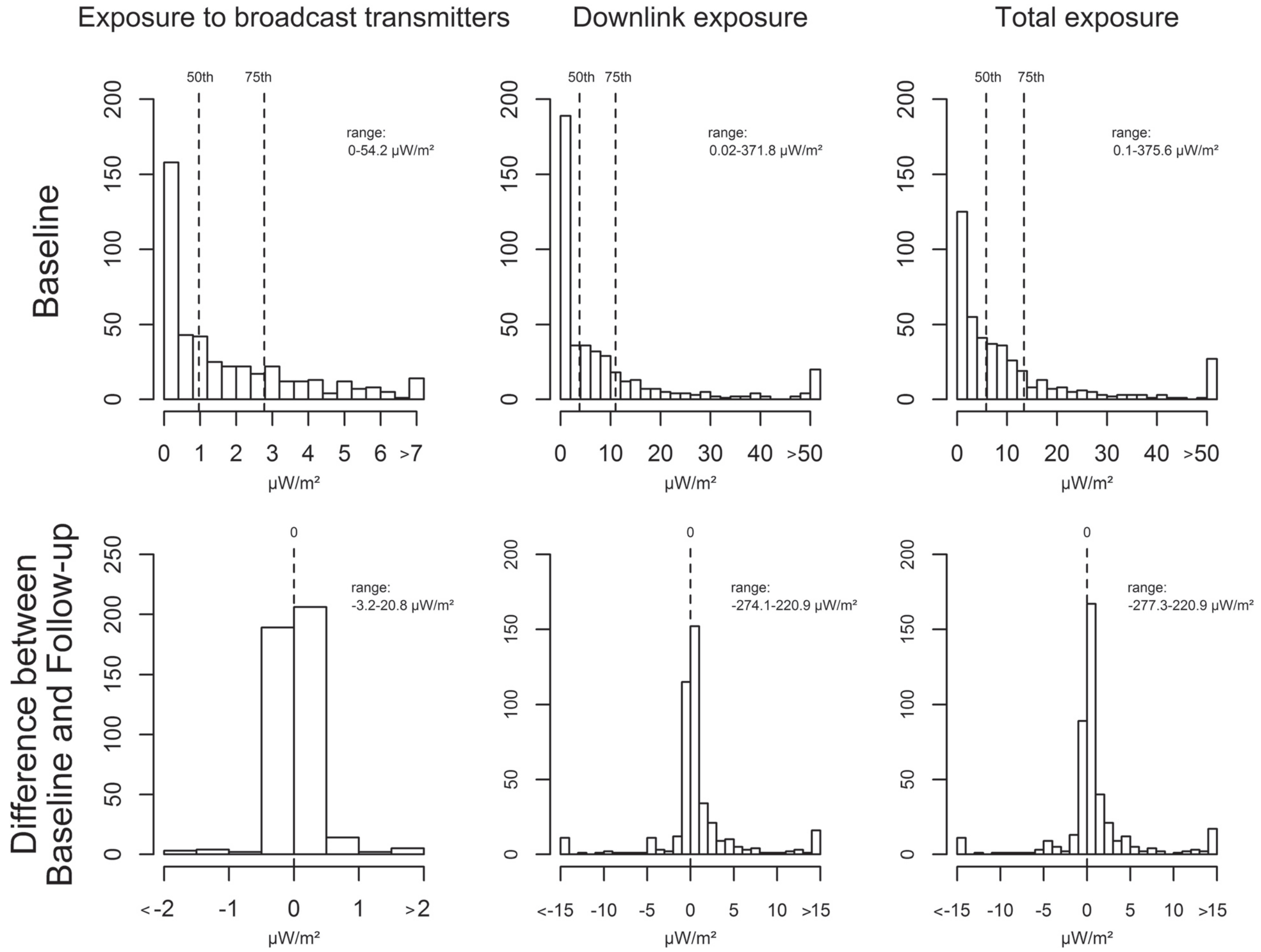

Fig. 1 Distribution of the exposure variables

50th and 75th percentiles and the distribution of the exposure difference between baseline and follow-up (reference).

Associations between symptoms and RF-EMF exposure from fixed site transmitters

Mixed-logistic cross-sectional analyses (a)

Table 1 shows the results of the mixed-logistic cross-sectional analysis of baseline and follow-up data based on categories. None of the symptoms was significantly associated with any of the exposure measures.

Cohort analyses (b)

Table 2 shows the results of the cohort analyses based on categories. Significant associations were found for increased tiredness and high downlink exposure (OR: 3.68; 95%CI: 1.76 to 7.66) and high total exposure to fixed site transmitters (OR: 2.94; 95%CI: 1.43 to 6.05), respectively and for increased lack of concentration and high exposure to broadcast transmitters (OR: 2.78; 95%CI: 1.23 to 6.27). High exposure refers to those in the top 25th percentile compared to those below the median (reference). Further significant results were found for increased lack of concentration for those in the medium broadcast transmitter exposure group (OR: 2.86; 95%CI: 1.28 to 6.42).

Change analyses (c)

In the change analyses two significant results were observed: an increase in downlink exposure was associated with a decrease in lack of concentration and an increase in total exposure to fixed site transmitters was associated with a decrease in exhaustibility (for numbers see Additional file 1: Table S1). None of the symptoms was increased for those with an increase in exposure between baseline and follow-up.

Discussion

In cross-sectional analyses of a combined dataset consisting of baseline and follow-up data no associations were observed between any symptom and RF-EMF exposure to fixed site transmitters. In the cohort

Table 1 Odds ratios (OR) of the mixed-logistic cross-sectional analysis of baseline and follow-up data based on exposure categories

	n with symptoms / n total	Medium exposure (>50th to ≤ 75th percentile)[b]			High exposure (>75th percentile)[b]		
		50th perc [μW/m²]	OR (95 % CI) crude	OR (95 % CI) adjusted[a]	75th perc [μW/m²]	OR (95 % CI) crude	OR (95 % CI) adjusted[a]
headache							
broadcast transmitter	158/858	0.97	1.23 (0.59 to 2.56)	1.26 (0.60 to 2.63)	2.8	1.79 (0.86 to 3.70)	1.70 (0.82 to 3.54)
total downlink	158/858	4.01	0.72 (0.34 to 1.52)	0.68 (0.32 to 1.45)	11.77	1.21 (0.59 to 2.48)	1.17 (0.57 to 2.38)
total	158/858	6.08	1.23 (0.59 to 2.55)	1.22 (0.58 to 2.55)	14.19	1.29 (0.62 to 2.70)	1.19 (0.57 to 2.49)
tiredness							
broadcast transmitter	404/861	0.97	1.03 (0.59 to 1.81)	1.00 (0.57 to 1.75)	2.8	1.05 (0.60 to 1.86)	1.02 (0.58 to 1.81)
total downlink	404/861	4.01	0.73 (0.42 to 1.27)	0.71 (0.41 to 1.24)	11.77	0.97 (0.56 to 1.69)	0.95 (0.55 to 1.65)
total	404/861	6.08	0.69 (0.40 to 1.21)	0.68 (0.39 to 1.19)	14.19	0.91 (0.52 to 1.59)	0.88 (0.51 to 1.53)
lack of concentration							
broadcast transmitter	163/861	0.97	1.42 (0.73 to 2.76)	1.58 (0.81 to 3.06)	2.8	1.08 (0.54 to 2.15)	1.24 (0.62 to 2.48)
total downlink	163/861	4.01	0.74 (0.37 to 1.44)	0.83 (0.42 to 1.63)	11.77	1.02 (0.52 to 2.01)	1.03 (0.53 to 2.00)
total	163/861	6.08	0.89 (0.46 to 1.74)	1.04 (0.53 to 2.04)	14.19	0.85 (0.43 to 1.69)	0.88 (0.45 to 1.75)
exhaustibility							
broadcast transmitter	131/857	0.97	1.19 (0.66 to 2.14)	1.13 (0.63 to 2.03)	2.8	1.07 (0.59 to 1.94)	0.98 (0.54 to 1.78)
total downlink	131/857	4.01	0.93 (0.52 to 1.66)	0.97 (0.54 to 1.74)	11.77	0.96 (0.54 to 1.74)	0.93 (0.52 to 1.66)
total	131/857	6.08	0.99 (0.56 to 1.77)	1.03 (0.57 to 1.83)	14.19	0.88 (0.48 to 1.60)	0.84 (0.46 to 1.51)
lack of energy							
broadcast transmitter	155/860	0.97	1.19 (0.63 to 2.24)	1.12 (0.60 to 2.11)	2.8	1.09 (0.58 to 2.08)	0.97 (0.51 to 1.86)
total downlink	155/860	4.01	0.70 (0.36 to 1.34)	0.66 (0.34 to 1.27)	11.77	1.10 (0.59 to 2.05)	1.04 (0.56 to 1.94)
total	155/860	6.08	0.90 (0.48 to 1.70)	0.85 (0.45 to 1.63)	14.19	1.13 (0.60 to 2.12)	1.08 (0.58 to 2.01)
physical ill-being							
broadcast transmitter	280/862	0.97	0.95 (0.52 to 1.74)	0.83 (0.46 to 1.48)	2.8	0.93 (0.51 to 1.72)	0.84 (0.47 to 1.50)
total downlink	280/862	4.01	0.97 (0.54 to 1.76)	1.02 (0.58 to 1.81)	11.77	1.39 (0.76 to 2.54)	1.38 (0.78 to 2.45)
total	280/862	6.08	0.83 (0.46 to 1.51)	0.93 (0.52 to 1.64)	14.19	1.20 (0.66 to 2.18)	1.21 (0.68 to 2.13)

[a] adjusted for age, sex, nationality, school level, physical activity, alcohol and education of parents
[b] < =50th percentile as reference group

analyses, where we investigated whether occurrence of the symptom was related to the exposure level at baseline, self-reported tiredness and concentration difficulties tended to be increased in relation to the exposure to fixed site transmitters. But such a pattern was not seen in the cross-sectional and the change analyses (Fig. 2). On the other hand, in the change analyses, where we investigated whether occurrence of symptoms was related to an increase in exposure between baseline and follow-up a decrease of exhaustibility was found for total RF-EMF increase and an improvement in concentration for increase in downlink exposure.

The highest calculated total mean exposure to fixed site transmitters was 375.6 μW/m² (=0.38 V/m), which is considerably below the current ICNIRP (International Commission on Non-Ionizing Radiation Protection [11]) guidelines, as well as lower than the approx. 10 times lower precautionary reference levels in Switzerland as defined by the ordinance relating to protection from non-ionising radiation [12].

