5 BRAIN PHYSIOLOGY AND FUNCTION

5.1 Epidemiology

Epidemiological studies on brain physiology address cognitive performance, behaviour, symptoms, well-being and the blood brain barrier integrity. The first studies on these outcomes appeared mainly in the Soviet and Eastern European literature and have been described in the previous Environmental Health Criteria Monograph 137 (WHO, 1993). These studies referred to "neurasthenic syndrome" or to "microwave sickness" and included mostly occupationally exposed groups like military radar workers, plastic sealers or radio operators. WHO (1993) concluded that these early studies suffered from various deficiencies. Some of the results could have been attributed to other working conditions, and it appeared that the working environments for exposed and control groups were not similar in essential aspects. Other factors could also have been operating to produce more subjective complaints among the exposed workers and a reporting bias because of enhanced awareness of the possible "microwave sickness" syndrome was of concern.

Little research on these outcomes has been conducted in the 1990s and mainly after 2000 a new body of literature emerged. Most studies addressed symptoms and well-being in relation to mobile phone use or far-field radiofrequency (RF) exposure sources such as mobile phone base stations. Conduct and interpretation of this research is challenging for several reasons. In relation to mobile phone use reverse causality is of concern, which means that subjective health status and also behavioural problems may affect the amount of mobile phone use and not vice versa. Alternatively, some common latent variables (confounders) may affect both quality of life and use of mobile phone or other life-style related RF-EMF sources (cordless phones, W-LAN). Further, these mobile phone studies almost exclusively rely on self-reported exposure data, which makes them vulnerable to reporting bias or nocebo effects, especially since the outcomes are also self-reported. The nocebo effect is the inverse of the placebo effect and means that adverse symptoms occur due to expectations (e.g. due to concerns). Human experimental research has consistently demonstrated the occurrence of nocebo phenomena in EMF research (Röösli, 2008; Rubin, Nieto-Hernandez & Wessely, 2010). With respect to far-field sources, exposure assessment is a challenge. The first studies used self-reported distance to the closest base-station as an exposure proxy, but it is now well-established that such an exposure measure is not correlated to RF exposure (Frei et al., 2010) and likely to be biased (Baliatsas et al., 2011). This is due to the fact that persons who are worried about base stations tend to underestimate the distance compared to persons without such worries (Blettner et al., 2009). As a consequence these studies applying self-reported distances to base stations are not further considered in this report. Selection bias, reporting bias and nocebo phenomena are of concern if people are aware of their exposure status, which is typically the case for large transmitters where exposure levels tends to be associated with distance to the source (Hauri et al., 2014; Schmiedel et al., 2009). For measured RF fields from base stations and other small transmitters exposure pattern is more complex and thus exposure is not related to distance (Frei et al., 2010) making nocebo and reporting bias in general less of a problem.

Reverse causality is expected to play a minor role for these studies on far-field EMF sources since they are not related to life style, but is a problem for studies dealing with mobile phones and other life-style related sources. Further, it is conceivable that using a mobile phone might have a training effect on cognitive performance, independent of any radiation effect. Also, the decision to use a mobile phone may depend on the cognitive performance (reverse causality). This is expected to be particularly relevant for the uptake of mobile phone use in the elderly generation.

There is also an emerging body of literature addressing the effects of mobile phone use on behaviour and well-being from a purely psychological point of view. These studies do not aim to and are not designed to address potential health risks associated with RF exposure, but point towards relevant potential confounding from psychological and life style aspects of mobile phone use. In this report their results are briefly summarized but not tabled in detail.

By the literature search 448 papers were identified and 54 were retrieved for detailed analysis, 50 were kept after excluding irrelevant outcomes and duplicate publications. Of these, 4 were excluded because they did not fulfil the inclusion criteria leaving 46 papers for review. To be included, studies had to be published after 1992 and should address the effects of RF exposure on outcomes relevant for brain physiology by applying an epidemiological study design, and fulfil the inclusion criteria outlined in Appendix X.

