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

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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.

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.

Keywords: Mobile phone use, RF-EMF dose, adolescents, 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 minutes 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 minutes, 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, 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. 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 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 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 minutes are 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 Figure S1 shows the distribution of the change in the verbal and figural memory tests between baseline and follow-up.

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)
	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

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/d, and still 13.3 min/d 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 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/d]	48.2	33.2	22.5	43.9	74.3	107.8
duration cordless phone calls [min/d]	7.3	7.6	2.5	4.8	9.4	53.2
duration mobile phone calls [min/d]	16.0	25.7	3.0	7.6	18.6	293.9
objective (sample with operator data)						
volume data traffic on mobile phone [MB/d]	9.0	19.0	0.01	0.9	10.9	140.2
duration mobile phone calls [min/d]	1.9	3.6	0.2	0.6	1.8	28.6
Negative control variables						
self-reported (whole sample)						
duration gaming [min/d]	45.2	54.7	6.4	23.6	65.0	257.9
texts sent [x/d]	30.9	20.8	12.0	31.5	48.8	76.4
objective (sample with operator data)						
SMS sent [x/d]	1.7	2.3	0.5	0.9	1.8	16.1
Dose						
whole sample [a]						
brain [mJ/kg/d]	1421	1979	275	710	1854	16233
whole body [mJ/kg/d]	322	431	120	205	380	6044
sample with operator data [b]						
brain [mJ/kg/d]	235	432	60	102	236	4787
whole body [mJ/kg/d]	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 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 phone call duration and brain dose of the sample with operator data (0.48). Also whole body RF-EMF exposure 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.

Table 3. Kappa coefficients of usage related factors and the RF-EMF doses.

	Dose: whole sample [mJ/kg/d]		**Dose: sample with operator data** [mJ/kg/d]	
	brain	whole body	brain	whole body
Usage				
self-reported (whole sample)				
duration data traffic on mobile phone [min/d]	0.15[a]	0.21[a]	0.08[a]	0.28[a]
duration cordless phone calls [min/d]	0.25[a]	0.22[a]	0.21[a]	0.11[a]
duration mobile phone calls [min/d]	0.62[a]	0.67[a]	0.32	0.32
objective (sample with operator data)				
volume data traffic on mobile phone [MB/d]	0.01	0.13	0.10	0.20
duration mobile phone calls [min/d]	0.20	0.25	0.48[a]	0.28[a]
Negative control variables				
self-reported (whole sample)				
duration gaming [min/d]	-0.02	0.10	0.04	0.15
texts sent [x/d]	0.13	0.19	0.15	0.24
objective (sample with operator data)				
SMS sent [x/d]	0.08	0.05	0.15	0.21

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

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).

Figure 1 shows the results of the linear exposure response modelling (for numbers see supplementary tableS1). 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 FigureS2 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).

Figure 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.

Table 4. Results of the usage measures of the categorical analyses.

	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/d]	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/d]	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/d]	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/d]	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/d]	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/d]	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/d]	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/d]	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/d]	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/d]	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/d]	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/d]	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/d]	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/d]	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/d]	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/d]	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.

	n	**Medium exposure (>50% to ≤ 75%)**		**High exposure (>75%)**	
		crude (95% CI)	adjusted [c] (95% CI)	crude (95% CI)	adjusted [c] (95% CI)
Cumulative Dose [mJ/kg/d]					
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.