A particular strength is the longitudinal design which allows for more robust conclusions compared to cross-sectional studies. To the best of our knowledge, this is the first cohort study on non-specific symptoms in adolescents using a geospatial propagation model to assess exposure from fixed site transmitters. Our model allows prediction of exposure from fixed site transmitters at the homes and at schools of the study participants. We applied different analysis strategies to evaluate varying hypotheses. In order to account for delayed effects with about one year latency (independent of dose relationship), we applied the cohort approach. On the other hand in the change analysis we would find effects if there is a linear relationship and thus we evaluated whether participants with an increase in exposure were more likely to develop symptoms. Thus, results have not to be entirely consistent as different hypotheses are tested but one would not expect to see

Table 2 Odds ratios (OR) of the cohort analysis based on exposure categories

	n with symptoms /	Medium exposure (>50th to ≤ 75th percentile)[b]			High exposure (>75th percentile)[b]		
	n total	50 th perc [μW/m^2]	OR (95 % CI) crude	OR (95 % CI) adjusted[a]	75 th perc [μW/m^2]	OR (95 % CI) crude	OR (95 % CI) adjusted[a]
headache							
broadcast transmitter	40/341	0.96	1.23 (0.55 to 2.73)	1.17 (0.52 to 2.66)	2.8	1.45 (0.65 to 3.25)	1.26 (0.55 to 2.91)
total downlink	40/341	3.79	0.65 (0.26 to 1.58)	0.57 (0.23 to 1.44)	11.01	1.20 (0.56 to 2.57)	1.07 (0.49 to 2.34)
total	40/341	5.82	0.77 (0.32 to 1.81)	0.67 (0.27 to 1.62)	13.38	1.11 (0.51 to 2.43)	0.95 (0.42 to 2.14)
tiredness							
broadcast transmitter	73/228	0.96	0.83 (0.41 to 1.67)	0.67 (0.32 to 1.41)	2.8	1.44 (0.74 to 2.81)	1.35 (0.66 to 2.77)
total downlink	73/228	3.79	1.98 (0.98 to 3.98)	1.71 (0.81 to 3.57)	11.01	3.24 (1.63 to 6.43)	3.68 (1.76 to 7.66)
total	73/228	5.82	1.57 (0.78 to 3.16)	1.47 (0.69 to 3.14)	13.38	2.81 (1.43 to 5.51)	2.94 (1.43 to 6.05)
lack of concentration							
broadcast transmitter	44/343	0.96	2.48 (1.14 to 5.43)	2.86 (1.28 to 6.42)	2.8	2.45 (1.12 to 5.35)	2.78 (1.23 to 6.27)
total downlink	44/343	3.79	1.35 (0.63 to 2.90)	1.51 (0.68 to 3.35)	11.01	1.48 (0.69 to 3.20)	1.51 (0.69 to 3.30)
total	44/343	5.82	1.33 (0.62 to 2.84)	1.64 (0.73 to 3.68)	13.38	1.25 (0.57 to 2.70)	1.31 (0.59 to 2.89)
exhaustibility							
broadcast transmitter	51/361	0.96	1.44 (0.71 to 2.94)	1.28 (0.61 to 2.68)	2.8	1.48 (0.72 to 3.06)	1.32 (0.62 to 2.84)
total downlink	51/361	3.79	1.16 (0.55 to 2.42)	1.00 (0.47 to 2.15)	11.01	1.41 (0.70 to 2.83)	1.33 (0.65 to 2.72)
total	51/361	5.82	1.26 (0.61 to 2.58)	1.08 (0.50 to 2.31)	13.38	1.18 (0.58 to 2.42)	1.10 (0.52 to 2.30)
lack of energy							
broadcast transmitter	53/353	0.96	1.08 (0.52 to 2.24)	1.07 (0.51 to 2.29)	2.8	1.49 (0.74 to 2.98)	1.45 (0.69 to 3.03)
total downlink	53/353	3.79	1.08 (0.52 to 2.25)	1.04 (0.49 to 2.21)	11.01	1.51 (0.76 to 3.00)	1.45 (0.72 to 2.95)
total	53/353	5.82	1.70 (0.84 to 3.41)	1.70 (0.81 to 3.58)	13.38	1.48 (0.72 to 3.03)	1.46 (0.69 to 3.08)
physical ill-being							
broadcast transmitter	55/280	0.96	0.61 (0.28 to 1.34)	0.71 (0.31 to 1.60)	2.8	0.87 (0.42 to 1.80)	0.91 (0.41 to 1.99)
total downlink	55/280	3.79	1.45 (0.70 to 3.00)	1.72 (0.78 to 3.77)	11.01	1.62 (0.80 to 3.27)	1.95 (0.92 to 4.11)
total	55/280	5.82	1.19 (0.57 to 2.47)	1.55 (0.67 to 3.58)	13.38	1.58 (0.78 to 3.19)	2.07 (0.97 to 4.39)

[a] adjusted for age, sex, nationality, school level, physical activity, alcohol, education of parents and change in body height between baseline and follow-up
[b] < =50th percentile as reference group

opposite results as it was the case for us. No longitudinal study with adolescents has been identified so far and only one study in adults was identified to be longitudinal. In this study of 1'124 adults aged between 30 and 60 years no evidence was found that exposure from fixed site transmitters is associated with the development of non-specific symptoms [13] or sleep disturbances [14] over one year.

A further strength is that no information bias can be introduced in the exposure assessment since the exposure is assigned on the basis of residential and school location using a geospatial propagation model and any exposure error is thus not related to the health status. Obviously, there are some uncertainties in the modelling. The uncertainty of these calculations depends on the quality of the input data such as the building and topographic data and the antenna characteristics. A previous validation study for this model in the city of Basel and surroundings found a Spearman correlation coefficient of 0.66 between modelling and indoor measurements conducted in bedrooms during approx. 5 min and a Spearman correlation coefficient of 0.72 between modelling and personal measurements taken during 1 week in the homes of study participants [15]. Additional exposure assessment uncertainty is introduced by the behaviour of the study participants, who do not only stay at home and at school. Exposure outside home and school is not considered in this study.

We are aware that exposure to fixed site transmitters is of minor relevance in comparison to exposure from wireless devices operating close to the body such as a mobile or cordless phone. According to the dose estimations by Roser et al. [16], the far-field exposure from fixed site transmitters contributed on average 0.7 % to the cumulative brain dose and 2.3 % to the cumulative whole body dose. Or expressed differently, the mean dose for the brain in our study sample obtained from mobile phone base stations (downlink exposure) for 24 h corresponds to a mobile phone call of 2.6 s on the

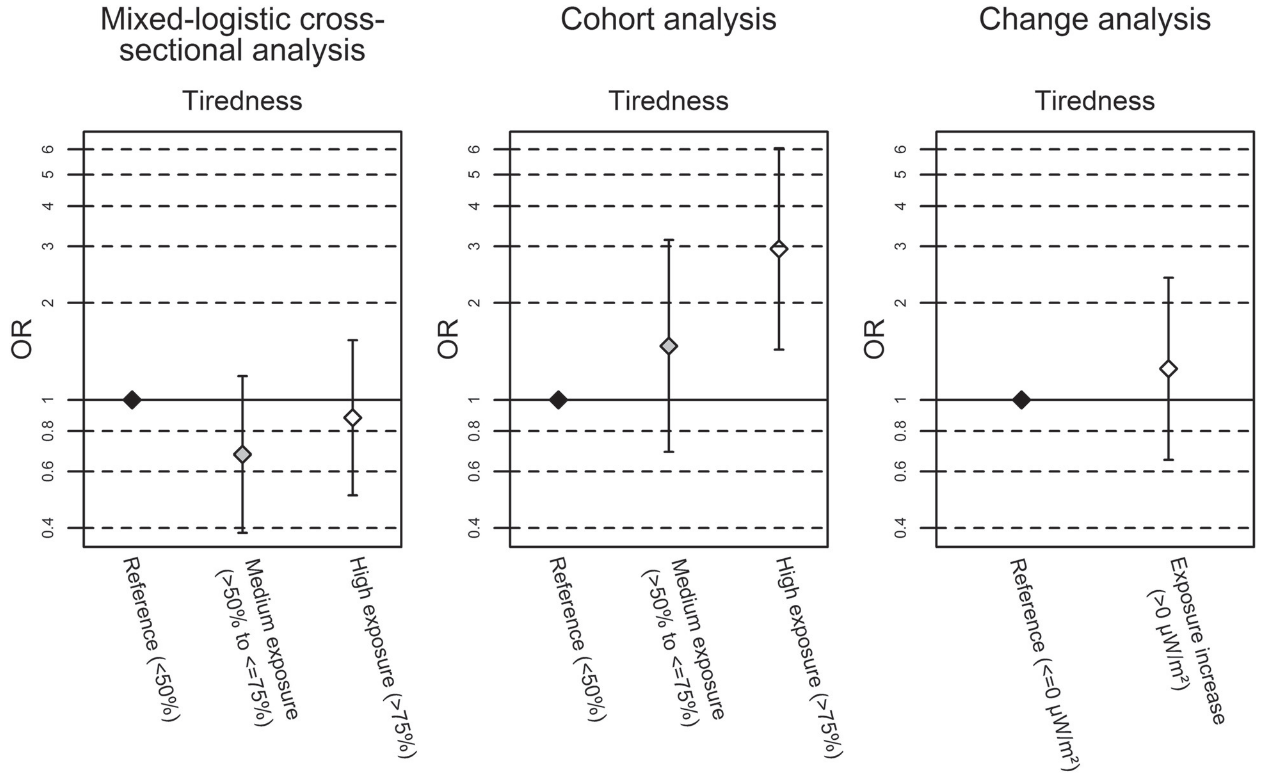

Fig. 2 Odds ratios (OR) of the association between tiredness and total exposure to fixed site transmitters. All models are adjusted for age, sex, nationality, school level, physical activity, alcohol and education of parents. The models for the cohort and change analysis are additionally adjusted for change in body height between baseline and follow-up

GSM (2nd generation Global System for Mobile Communications) network or of a 6.1 min call on the UMTS (3rd generation Universal Mobile Telecommunications System) network. Concerning the exposure to the whole body, 24 h downlink exposure from mobile phone base stations corresponds to a 15.0 s call on the GSM network or to a 34.2 min call on the UMTS network.

However, exposure to fixed site transmitters has different features; the exposure is indeed low, but the levels are more or less constant for several hours a day, especially during night. Further, it is not voluntary and thus not related to lifestyle like wireless device use. Confounding and reverse causality is therefore expected to be less relevant compared to studies focussing on the health effects of mobile phone use.

Nonetheless, we also investigated in our study sample whether self-reported general well-being is associated with a comprehensive RF-EMF brain and whole body dose measure taking into account not only exposure from fixed site transmitters, but exposure from devices operating close to the body such as mobile phones or cordless phones and did not find any indication that symptoms are related to RF-EMF exposure (Schoeni A, Roser K, Röösli M: Symptoms and the use of wireless communication devices: a prospective cohort study in Swiss adolescents, submitted). The absence of associations for these stronger RF-EMF exposure sources calls for a prudent interpretation of the few significant associations observed in our cohort approach. These findings could have happened by chance unless the effect is very frequency or signal specific, for which little evidence is available so far in the low dose range. In particular, the significant association between broadcast transmitters and lack of concentration of the cohort analysis may be due to chance since no exposure response pattern was found. A limitation of the study is the small sample size producing relative large 95 % confidence interval. Our results of the cross-sectional analyses, where we did not find decreased self-reported general well-being in relation to exposure to fixed site transmitters, are in line with other cross-sectional studies on symptoms [2–4].