5.1.1 Cognitive performance

5.1.1.1 Use of mobile phones or other RF devices operating close to the body

Although provocation studies on short term effects of mobile phone use on cognitive functions are numerous (see chapter 5.2.1), only a few epidemiological studies addressed possible longer term consequences of regular mobile phone use. In Hong Kong, the effect of regular mobile phone use on human attention was investigated in a cross-sectional study (Lee et al., 2001). All Form Five students (corresponding to grade 11 in the US) in two girls' and two boys' schools were invited to participate in the study, in total 158 adolescents. After exclusion of students with medical and/or psychiatric histories, 79 students reported to regularly use mobile phones. Thereof, those 37 with the highest amount of use (175 to 27240 minutes) were included in the study together with 35 students who reported not to use a mobile phone. The groups were matched in terms of age (16.08, vs. 16.06 years) and gender distribution. During classroom hours students conducted the Symbol Digit Modalities Test (SDMT), the Stroop Color Word Test (CST), and the Trail Making Test (TMT) part A and B. Data of CST and SDMT were analysed by means of a two-way ANOVA and data of both TMT test parts were analysed with a multivariate ANOVA. Number of correct matches in the SDMT and colour naming time in the CST did not differ between the two groups. Time for completion of part A and part B of the TMT was significantly lower for the mobile phone users compared to the non-users. The authors concluded that these results either indicate that use of mobile phones may be facilitatory to human attention or it may reflect a self-selection process in a way that one is more likely not use a mobile phone if one does demonstrate a sufficient level of integrative attention function for multiple tasking. [A further explanation could be that regular using mobile phones for texting and gaming has a training effect on this type of task. Apart from gender and age matching no other potential confounding factors were considered in the analysis. Thus, confounding may be a fourth explanation for this observation. The study sample is small for this type of cross-sectional analysis.].

In an Australian study 479 7th grade students aged between 11 and 14 years were invited to carry out a computerized test battery and the Stroop Color Word Test (Abramson et al., 2009). Mobile phone use was assessed by a modified version of the INTERPHONE questionnaire. Finally, 317 (66%) students took part in the examination. In 9 out of 14 tests accuracy or reaction time was not related to cumulative number of calls. However, with increasing number of mobile phone calls, the accuracy of working memory was poorer, reaction time for a simple learning task shorter, and associative learning response time shorter and accuracy poorer. The completion time for form B of the Stroop word naming tasks was longer for those reporting more mobile phone voice calls. Since the findings were similar for total amount of text messages (SMS) per week, the authors suggest that these cognitive changes were unlikely due to RF exposure. In particular, faster but less accurate response may have been learnt through frequent use of a mobile phone. Subsequently, a follow-up examination was conducted one year later and it was investigated whether change in cognition between follow-up and baseline was related to baseline exposure or change in exposure between follow-up and baseline (Thomas et al., 2010a). Two hundred and thirty-six students participated in both examinations. At follow-up, the median numbers of voice calls and SMS had increased from 8 to 10 per week. Participants with a high baseline mobile phone exposure showed less reduction in response time over the 1-year period in various computerized tasks. Again, results were comparable for number of SMS and number of voice calls. The change analysis revealed that increase in the number of voice calls between baseline and follow-up was related to changes in the response time in two out of nine tasks. Further analyses indicated that observed changes occurred mainly in those who had fewer voice calls and SMS at baseline. Thus, according to the authors, the observed changes over time may relate to statistical regression to the mean and not represent the effect of mobile phone exposure. [The prospective design is a strength although self-reported exposure data introduce some uncertainty to the analyses. Since exposure from calling is much higher than from texting, a comparison of these results is useful for evaluating causality. At baseline the correlation between number of SMS and the number of calls was 0.4. Thus, it is not clear whether similar effects for amount of mobile phone use and amount of SMS just reflects some correlation of these two exposure measures or whether it indicates a non-radiation induced training effect of mobile phone use, as the authors suggest or any other type of confounding related to frequent use of mobile phone. If results in the first study are explained by a training effect among frequent mobile phone users, the finding in the follow-up study of improved results mainly among those who had few voice calls and SMS at baseline, but had increased their mobile phone use during follow-up, would be expected]