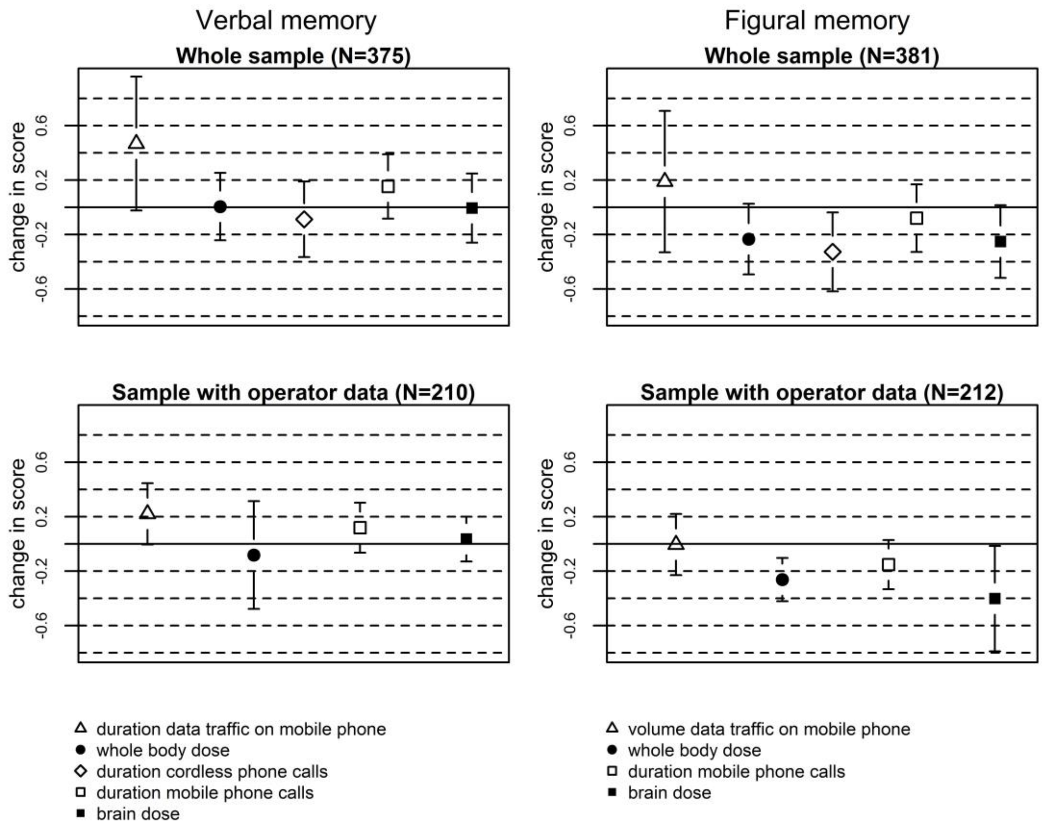

Figure 1. Results of the linear exposure response modelling. All models are adjusted for age, sex, nationality, school level, physical activity, alcohol, education of parents, change in height and time between baseline and follow-up investigation. Change in score per inter quartile range.

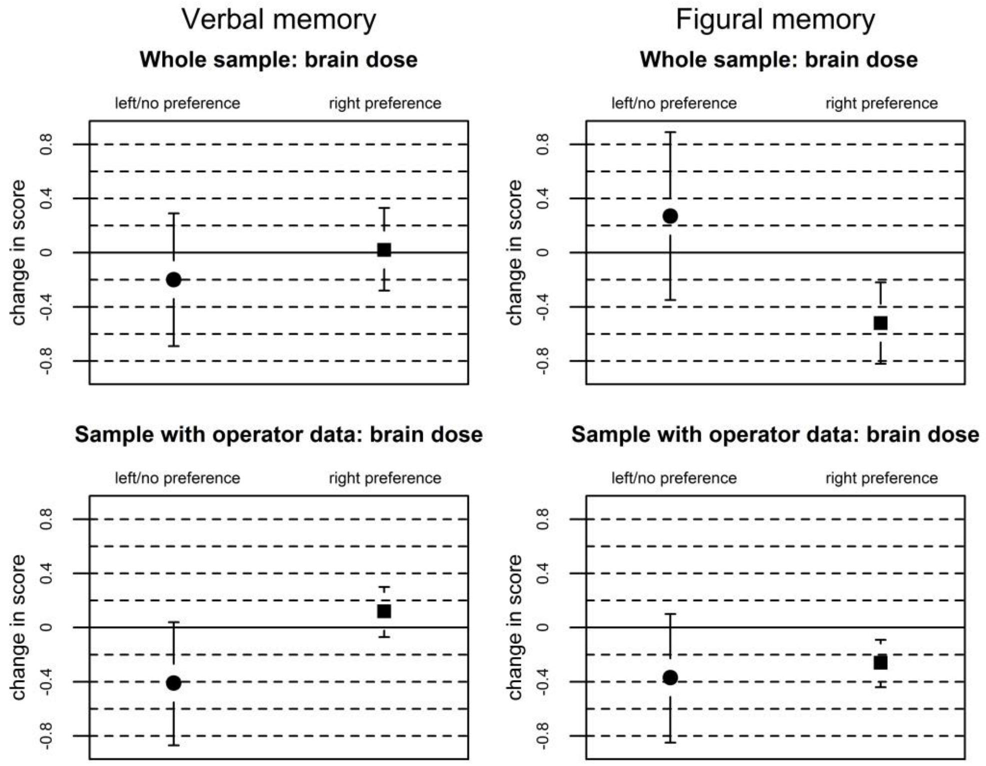

Figure 2. Results of the laterality analyses (linear exposure response). All models are adjusted for age, sex, nationality, school level, physical activity, alcohol, education of parents, change in height and time between baseline and follow-up investigation. Change in score per inter quartile range.

4. DISCUSSION

In longitudinal analyses 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 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 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 marginally associated with RF-EMF were not associated with figural memory performance (e.g. sending text messages, playing games, 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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