Conclusions

Exposure from fixed site transmitters was low in our study area (≤0.38 V/m). In cross-sectional analyses no associations between self-reported symptoms and RF-EMF exposure was observed. In the change analyses a decrease of exhaustibility was found for total RF-EMF increase and an improvement in concentration for increase in downlink exposure, whereas in the cohort approach an association between modelled RF-EMF exposure from fixed site transmitters and tiredness and concentration difficulties in Swiss adolescents was seen. Given the high number of analyses conducted in this study, the observed associations need confirmation before firm conclusions can be drawn.

Additional file

Additional file 1: Table S1: Odds ratios (OR) of the change analysis. (DOCX 17 kb)

Abbreviations

GSM, global system for mobile communications network; HERMES, health effects related to mobile phone use in adolescents; RF-EMF, radiofrequency electromagnetic fields; UMTS, universal mobile telecommunications system network

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Availability of data and materials

The data contain personal and sensitive information. Persons may be easily identifiable from a combination of these variables. This could be a serious problem for the study participants, e.g., when searching for a job. We are willing to share the data on request. In this case we reduce identifying information to a minimum.

Authors' contributions

AS coordinated data collection, carried out the analyses, drafted the initial manuscript, and approved the final manuscript as submitted. KR coordinated data collection, reviewed and revised the manuscript, and approved the final manuscript as submitted. AB developed the propagation model and calculated the exposure values, reviewed and revised the manuscript, and approved the final manuscript as submitted. MR conceptualized and designed the study, obtained funding, reviewed and revised the manuscript and approved the final manuscript as submitted.

Competing interests

The authors declare that they have no competing interests.

Consent for publication

Not applicable.

Ethics approval and consent to participate

Ethical approval for the conduct of the study was received from the ethical committee of Lucerne, Switzerland (Dienststelle Gesundheit, Ethikkommission des Kantons Luzern, Schweiz) on May 9th, 2012 (Ref. Nr. EK: 12025). Written informed consent was obtained from the adolescents and their parents for the participation in the study.

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Table S1. Odds ratios (OR) of the change analysis.

	n with symptoms / n total	n with exposure increase	exposure increase (> 0 µW/m²)**	
			OR (95% CI) crude	OR (95% CI) adjusted*
headache				
broadcast transmitter	40/341	184	1.49 (0.75 to 2.93)	1.35 (0.63 to 2.89)
total downlink	40/341	224	0.60 (0.31 to 1.17)	0.60 (0.30 to 1.19)
total	40/341	243	0.72 (0.36 to 1.44)	0.73 (0.35 to 1.49)
tiredness				
broadcast transmitter	73/228	132	1.16 (0.66 to 2.04)	1.09 (0.57 to 2.09)
total downlink	73/228	149	1.12 (0.62 to 2.02)	1.16 (0.62 to 2.15)
total	73/228	160	1.31 (0.70 to 2.45)	1.25 (0.65 to 2.40)
lack of concentration				
broadcast transmitter	44/343	184	0.85 (0.45 to 1.59)	0.91 (0.45 to 1.84)
total downlink	44/343	219	**0.47 (0.25 to 0.88)**	**0.46 (0.24 to 0.88)**
total	44/343	238	0.66 (0.34 to 1.28)	0.68 (0.35 to 1.32)
exhaustibility				
broadcast transmitter	51/361	185	1.30 (0.72 to 2.36)	1.39 (0.71 to 2.72)
total downlink	51/361	230	0.59 (0.33 to 1.08)	0.55 (0.30 to 1.03)
total	51/361	248	0.55 (0.30 to 1.00)	**0.50 (0.27 to 0.93)**
lack of energy				
broadcast transmitter	53/353	181	0.90 (0.50 to 1.62)	1.02 (0.53 to 1.98)
total downlink	53/353	231	0.77 (0.42 to 1.41)	0.68 (0.37 to 1.27)
total	53/353	247	0.60 (0.33 to 1.10)	0.55 (0.30 to 1.04)
physical ill-being				
broadcast transmitter	55/280	150	0.61 (0.34 to 1.10)	0.83 (0.42 to 1.64)
total downlink	55/280	180	1.07 (0.57 to 1.98)	1.08 (0.56 to 2.10)
total	55/280	197	0.93 (0.49 to 1.76)	1.02 (0.51 to 2.02)

* adjusted for age, sex, nationality, school level, physical activity, alcohol, education of parents and change in height between baseline and follow-up.
** compared to the remaining study participants who did not experience an exposure increase between baseline and follow-up (reference).

6 Summary of the main findings

In this section short summaries according to the objectives outlined in chapter 2.2 are presented. Detailed results can be found in the respective articles.

Objective 1: To study health symptoms and cognitive function (memory performance and concentration capacity) in relation to mobile phone use during night.

We could demonstrate that mobile phone use during night is common among adolescents. Being awakened during night by an incoming text message or call was associated with an increase in health symptom reports such as tiredness, rapid exhaustibility, headache and physical ill-being. These findings were confirmed by analyzing objectively operator recorded mobile phone use data during night. Concentration capacity and memory performance were not related to mobile phone use during night.

Objective 2: To apply the newly developped RF-EMF dose measures on the study participants to investigate whether memory performance or health are affected by RF-EMF from wireless devices or by the wireless device use itself due to non-radiation related factors in that context.

Development of the RF-EMF dose measures:
An integrative exposure surrogate combining exposure from near-field (use of wireless devices) and far-field (environmental sources) RF-EMF sources to one single whole body and brain exposure measure was developed. This was achieved by combining data from questionnaires, objectively recorded mobile phone use data, personal measurements and a separately developed geospatial propagation model.
The most relevant contributor for the brain and the whole body dose were duration of mobile phone calls (93.3% and 66.9%, respectively).

Application of the RF-EMF dose measures on study participants:
Memory performance:
We found that changes in figural memory performance score over one year tended to be decreased in relation to various RF-EMF dose measures but less so with respect to wireless device use and to other media usage measures such as sending text messages or duration

of gaming, which are scarcely related to RF-EMF exposure. This indicates that RF-EMF may indeed impair the memory performance in adolescents.

Health symptoms:
We found a stronger increase in health symptom reports in relation to wireless device use compared to RF-EMF dose measures. Associations between wireless device use and health symptoms are thus unlikely related to RF-EMF exposure but due to other factors related to wireless device use such as sleep deprivation or accessibility stress.

Objective 3: To investigate whether adolescents‘ perceived health is affected by RF-EMF exposure from fixed site transmitters using a geospatial propagation model.

The observed highest total exposure from fixed site transmitter was 376 µW/m2 (=0.38 V/m), which is considerably below the current ICNIRP (International Commission on Non-Ionizing Radiation Protection) guidelines, as well as lower than the precautionary reference levels for Switzerland. We observed an association between RF-EMF exposure from fixed site transmitters and tiredness in Swiss adolescents whereas other health symptoms were not related. The observed associations however have to be interpreted with caution and might represent a chance finding.

7 General discussion

The specific findings of the different objectives are discussed in detail in the corresponding articles. The following section gives room for speculations and more general aspects of the results. The strengths and limitations of the HERMES study and the public health relevance of the results are discussed and implications for future research are provided. The structure of the discussion is following the different objectives stated in chapter 2.2.

7.1 Mobile phone use during night

The mobile phone has become an integral part of the everyday life of children and adolescents and the use of it does not even stop after lights out. We aimed thus to investigate whether being awakened during night by an incoming text message or call is associated with negative consequences for their health or cognitive function by using both self-reported and objectively operator recorded mobile phone use data. Overall, being awakened during night by mobile phone was associated with an increase in health symptom reports such as tiredness, rapid exhaustibility, headache and physical ill-being, but not with memory and concentration capacity. We hypothesized that the interruption of sleep due to an incoming text message or call, which results in reduced sleep quality and sleep quantity, may be the underlying mechanisms for the observed increase in symptom reports in our study. Several studies have shown a strong relationship between too short and poor sleep and health consequences such as fatigue (Fallone et al. 2002), headache (Rains et al. 2008), subjective psychological well-being (Kalak et al. 2014; Nuutinen et al. 2014), respiratory disorders (Iber 2005) or cardiovascular diseases (Gangwisch et al. 2006; von Ruesten et al. 2012). The exact underlying mechanisms are not known, but may be mediated by inflammatory responses (Irwin et al. 2006) or by neurophysiological mechanisms (Dodick et al. 2003). Concerning the results of the cognitive function, which was not impaired when study participants were being awakened by an incoming text message or call during night, we hypothesized as suggested by a meta-analysis (Pilcher and Huffcutt 1996) that the effects of sleep deprivation have greater influences on feelings of fatigue and other related mood conditions than on cognitive performance. Other explanations could be that these two cognitive tests on concentration capacity and memory performance are not sensitive enough or the sample size was just too small.

It was the first time that objectivey recorded mobile phone use data was used to assess incoming text messages or calls during night. Objectively recorded mobile phone use data has several advantages over self-reported mobile phone use data, which is discussed in detail in Article 1. Here I will shortly talk about one of the biggest disadvantages that will have implications for future research. The biggest disadvantage is that the duration of using the internet on the mobile phone (over the network or over WLAN) is not recorded. Todays adolescents mostly use applications (apps) such as „WhatsApp“ or „Line“ to communicate with their peers, which only work over an internet connection (over the network or over WLAN) and is therefore not recorded in the operator recorded data. The traditional short message service (SMS) is not used that frequently anymore, which can be shown when analysing the operator recorded data at baseline and at follow-up.

Table1. Operator recorded mobile phone use data at baseline and follow-up.

	Baseline (N=233)			Follow-up (N=229)		
	mean (SD)	Min	Max	mean (SD)	Min	Max
Number of incoming SMS per day	3.66 (5.42)	0.08	50.55	1.93 (2.17)	0	17.31
Number of outgoing SMS per day	2.82 (5.05)	0	40.77	1.36 (2.08)	0	16.05
Duration of incoming calls per day [sec]	53.71 (111.32)	0	1099.54	47.39 (81.69)	0	611.94
Duration of outgoing calls per day [sec]	57.49 (161.65)	0	1190.67	52.58 (127.8)	0	1305.8

The mean number of SMS per day at follow-up is almost half as much compared to baseline. The permanent increase in new technologies will decrease the use of SMS in a significant manner and it will be impossible to use operator recorded text messages for research in the future anymore. The same applies for the duration of calls recorded by mobile phone operators. A decrease of duration of calls from baseline to follow-up can be observed. A huge effort is made by apps developer to release apps which can be used to make calls. All the calls that are made with apps would neither be recorded by mobile phone operators. Although we still argue that using operator recorded mobile phone use data is an advantage over self-reported mobile phone use data, it will not be that useful anymore in the future. Unfortunately, there is no way yet to consider the amount of data traffic [MB/day] to quantify the number of text messages or calls. In the data traffic records every download, every up-date of any app is included and to distinguish text messages and calls from those is impossible at that time. Therefore one has to rely on self-reported data or find another way to record all kind of activities on the mobile phone. One can take advantage of this problem and use apps that record such information more properly than mobile phone operators.

When using self-reported mobile phone use data, recall bias (inaccurately recall exposure data) is always of concern. Although recall bias cannot be fully ruled out, in this context however, we think it is rather unlikely that recall bias is specifically linked to the question on being awakened by mobile phone during night with health questions since the questionnaire contained around 100 questions not only on their mobile phone use and their health but also on several other aspects such as hobbies, drinking alcohol, friends, pocket money and school. It would be more likely to be linked to mobile phone use in general. But since we adjusted for this (see below the discussion on confounding and adjustment), it will not bias the results.

In our analyses of the effect of being awakened by mobile phone during night on health symptoms and cognitive function we presented two adjusted models. We adjusted for relevant confounders in the first adjusted model (adjusted 1) and additionally for mobile phone call duration per day in the second adjusted model (adjusted 2). Confounding can bias study results in any direction and is an important issue in all epidemiological studies. In a traditional definition, a confounder variable fulfills the following three criteria: 1) it is a risk factor for the outcome of interest, 2) it is also associated with the exposure and 3) it does not lie on the causal pathway between exposure and outcome under study (Rothman 2002).
In the context of causal inference and its directed acyclic graphs (DAGs), there is confounding if exposure and outcome share a common cause, graphically speaking, when a backdoor paths exist. Figure 4 shows a DAG of an exposure A and an outcome Y with the common cause L. The path from A to Y represents the causal effect of A on Y. The path that links A and Y through their common cause L is an example of a backdoor path. In this case the presence of the common cause L creates an additional source of association between the exposure A and the outcome Y, which we refer to as confounding for the effect of A on Y. Such a packdoor path can be blocked by conditioning (adjusting) on the common cause L and confounding will be removed (Hernán and Robins 2016). The following figures are adapted from Hernán and Robins (2016), a book on Causal inference.

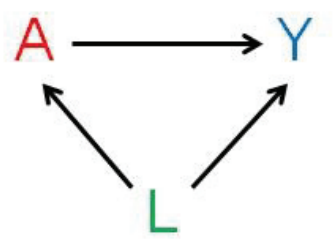

Figure 4: DAG of an exposure (A), an outcome (Y) and a common cause (L).

In the case of our models, age is an example of a common cause of the exposure and the outcome as depicted in Figure 5. When conditioning (adjusting) on age, we remove confounding.

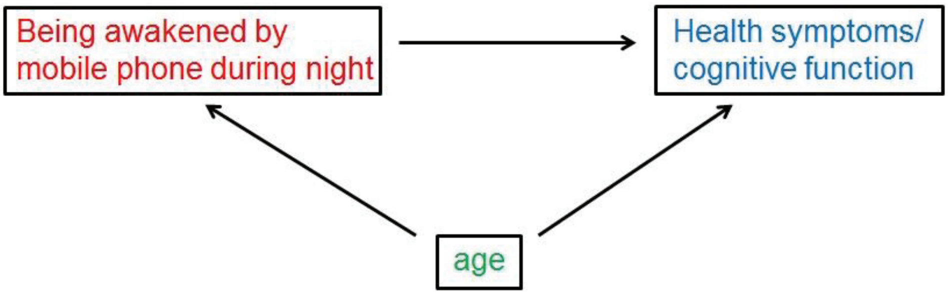

Figure 5: DAG of our model with the exposure (“being awakened by mobile phone during night”), the outcome (“Health symptoms/cognitive function”) and the common cause (“age”).

No adjustment is needed when a variable lies on the causal pathway between exposure and outcome since one would remove the direct link between exposure and outcome. In our case, sleep disturbances for example is the consequence of being awakened by mobile phone during night and therefore lies on the the causal pathway between exposure (being awakened by mobile phone during night) and outcome (Health symptoms / cognitive function). For that reason no adjustment for sleep disturbances is needed (Figure 6).

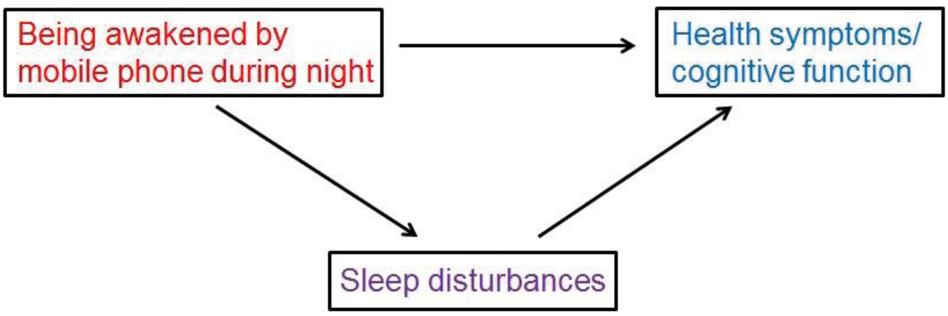

Figure 6: DAG with “sleep disturbances” lying on the pathway between exposure and outcomes.

The question in our analyses was if we would need to adjust for „Mobile phone call duration“, which was used as a proxy for overall mobile phone use. The effect of being awakened by mobile phone during night on the risk of having more health symptoms/ impaired cognitive function will be confounded if being awakened by mobile phone during night is more likely in individuals with higher mobile phone use. Mobile phone call duration is correlated with being awakened by mobile phone during night: The longer the mobile phone call duration, the more likely they were being awakened by mobile phone during night. On the other side, we do not think that there is a direct association between mobile phone use and for example health symptoms (Figure 7), although there have been several cross-sectional studies that found associations between the amount of mobile phone use and health symptoms such as fatigue (Byun et al. 2013; Ikeda and Nakamura 2014; Soderqvist et al. 2008), headache (Chiu et al.

2014; Redmayne et al. 2013) or depressed mood (Ikeda and Nakamura 2014; Koivusilta et al. 2007).

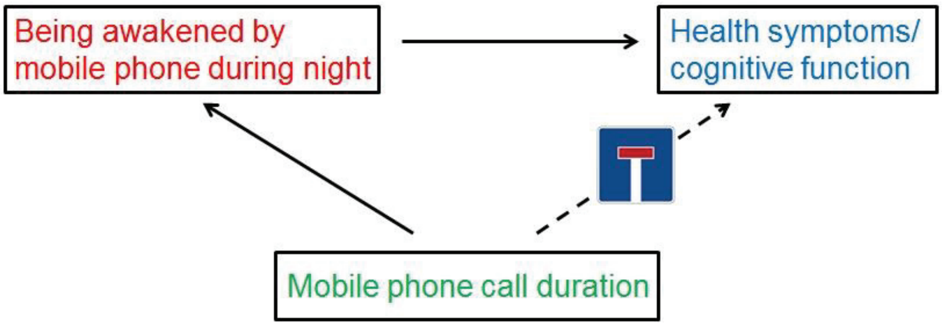

Figure 7: DAG with "Mobile phone call duration" correlated with being awakened by mobile phone during night but not with health symptoms and cognitive function.

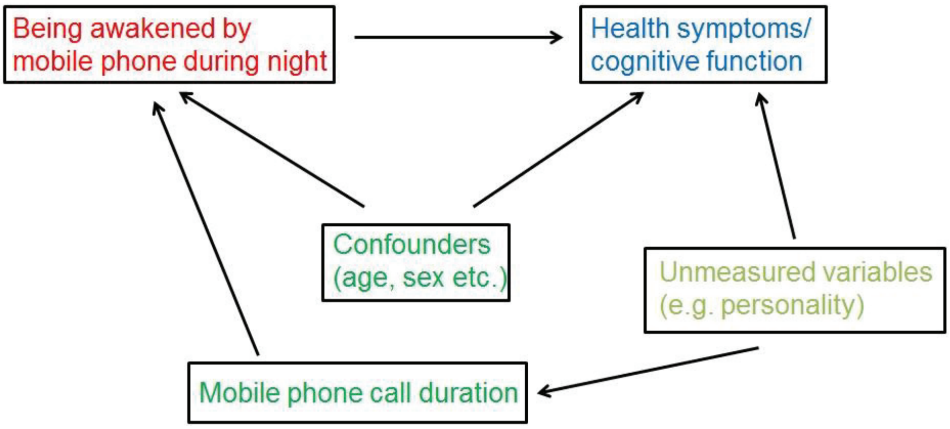

Figure 8: DAG with "Mobile phone call duration" caused by an unmeasured variable such as "personality".

We hypothesize that such associations may be, at least partly, not directly caused by mobile phone use itself but by unmeasured variables related to mobile phone use such as „personality“. Therefore we suspected confounding by indication as depicted in Figure 8. So, there is confounding because the exposure (being awakened by mobile phone during night) and the outcomes (health symptoms or cognitive function) share a common cause (unmeasured variables), i.e. there is a backdoor path between the exposure and the outcomes through the unmeasured variables. This backdoor path could be theoretically blocked, and thus confounding eliminated, by conditioning (adjusting) on the unmeasured variables, had data on these variables been collected (Hernán and Robins 2016). However, this backdoor path can also be blocked by conditioning (adjusting) on mobile phone call duration. We claim that mobile phone use is a confounder because it is needed to eliminate confounding, even though the confounding resulted from the presence of the unmeasured variables. We presented both models in Article 1: adjusted 1 and adjusted 2, which allows the reader to judge how relevant confounding by indication is for our outcomes. To come back to our results, the symptom risk estimates for models with (adjusted 2) and without (adjusted 1) mobile phone call duration adjustments were similar for operator recorded exposure data and only a little reduced for self-reported exposure data (details on numbers can be found in Article 1).

As just outlined, confounding is not an easy issue. Suboptimal adjustment due to errors in confounder measurements may result in residual confounding. Additionnally, there are situations where the traditional definiton of a confounder variable fails and conditioning (adjusting) on the confounder introduces a bias (Figure 9) (Hernán and Robins 2016).

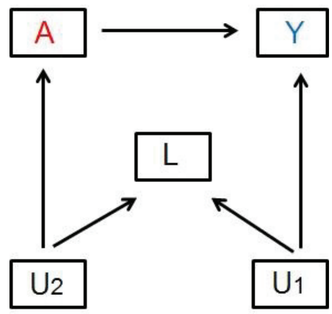

Figure 9: DAG where the traditional definition of a confounder variable fails.

In this causal diagram there are no common causes of exposure A and outcome Y, and therefore there is no confounding. By standard definition however, L, a measured covariate, is both associated with the exposure A and the outcome Y and does not lie on the causal pathway between A and Y and is therefore a confounder. But, adjusting for L would lead to bias. The backdoor path between A and Y through L (over the unmeasured variables U_1 and U_2) is blocked because L is a collider on that path. In graph theory the common effect is referred to as a collider because two arrowheads collide on this node and colliders, unlike other variables, block the flow of association along the path on which they lie. Adjusting for L would open the otherwise blocked backdoor path between A and Y and introduce bias. This example showes that confounding is a causal concept and that associations or statistical criteria are insufficient to characterize confounding (Hernán and Robins 2016).

The cross-sectional study design is a limitation in the study on mobile phone use during night. Like in all cross-sectional studies, reverse causality is of concern. Outcome prevalence and exposure status are measured at the same timepoint, thus, drawing any conclusions about causal associations is limited. Usually such a causal association is based on the assumption that the present exposure is correlated to the past exposure. In our study, we hypothesized that being awakened by mobile phone during night affects sleep which in turn leads to more symptoms. In case of reverse causality due to the cross-sectional design, study participants with sleep disturbances and therefore more symptoms use the mobile phone during night more often than their peers without sleep disturbances. Therefore, caution in interpreting the directions of the associations is always needed in cross-sectional studies.

Nighttime mobile phone use is a particular threat to a healthy sleeping pattern in adolescents. Since the mobile phone has become a lifestyle factor that cannot be cleared away easily, adolescents should get sleep hygiene education in the framework of health education in high schools and prevention strategies should focus on helping adolescents set limits for their accessibility by mobile phone, especially during night.

7.2 RF-EMF dose measures and its application

Development of the RF-EMF dose measures:

An integrative RF-EMF exposure surrogate including various factors affecting near-field and far-field RF-EMF exposure was developed to calculate an RF-EMF dose of the brain and the whole body of the participating adolescents.

In order to calculate such an RF-EMF dose, various exposure assessment methods have been used. The quality of the exposure assessment determines to a large extent the validity of an environmental epidemiological study. An exposure assessment makes use of temporal and/or spatial variability to improve the exposure estimates. The selection of the appropriate exposure assessment method in the HERMES study was determined by time, cost and feasibility. All of the exposure assessment methods used have their merits and limitations.

In a first place questionnaires were used to obtain individual exposure information and confounding factors. Questionnaires are widely used in epidemiological studies and can be designed to meet a specific goal of the question to answer. Questionnaires can be distributed to a large number of study participants, however, the accuracy of the answers is difficult to check and recall bias (inaccurately recall exposure data) is of concern. From our analyses we know that the adolescents did not accurately recall their mobile phone use since we could compare self-reported with objectively recorded mobile phone use data. Adolescents tended to overestimate their mobile phone call duration per day by a factor of 7. However, spearman correlation between self-reported call duration and operator recorded call duration per day at baseline was 0.55. The same correlation was found for frequency of calls between self-reported and operator recorded data. Another bias that can happen when using questionnaires is the selection bias. Selection bias occurs when participants and non-participants differ systematically in a characteristic such as socioeconomic or demographic factors. Selection bias manifests only if the selection to participate in the study is associated with exposure and the outcome. Selection bias in the HERMES study cannot completely be ruled out but we do not think that selection bias is of major concern although participation rate at baseline was not impressive (participation rate 36.8%). On the school level decision to participate in the study has been taken by the school master. On the class level, the teacher played an important role and we observed that participation per class were either very high or very low (both providing little possibility for selection bias). It seems unlikely that the decision by school master or the motivation of the teacher is related to both, the outcomes and the exposure of the adolescents, a criterion that has to be met when claiming selection bias.

Personal measurements were conducted in a subgroup of 121 study participants collecting exposure data during two to three consecutive days. Additionally the study participants filled in a time-activity diary installed as an application on a smartphone operating in flight mode. When applied correctly, personal measurements take into account the exposure-relevant behavior of the study participants including other activities than just the use of mobile phones since the exposure data is collected during normal daily activities. This exposure assessment method however needs a lot of willingness and compliance from the study participants, therefore personal measurements cannot last for too long. Especially adolescents may not perfectly understand the purpose of personal measurements and may not track correctly their daily activities or may forget the measurement device at home. The risk of manipulating the personal measurements is an additional disadvantage. The measurement device can be placed next to an exposure source such as a WLAN modem and record far too high exposure levels. The unknown position of the emitting source in relation to the body, which is expected to show a high variability, is a further disadvantage in personal measurements as exposure assessment method. In the HERMES study, 95 personal measurements could be used after data cleaning, more than one quarter had to be discarded, due to technical failures of the measurement device because the measurement was not charged by the study participants or when no dairy entries were available. This already shows that personal measurements are very elaborate and the compliance of the study participants has to be very high. Although exposimeters (measurement device) for personal measurements are considered as one of the most sophisticated method to assess personal exposure levels, there are some difficulties which have been discussed in several studies (Frei et al. 2009b; Inyang et al. 2008; Röösli et al. 2010a). One of those difficulties is the assessment of exposure from close to body sources. Measurements that are taken during mobile or cordless phone calls depend heavily on the distance between the measurement device and

the emitting source. Therefore it does not properly reflect the exposure at the head of the person that makes a call (Frei et al. 2009b).
A last exposure assessment method used in the HERMES study was modelling. Geospatial propagation modelling was used to estimate the far-field exposure from fixed site transmitters (mobile phone base stations and radio and TV broadcast transmitters). Modelling can only be applied when the emission and propagation pattern of all the fixed site transmitters is known. The quality of the model depends heavily on the input parameter such as topography, building geography and source emission characteristics. The geospatial propagation modelling can be applied to a large number of study participants without consent form as long as the coordinates of the residential location are known. The model can be seen as long-term exposure measurement because when constructed once it is easy to update the input data. The first construction of the model, however, may be difficult and time-consuming. And one has to be aware that the geospatial propagation model does not take into account that study participants move around- it is only modestly correlated with personal measurements (Frei et al. 2010). In the HERMES study a big challenge was to find out the correct geocodes for the study participants' homes which were used as input data.

The HERMES study is the first study worldwide that did not only use mobile phone call duration as an exposure proxy but calculated an integrative exposure surrogate taking into account relevant near- and far-field components to get one single brain and whole body RF-EMF dose. This was achieved by combining data from all the just introduced exposure assessment methods.
Most relevant contributors for the brain dose are mobile phone calls (on average 93.3% for the whole sample based on self-reported data and 58.7% for the sample with operator data using operator recorded information) followed by calls with the cordless phones (4.2% and 21.0%, respectively). For the whole body dose, mobile phone calls (on average 66.9% for the whole sample and 19.5% for the sample with operator data), the use of computer/laptop/tablet connected to WLAN (12.0% and 29.1%, respectively) and data traffic on mobile phones over WLAN (8.1% and 22.3%, respectively) counted for the most part. Less important for the dose measures were exposure from radio and TV broadcast transmitters (brain dose: 0.1% and 0.4%, respectively; whole body dose: 0.3% and 0.9%, respectively) and mobile phone base stations (brain dose: 0.6% and 3.5%, respectively; whole body dose: 2.0% and 4.8%, respectively).

A limitation of the RF-EMF dose measures is the large uncertainty since it is impossible to directly measure the RF-EMF dose that is absorbed by the body due to the absence of an established biomarker. For example the position from the emitting source in relation to the body determines the absorbed radiation by the body. Further uncertainties are the emitted exposure from mobile phones in stand-by mode, errors in personal measurements and modelling. A comprehensive discussion on all the uncertainties can be found in the Article 2. Although the list of uncertainties seems endless, it is a first approach to quantify RF-EMF exposure not only dependent on the duration of mobile phone calls but the network used (GSM vs. UMTS) for calls and other relevant RF-EMF emitting sources. Due to the rapid development of new devices and new networks, the RF-EMF exposure assessment is becoming more and more complex. It will always be a challenge to adapt the dose measures to these new devices and its emitting exposure. However, the dose measures are more accurate than mobile phone call duration as en exposure proxy. Already today, mobile phone operators have introduced cheap flat rate subscriptions with unlimited amount of data traffic. Especially adolescents do not use the mobile phone for calling regularly. They mostly use applications such as "WhatsApp" or other communicating apps to communicate with their peers, which will make it difficult to use mobile phone call duration as an exposure proxy in the future. Therefore other components will have to be incorporated into the dose measures such as data on recorded volume of data traffic or data on emitted exposure when the mobile phone is in stand-by mode. However, no data is available yet to transfer data traffic volume into absorbed RF-EMF dose or quantification of the emitted exposure of mobile phones in stand-by mode. So far, the dose calculation had to rely on self-reported data traffic duration and on an estimation of the quantification of the emitted exposure of mobile phones in stand-by mode.

Such a RF-EMF dose measure can be applied to a large study population as long as the input data are available. The newly developed approach to combine near- and far-field exposure to one integrative exposure surrogate is considered useful for exposure assessment in epidemiological studies.

Application of the RF-EMF dose measures on study participants:

Memory performance:

The first time the RF-EMF dose measures were applied to the HERMES cohort was to investigate whether memory performance is affected by RF-EMF from wireless devices or by the wireless device use itself due to non-radiation related factors in that context. Changes in figural memory performance score over one year tended to be decreased in relation to various RF-EMF dose measures but less so with respect to usage measures. This may indicate that RF-RMF exposure might indeed play a role for memory processes in adolescents.

For the RF-EMF dose measures, two different calculations were done which resulted in a brain and whole body dose measure based on self-reported mobile phone call duration for the whole cohort (dose for the whole sample) and a brain and whole body dose measure based on objectively recorded mobile phone call duration (dose for the sample with operator data) for the subgroup of study participants with operator recorded mobile phone data. As graphically depicted in Figure 10, the two brain doses are quite different due to the highly overestimated self-reported mobile phone call duration.

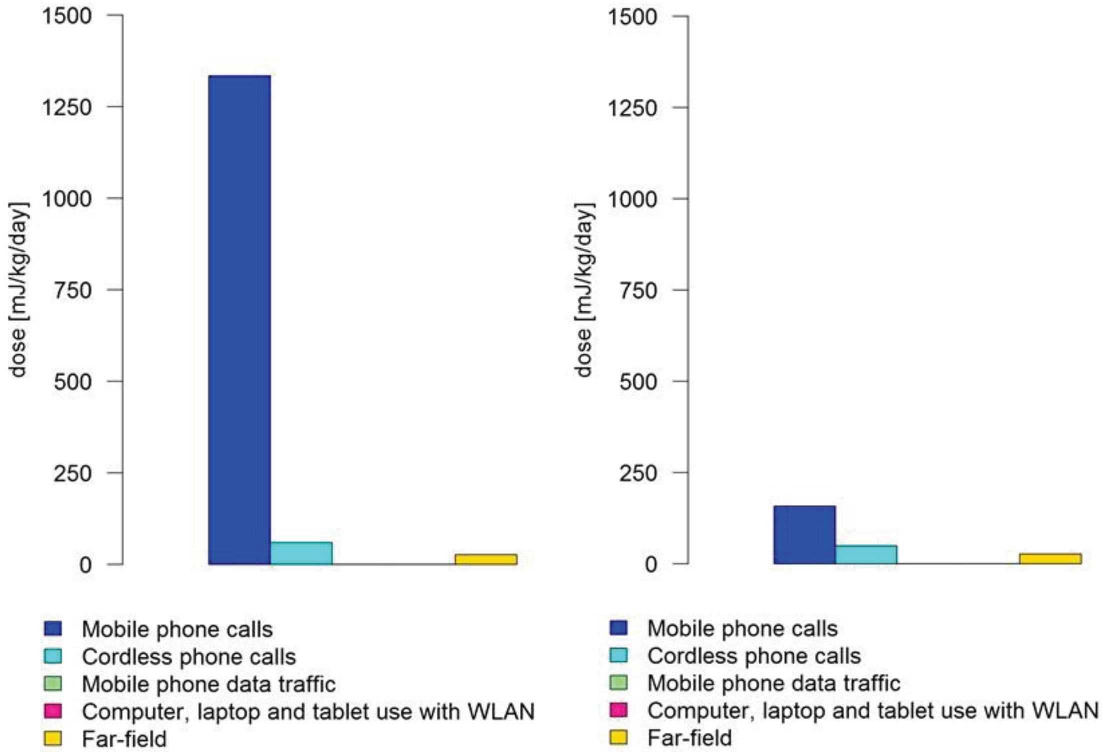

Figure 10: The two different brain dose measures. Left: calculation based on self-reported mobile phone call duration; Right: calculation based on objectively recorded mobile phone call duration.

To obtain a real objective dose measure, one would need all measures objectively recorded; however this is impossible. There is no way to consider operator recorded cordless phone use for adolescents because adolescents usually do not live in a one-person household. So many people use the same cordless phone; therefore it would be very difficult to assign the duration of cordless phone use to one specific person. The same applies to the other measures that were used to calculate the dose measures such as computer, laptop and tablet use with WLAN.

We tried to disentangle effects due to RF-EMF exposure or due to other factors associated with mobile phone use, however, this resulted to be difficult due to the relative high correlation between RF-EMF dose measures and mobile phone call duration. Nevertheless, the differentiation between mobile phone calls made on the different networks (GSM vs

UMTS) removed some co-linearity which helped us to obtain some indications about RF-EMF effects and indeed we found stronger associations for various dose measures than for the single usage measures indicating a causal association between RF-EMF exposure and memory performance.

To demonstrate a causal association is the principal aim of epidemiology. The recognition of a causal factor is necessary when implementing preventive actions. However, since most epidemiological research is observational rather than experimental and conducted in a “noisy” environment, a number of possible explanations for an observed association need to be considered before a cause-effect relationship can be inferred. The observed association may in fact be due to chance (random error), bias (systematic error) and/or confounding (logical error). Therefore, the maximization of the signal-to-noise ratio by applying an appropriate research setting and study design is what epidemiologists are seeking for. The judgement if the observed association between an exposure and an outcome represents a cause-effect relationship requires the full consideration of epidemiological noise- chance, bias and confounding. Research situations, in which full consideration of epidemiological noise can be accounted for, are limited to clinical trials and maybe to really large observational studies with an unflawed study design and performance.

Sir Austin Bradford Hill (1897-1991) was the first one to describe ideas about causal inference. The Hills Criteria of Causation (Hill 1965) outline conditions to assess whether an observed association is likely to be causal. While it is easy to claim that an exposure causes an outcome, it is another issue to establish a statistically valid and meaningful connection between the exposure and the outcome.

Hills Criteria are presented here as they were used in epidemiological research:

1. Strength of the association: The stronger the association between a risk factor and outcome, the more likely the relationship is to be causal.

2. Consistency of findings: The association is repeatedly observed in different populations under different circumstances.

3. Specificity of the association: There must be a one to one relationship between cause and outcome.

4. Temporal sequence of association: Exposure must precede outcome.

5. Biological gradient: Change in disease rates should follow from corresponding changes in exposure (dose-response curve).

6. Biological plausibility: Presence of a potential biological mechanism.

7. Coherence: The cause-and-effect interpretation for an association does not conflict with what is known of the natural history and biology of the disease.

8. Experimental evidence: Experimental evidence exists to support the causation hypothesis.

9. Analogy: Judgment from analogy, such as observing what effect a similar drug has on a disease.

Although Sir Austin Bradford Hill did not claim that the proposed criteria should be used for evaluating a causal relationship, they have been widely applied in this way.

> “None of my nine viewpoints can bring indisputable evidence for or against the cause-and-effect hypothesis and none can be required as a *sine qua non*. What they can do, with greater or less strength, is to help answer the fundamental question- is there any other way of explaining the set of facts before us, is there any other answer equally, or more, likely than cause and effect?” (Hill 1965)

If we would apply those Hill criteria to our study, we would not describe our observed associations between RF-EMF doses and memory performance to be causal. Several criteria would be violated- to name just two: the strength of the association or the specificity of the association.
Strength of the association: The stronger the association between a risk factor and outcome, the more likely the relationship is to be causal. The strong associations are more confident since they are less likely to be assignable to uncontrolled residual confounding (Hill 1965). However, weak associations are quite common in contemporary epidemiology as shown as well in our research. For a valid measure of association a strong study design and methodology are inevitable to minimize bias, to measure possible confounding factors and to rule out chance findings.
Specificity of the association: There must be a one to one relationship between cause and outcome (Hill 1965). Causes of a given effect cannot be expected to lack all other effects. In fact, everyday experience teaches us repeatedly that single events or conditions may have many effects (Rothman and Greenland 2005). If we would apply the criteria of specificity to our research, we would argue that RF-EMF doses only lead to decreased memory performance, however it may have other effects. The existence of one effect of an exposure does not detract from the possibility that another effect exists (Rothman and Greenland 2005).

Sir Austin Bradford Hill recognized already at that time that it is important to move from association to causation in order to implement preventive action against environmental causes. The validity and applicability of those criteria however have been questioned just ten years after Sir Austin Bradford Hill published these criteria. It was Kenneth J. Rothman who argued that the Hill criteria fail to distinguish causal from non-causal relationships and presented a model of causation with multiple component causes and diverse causal pathways (Rothman 1976). On a later stage, Kenneth J. Rothman and Sander Greenland noted that none of Hills criteria alone is sufficient to establish causality. Temporality, the requirement that the exposure precede the effect, is the only necessary criterion for a causal relationship between an exposure and an outcome (Rothman and Greenland 1998). As just outlined in two examples, several criteria would be violated in our study. However, the criterion of temporality, the only necessary criterion needed for a causal relationship is accepted as true in our research. The exposure preceded the outcome.

The process of causal inference is a complex issue. In our case, we tried to consider all the noise (confounding, bias and chance) in our research. To address confounding, we adjusted for a number of potential confounders. The use of mobile phones and other wireless devices and thus exposure to RF-EMF is related to lifestyle factors such as smoking, drinking alcohol or BMI (body mass index) which are as well expected to be related to adverse health effects or cognitive function in adolescents. Lajunen et al. (2007) for example found a positive linear relationship between an increasing monthly mobile phone bill and the BMI in a twin study in Finland. In another Finnish study, Koivusilta et al. (2005) found that the mobile phone use was related to smoking and drinking alcohol in 3485 14 to 16 years old adolescents. The fact that such lifestyle factors are related to the use of mobile phones complicates the research. However, as the adjusted model estimates in the study on memory performance were relatively similar to the crude model estimates, we concluded that confounding does not seem to have a substantial impact on the results, although it is always possible to miss an important confounder.

Concerning bias, we can distinguish between selection and information bias. Selection bias in our study cannot completely be ruled out but we do not think that selection bias is of major concern as already discussed in this same chapter in the paragraph on the “Development of the RF-EMF dose measure”. Additionally, with a participation rate of 96.8% in the follow-up investigation potential bias in the effect estimates from lost to follow-up is rather low and can be neglected. Information bias occurs when information collected about or from study participants is erroneous. Information bias is of major concern when using self-reported data such as self-reported mobile phone use data (recall bias). To deal with such kind of bias, objective data needs to be obtained although this might not always be possible. In our case we were able to obtain objectively recorded mobile phone use data to avoid recall bias. In the context of information bias, exposure misclassification should be mentioned. Exposure misclassification is called differential when the likelihood of being misclassified differs across groups of study participants. The observed effects of differential exposure misclassification can either be overestimated or underestimated of the true value. On the other hand exposure misclassification is called non-differential if the likelihood of being misclassified is the same for all study participants. In this case, the effect estimates would be biased towards unity.

The RF-EMF dose measure gives a good example for non-differential exposure misclassification. The RF-EMF dose measure calculations are subject to large uncertainties (a comprehensive discussion on all the uncertainties can be found in Article 2). We found negative associations between RF-EMF doses and memory performance. We do not expect a correlation between RF-EMF dose measures and memory performance; therefore the more the uncertainty of the RF-EMF dose measure calculation, the more the effect estimates would bias towards unity since the probability of the exposure being misclassified is independent of the outcome. We can only assume how much the uncertainties of the dose measure calculation biased the effect estimates towards unity. We would therefore expect even stronger negative associations between RF-EMF dose measures and memory performance if there were no uncertainties in the dose calculations.
If there is random error, an association between an exposure and an outcome can be introduced. Since it is impossible to study an entire population, we draw inference on the entire population based on the evaluation of a sample of the population. The play of chance however can have an effect on the results of an epidemiological study when drawing such inferences. This is due to the effects of random variation from one sample to another. The effect of random error can result in an overestimation or in an underestimation of the true value. The smaller the sample population, the higher the random error will be. Therefore, an increase in sample size will reduce the random error. In our case there is a possibility that the observed results happened by chance. In order to rule out that the observed results did not happen by chance an increase in sample size is needed. The HERMES study is being continued as HERMES II; a second cohort has already been established. Pooling all study participants from both cohorts will increase the sample size and we will be able to reveal if the observed results happened by chance or not.

We found stronger associations between RF-EMF doses and figural memory performance; therefore we performed stratified analyses according to preferred side of mobile phone use since the observed results might be due to different areas involved in the verbal and figural memory tasks. Figural memory processes seem to involve predominantly the right hemisphere whereas the verbal memory tasks mostly involve the left hemisphere. Although the sample size was small, at least for those who prefer to use the mobile phone at the left side or have no side preference, our laterality analyses indicated indeed stronger associations for right side users for the figural memory task whereas the reverse pattern was seen for the verbal memory task. Details on the numbers can be found in Article 3. The observed results may indeed indicate that RF-EMF exposure affects memory performance in adolescents. Studies on the effects of RF-EMF on the modification of brain activity conducted so far have been controversial and failed in pointing out a final conclusion. Reviews on metabolic and neurophysiological effects suggested that rigorous study design and data analysis considering multiple comparisons and effect size are required to reduce controversy in this important field of research (Kwon and Hamalainen 2011; Valentini et al. 2007; Valentini et al. 2010). Therefore, we can only speculate about the biological effects behind if our results are proven to be true.

So far, I only considered epidemiological “noise” that could have possibly provoked the results on memory performance. However, there might be an alternative explanation. The RF-EMF dose measures include amongst others all kind of wireless device activities, such as using the mobile or cordless phone or using a laptop/ tablet or computer connected to WLAN etc. The RF-EMF dose measure would therefore represent an integral measure for the usage of wireless devices. In this case, the explanation of the observed results would be different: The more somebody is involved in all these kind of wireless activities, the poorer their ability to remember things (memory performance) - to name it: “digital dementia”. The term “digital dementia” was not widely known until a report in Seoul, Korea has revealed some alarming information about degenerative memory loss that is attributed to the overuse of mobile phones and other wireless devices. Digital dementia is the kind of early onset dementia, or deterioration of cognitive abilities, that usually only comes about following a head injury or psychiatric illness (Korea Joongang daily 2013). According to Dr. Byun Gi-won from the Balance Brain Center in Seoul, the over-use of mobile phones hampers the balanced development of the brain. Heavy users are likely to develop the left side of their brains, leaving the right side untapped or under developed. Engaging with computer or mobile devices is the kind of activity that is handled by the left side of the brain and the right side, which is linked with concentration, short attention and memory span, eventually degenerates (Korea Joongang daily 2013).
The explanation of digital dementia would perfectly fit to our results since we found stronger associations between RF-EMF doses and figural memory performance than between RF-EMF doses and verbal memory performance. Figural memory performance seems to involve predominantly the right hemisphere whereas the verbal memory tasks mostly involve the left hemisphere; however, the scientific evidence for “digital dementia” is limited, the evidence seems to be rooted in anecdotal observation.

In epidemiological studies it is common that large amount of data has to be condensed to one single exposure proxy for every study participant to perform a meaningful analysis. From a biological point of view however, there might be more relevant exposure proxies. For example, there may be a biological effect only above a certain threshold or there may be a biological response proportional to the amount of exposure. Assuming that two study participants have the same RF-EMF dose measures and all the same composition of the RF-EMF dose measures except for the mobile phone call duration. One of those calls with the mobile phone 20 times for 30 seconds, the other one calls once for 10 minutes which results in the same average mobile phone call duration. Would the effect of both RF-EMF dose measures be the same for both study participants? The thermal effects of biological tissue resulting from the exposure to radiofrequency electromagnetic fields is known and beyond dispute, however, since the threshold that is linked to a biological effect is not known it is difficult to answer such a question. One might speculate that for the study participant who calls 10 minutes continuously the thermal effect might be increased compared to the one that calls 20 times for 30 seconds. Another explication would be, and that is what we assume for our results, that cumulative dose best represents an irreversible proportional process model like it has been observed for silicosis, lung fibrosis caused by inhalation of dust that contains silica, or for the lead concentrations in childrens' blood which are associated with cognitive deficits. In this case the effect would be the same for both study participants. A way to answer such a question would be to find a biomarker that measures the absorbed dose; however this is difficult or even impossible.

Health symptoms:

The RF-EMF dose measures were also applied to investigate whether radiofrequency electromagnetic fields (RF-EMF) from mobile phones and other wireless devices affects the adolescents' health. We observed that the occurrence of health symptoms in adolescents is stronger associated with wireless device use than with RF-EMF dose for the brain or the whole body. Negative associations between wireless device use and health symptoms are thus unlikely to be related to RF-EMF exposure but due to other factors related to wireless device use such as sleep deprivation or accessibility stress.

There have been several studies focussing on mobile phone use and health symptoms in children and adolescents (Byun et al. 2013; Chiu et al. 2014; Ikeda and Nakamura 2014; Redmayne et al. 2013; Roser et al. 2015b; Soderqvist et al. 2008). Most of the evidence on adverse health effects in adolescents however comes from cross-sectional studies, where changes over time cannot be assessed and where reverse causality as well as confounding by lifestyle factors related to mobile phone use and health are of concern. There is only one longitudinal study on mobile phone use in adolescents on health (Thomee et al. 2011). They found that perceived stressfulness of accessibility around the clock was the strongest predictor of mental health outcomes. Only one longitudinal study in adults was identified (Frei et al. 2012) where objectively recorded mobile phone use was used. In this study of 1'124 adults aged between 30 and 60 years results showed a tendency of a negative correlation between health symptoms and self-reported mobile phone use and no indication of an association for operator recorded mobile phone use, which was available for 451 study participants.

A further limitation in most of these studies is that they used self-reported mobile phone use as an exposure proxy. Thus, to address RF-EMF effects from mobile phones and other wireless devices on adolescents' health, the application of the RF-EMF dose measures was necessary. This time we did not find a causal association between RF-EMF exposure and health of adolescents. If there was a causal association between RF-EMF exposure and health, one would expect more pronounced associations for RF-EMF dose measures compared to single usage measures, which was not the case.

In the same study sample, the dose measures were applied in order to investigate whether exposure to RF-EMF emitted by mobile phones and other wireless devices causes behavioral problems or affects concentration capacity in adolescents (Roser et al. 2016a). Conclusively they suggested that behavioral problems and concentration capacity are not affected by the use of wireless devices or RF-EMF exposure due to a lack of consistent exposure-response patterns in the longitudinal analyses. Observed cross-sectional findings were attributed to information bias and/or reverse causality.

The RF-EMF dose measures have been applied to investigate whether memory performance, health, concentration capacity or behavior in adolescents are affected by RF-EMF from wireless devices or by the wireless device use itself due to non-radiation related factors in that context. The only consistent associations of RF-EMF exposure were found in relation to memory performance. This may create legitimate doubt that the observed results concerning RF-EMF dose measures and memory performance indeed happened by chance. One might expect that there must be at least one other outcome affected by RF-EMF, however, this was not the case for any of the outcomes. The answer to the question if the result pattern indicating that RF-EMF exposure affects memory performance in adolescents will be given at a later stage, in HERMES II, when the study participants of both cohorts are pooled together in order to increase the sample size. In case the results will be the same with an increased sample size, the public health impact would be tremendous because so far the scientific evidence that RF-EMF has any major effect on humans is limited. More on this issue is discussed in chapter 7.4 Public Health relevance.

The possibility that the findings on memory performance could have happened due to the so-called "digital dementia" has been discussed. The explanation would fit quite well to our results on memory performance. However, if we explain the results by "digital dementia" we would probably expect at least concentration capacity to be affected as well by RF-EMF since the right side of the brain seems not only be linked with memory but with concentration, as suggested by the Corean doctors (Korea Joongang daily 2013). As already mentioned, concentration capacity in the HERMES cohort was not affected by the use of wireless devices or RF-EMF exposure. For this reason, one might think that “digital dementia” may probably not be the reason for the observed results.

7.3 Far-field exposure and health symptoms

We investigated whether adolescents’ health is affected by RF-EMF exposure from fixed site transmitters (radio and TV broadcast transmitters and mobile phone base stations) using a geospatial propagation model. We observed an association between RF-EMF exposure from fixed site transmitters and tiredness in Swiss adolescents whereas other health symptoms were not related. Since the geospatial propagation model only takes exposure at the residential location and only exposure from fixed site transmitters into account, which is small compared to exposure from close to body sources, the observed associations have to be interpreted with caution and might represent a chance finding.

The observed highest total exposure to fixed site transmitter was 376 $\mu W/m^2$ (=0.38 V/m), which is considerably below the current ICNIRP (International Commission on Non-Ionizing Radiation 1998) guidelines, as well as lower than the precautionary reference levels as defined by the Federal Office for the Environment for Switzerland (FOEN 2012), which are 10 times lower than the ICNIRP guidelines.

Several studies have shown that exposure from fixed site transmitters is clearly lower than exposure from close to body sources (Neubauer et al. 2007; Regel et al. 2006). Regarding exposure to the head, exposure from an operating mobile phone is remarkably higher compared to the everyday exposure from a mobile phone base station. With respect to exposure to the whole body it is estimated that 24h exposure from a base station corresponds to about 30 minutes of mobile phone call duration (Neubauer et al. 2007). According to the dose estimations (Roser et al. 2015a), the mean dose for the brain obtained from mobile phone base stations (downlink exposure) for 24 hours corresponds to a mobile phone call of 2.6 seconds on the GSM network or of a 6.1 minutes call on the UMTS network. For the whole body exposure, 24 hours downlink exposure from mobile phone base stations corresponds to a 15.0 seconds call on the GSM network or to a 34.2 minutes call on the UMTS network.

The exposure from radio and TV broadcast transmitters is even lower than from mobile phone base stations. Normally, broadcast transmitters can be found in elevated locations for example on hills or mountains, which leads to low exposure levels in residential areas due to the large distance between the emitting source and residential locations.

Although the evidence is clear that exposure from mobile phone base stations is much lower compared to the exposure from the own mobile phone, people are still more afraid to live in the vicinity of a mobile phone base station than to use their own mobile phone. In the year 2005 there was even a postulate filed to the Swiss National Council asking to write a report on how the rent of apartments and houses and the value for real estates are influenced by the construction of mobile phone base stations (Parlament 2005). According to the EUROBAROMETER 2010 survey (Eurobarometer 2010) mobile phone base stations are the second most frequently cited area of health concern after high voltage power lines. 33% of respondents believe these mobile phone base stations have a major effect on people's health, whereas only 26% of respondent think that mobile phones affect people's health to a major extent. However, looking at the physical properties of RF-EMF, we rapidly recognize that RF-EMF exposure from fixed site transmitter must be lower than from mobile phones since RF-EMF levels decrease rapidly with distance. The propagation pattern changes depending on the type of source and the type of dispersion. For point sources with nondirectional dispersion, RF-EMF levels decrease with the square of distance from the source ($1/r^2$), whereas for point sources with directional dispersion, RF-EMF levels decrease inversely with the distance from the source ($1/r$). RF-EMF emitted by fixed site transmitters are regarded as a mixture between these two different propagation pattern. RF-EMF levels are therefore decreased between $1/r$ and $1/r^2$ (Röösli 2014). Hence, the fear of fixed site transmitters in close vicinity is in fact unjustified.

7.4 Strengths and limitations of the HERMES study

A particular strength of the HERMES study is the longitudinal design. The longitudinal design is in many aspects preferable to a cross-sectional design where changes over time cannot be assessed and where reverse causality is of concern. The prospective cohort design is a further strength in our study. Prospective cohort studies are regarded as superior to retrospective studies since they usually start with the exposure assessment and during the follow-up period the events of interest are recorded as they are developed.

A further strength of the study is the consideration of objectively recorded mobile phone use data. Adolescents tend to considerably overestimate their mobile phone use. Objectively recorded mobile phone use data is still considered more reliable and less prone to recall bias than self-reported mobile phone use data. Nevertheless, mobile phone operator do not record duration of using the internet on the mobile phone (over the network or over WLAN), which is a drawback when we think of how much time adolescents spend using apps on their mobile phone or of how much time they are connected to WLAN. Luckily, at the time of data collection, mobile phones which could connect to WLAN and install apps were quite new, therefore we still consider operator recorded data more reliable than self-reported data.

Another strength is the most comprehensive exposure assessment methods considering most relevant RF-EMF sources and exposure relevant behaviors (Roser et al. 2015a). The cumulative RF-EMF dose measures for the brain and the whole body over one year combined from questionnaire data, objectively recorded mobile phone use data, propagation modelling and personal measurements are unique and have not been applied ever before. The aim to disentangle effects due to RF-EMF exposure or due to other factors associated with mobile phone use, however, could not fully be achieved. Due to the high correlation between dose measures and self-reported and objectively recorded mobile phone call duration respectively, the confidence intervals of the effect estimates for usage related measures were overlapping with the effects of RF-EMF dose measures.

A limitation of the study was the low participation rate at baseline (36.8%) which may affect the representativeness of the cohort. Selection bias cannot completely be ruled out, as already discussed in chapter 7.2 in the paragraph on the “Development of the RF-EMF dose measure”, but we do not think that selection bias is of major concern although participation rate at baseline was not impressive. Additionally, with a participation rate of 96.8% in the follow-up investigation potential bias in the effect estimates from lost to follow-up is rather low and can be neglected.

A further limitation is the large uncertainty of the dose measure calculation. It is impossible to directly measure the absorbed RF-EMF dose and a validation of our dose calculations could not be done. Thus, it is difficult to quantify the uncertainty at that time. For example the absorbed radiation by the body depends heavily on the unknown position of the emitting device in relation to the body, which is expected to show a high variability. A further source of uncertainty is the emitted exposure from mobile phones, in particular during data traffic and in stand-by mode (Urbinello and Röösli 2013) and errors in modelling and personal measurements (Roser et al. 2015a).

7.5 Public Health relevance

The use of mobile phones and other wireless devices has increased remarkably in the last few years, especially in children and adolescents. This increase has been accompanied by a growing public concern regarding potential effects of RF-EMF emitted by such devices on health, cognitive function and behavior in adolescents. Additionally, there is considerable public confusion and misunderstandings regarding the ratio and magnitude of the electromagnetic fields within the different frequency bands as well as the qualitative differences between various sources, for instance close-to-body sources, such as mobile phones, and infrastructure installations, and their contribution to the total exposure (Dürrenberger et al. 2014). To address such concerns and misunderstandings robust evidence is required in order to appropriately communicate possible risks and to implement preventive measures if needed.

Preventive measures and awareness training might be the best option if our scientific results are taken into account. Our results show that RF-EMF exposure does not affect the health (Schoeni et al. 2017; Schoeni et al. 2016), concentration capacity or the behavior (Roser et al. 2016a), but memory performance in adolescents (Schoeni et al. 2015a). Effects on health (Schoeni et al. 2015b; Schoeni et al. 2017), concentration capacity or the behavior (Roser et al. 2016a) in adolescents are attributed to the use of mobile phones and other wireless devices per se and to other factors such as sleep deprivation or accessibility stress. It is important that adolescents learn how to appropriately deal with their mobile phones and other wireless devices. Adolescents should get educated about consequences of use of mobile phones and other wireless devices in the framework of health education in high schools. Nowadays the mobile phone is a lifestyle factor which adds new complexities to daily life due to perceived stress resulting from information overload and constant availability. We are responsible that adolescents are equipped with skills to deal with such pressures and to guide them safely into adulthood. Prevention strategies should focus on helping adolescents set limits for their accessibility by mobile phone.

Concerning the results on memory performance (Schoeni et al. 2015a) precautionary strategies should be considered as long as the results are not confirmed with an increased sample size. Adolescents should get educated what precautionary measures can be undertaken in order to reduce personal exposure. The following advices can reduce the RF-EMF exposure:

- Minimise the use of mobile phones and other wireless devices or use a headset for the mobile phone to increase the distance between the RF-EMF emitting device and the head.
- Never use radiation shields or other such protective devices. By reducing the connection quality with such radiation shields, the mobile phone is forced to transmit at a higher output power.
- Low radiation cordless phones are available. Don’t place the cordless phone base station too close to places you occupy for longer periods.
- Switch WLAN off during night or switch it on only when needed and place it centrally so that all the devices have a good reception. Don’t place the WLAN access point too close to places you occupy for longer periods.

As generally applies, turning off the devices or keeping the RF-EMF emitting sources at bay are the most efficient ways to reduce personal exposure. However, everybody remains free to decide on what extent such precautionary strategies are adapted.
It would have tremendous consequences if one day the observed results concerning memory performance could be replicated and other effects due to RF-EMF exposure would be identified. The mobile phone industry, a multi-million-dollar industry with a sizeable lobbying arm, would make every endeavour to trivialize the results i.e. as the trivialization to new wireless devices. The anti-mobile lobby in contrast, that says that mobile phones are the smoking gun of the 21st century, will probably grow bigger and will demand to forbid mobile phone use in adolescents in certain context and special instances i.e. in public schools. Anyway, the crux of the debate will be going on for the next couple of years. Meanwhile countries such as France have already gone a little step further. The French government has banned any advertisements encouraging children under 12 to use mobile phones. Such preventive measures would probably grow in the next few years.

Our results showed that exposure from mobile phone base stations in terms of dose measures is quite low compared to exposure from mobile phones or other wirelss devices. Far-field exposure from fixed site transmitters contributed about 0.7% to the brain dose and 2.3% to the whole body dose (Roser et al. 2015a; Schoeni et al. 2015a). The observed highest exposure from mobile phone base stations at home and in school using the geospatial propagation model was 372 µW/m^2 (=0.37 V/m) (Schoeni et al. 2016), which easily complies with current ICNIRP guidelines (International Commission on Non-Ionizing Radiation 1998), as well as with the precautionary reference levels as defined by the Federal Office for the Environment for Switzerland (FOEN 2012). The latter are currently 10 times lower than the ICNIRP's. Such results of the levels are important for the public since the construction of new base stations still faces great resistance. People nowadays expect good quality reception on their mobile devices everywhere, especially where they spend their daily life, but nobody wants to live in the vicinity of a base station. Therefore, our research is also important to change the idea in people's mind that exposure from their own mobile phone is much greater as compared to the exposure from mobile phone base stations.

The results observed in the framework of this thesis allow making statements about the current situation and exposure levels in the low dose range. We cannot comment on effects in the long run and at higher exposure levels. But in conclusion, minimizing personal exposure is one reasonable way to overcome possible harm to health or cognitive function.

7.6 Outlook

The here reported HERMES study has already started its follow-up. A next cohort with 458 study participants has already been established (HERMES II). The set-up of the two HERMES studies is the same and thus will enable us to perform pooled analyses with the study participants from both cohorts. This helps to increase the sample size and make even firmer conclusions. Furthermore, HERMES II is embedded in a five year European project called GERoNiMO (Generalised EMF Research using Novel Methods). The project proposes to build upon existing European resources such as the HERMES study or case-control studies, exposure assessment techniques and novel methods to better understand possible effects of RF-EMF on health, to improve health risk assessment, to characterize population levels of RF-EMF exposure in Europe and to reinforce policy development to reduce RF-EMF exposure (CREAL 2015). The exposure assessment methods and the resulting RF-EMF dose measures that have been developed and used in the HERMES study will be adapted to the European-wide project.

By the end of 2015, according to the International Telecommunication Union (ITU), there will be more than 7 billion mobile phone subscriptions, corresponding to a penetration rate of 97%. This is an enormous increase compared to 738 million in the year 2000. Current estimates show that there will be a massive growth in connected devices (communicating devices): estimated increase of mobile phones, multi-antenna systems, and electronic article surveillance systems etc. to 50 billion devices in 2020. Emitting sources are becoming more diverse, new infrastructures are deployed, frequency bands will be used more efficiently and unused frequency bands will be filled. People will be exposed to RF-EMF everywhere, either from carrying own devices or from far-field sources. The absence of an established biological mechanism for RF-EMF exposure makes it challenging to focus on specific health symptoms or cognitive function. Furthermore, changes in exposure-related user behaviors will hamper the RF-EMF research in a significant manner. Exposure assessment in the near future will become even more complex but also inevitably necessary in order to establish evidence-based management measures and effective health risk communication programs (Dürrenberger et al. 2014).

In our epidemiological study we showed how an integrated exposure assessment approach is incorporated into a prospective study design. This was achieved by combining questionnaires to obtain information about exposure-relevant behaviors, the use of exposimeters to assess personal exposure and modelling. Additionally, self-reported data was supplemented by objectively recorded mobile phone use data.

In future RF-EMF epidemiological studies such an approach should be adapted. Instead of using objectively recorded mobile phone use data, apps that automatically record information about duration of mobile phone use, use of hands-free sets, the laterality (on which side of the head the mobile phone is used), output power and the frequency band should be used. There is already such an app, which has been developed; however, it will still take some time until such an app can reliably record all this information. In a further step, epidemiological studies should cooperate more extensively with biomedical research to assess possible biological mechanisms of RF-EMF exposure. In vitro studies of RF-EMF and experimental studies in humans where for example blood from exposed people is sampled could provide insights into biological mechanisms and possible new biomarkers which would make it easier to focus on a specific health outcome.

8 Conclusions

The topic of RF-EMF is characterized by general public concern regarding potential adverse effects on health, cognitive function and behavior. To address such public concerns robust evidence on effects of RF-EMF is required. With our small, but well documented HERMES study we contributed to the evaluation of complex associations which are difficult to be addressed with large datasets where i.e. detailed exposure information is lacking. Conclusively, we observed that rather the use of mobile phones or other wireless devices than RF-EMF exposure affect the health of adolescents. In contrast we found that memory performance was more strongly associated with RF-EMF exposure than with the use of mobile phones or other wireless devices per se. This may indicate that RF-EMF exposure affects memory performance of adolescents. The observed results, however, have to be interpreted with caution due to the complexity of the applied RF-EMF dose measures. Based on the results we conclude that precautionary measures to reduce the mobile phone use and thus personal exposure to RF-EMF should be applied.

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