In another study cognitive decline of mobile phone users aged 55 years and older was investigated in 871 non-demented Chinese participants of the Singapore Longitudinal Ageing Studies (SLAS) cohort (Ng et al., 2012). Baseline examination took place between 2004 and 2005 and included the conduct of a Mini-Mental State Examination (MMSE) and a face-to-face interview. The frequency of mobile phone use was inquired on a three-point Likert scale (ranging from "never or rarely, i.e. less than one call per week"; to "often, i.e., daily"). Follow-up examination of the MMSE was conducted 4 years after baseline. In cross-sectional analyses at baseline, adjusted for relevant confounding factors, global MMSE score and a few executive function sub-scores of the MMSE did significantly improve with increasing use of mobile phone. Various other aspects of memory were, however, not related to mobile phone use. In longitudinal analyses, the change of MMSE between follow-up and baseline was not related to extent of self-reported mobile phone use at baseline. Risk of cognitive decline was also not associated with mobile phone use. According to the authors, the cross-sectional analyses suggest that mobile phone use among elderly is a self-selecting process. People with better cognitive functioning are apparently more likely to use mobile phones. The longitudinal analyses indicate that mobile phone use among older people does neither result in deleterious nor in beneficial effects on cognitive functioning. [The crude exposure assessment, based on self-reports only, is a limitation in this otherwise well conducted longitudinal study. The mobile phone users differed substantially from the non-user groups in terms of various characteristics such as age, sex, education and physical activity. Although these factors are included in the statistical analysis, residual confounding is a strong concern. Reverse causation is also a concern, in particular for the cross-sectional analyses.]

Studies with uncertainties related to inclusion criteria

One study described below recruited subjects in a way that does not allow assessment of potential selection bias. It is briefly described, but results are not included in the table, and it is given little weight in the overall assessment.

In a cross-sectional study Arns et al. (2007) compared 100 right-handed healthy heavy mobile phone users, 100 intermediate users and 100 non-users in terms of EEG and a battery of neuropsychological tests. Participants were selected from the Brain Resource International Database. Personality characteristics of the three exposure groups were compared. The heavy user group scored higher on Extraversion (p=0.01) and on openness (not significant) as compared to the non-user group and as a consequence these factors were considered in the data analyses. Overall neuropsychological performance was significantly different for the heavy mobile phone user group which was mostly due to the Word Inference Test, which is equivalent to the Stroop test. Post-hoc analyses revealed that mobile phone users showed least inference, although statistical significance was not obtained after Bonferroni correction. The EEG results are discussed in section 5.1.5. The authors discuss the possibility that the more focused attention of mobile phone users may be due to a cognitive training effect, rather than a direct effect of mobile phone use on cognition. [The amount of mobile phone use was obtained by multiplying the answers of various questions and not expressed in interpretable units. Recruitment process is unclear and subsequently the comparability of the groups is difficult to judge.]

Table 5.1.1. Overview on studies about cognitive functions and exposure to RF-EMF sources operating close to body

Endpoint	Study population	Exposure assessment	Results	Comments	Reference
Symbol Digit Modalities Test (SDMT) Stroop Color Word Test (CST) Trail Making Test (TMT)	Cross-sectional 72 adolescents from 4 schools from Hongkong mean age: ca. 16 y	Self-reported amount of mobile phone use 37 heaviest mobile phone users (median use: 3713 min) out of 79 compared to all 35 non-mobile phone users	Mobile phone users performed better in the TMT test. No differences for CST and SDMT.	Unadjusted ANOVA, same age and sex distribution between exposed and unexposed subjects. Training effect potential explanation for differences.	(Lee et al., 2001)
Response time and accuracy of a computerised psychometric test battery (7 tests), Stroop Color Word Test (CST)	Cross-sectional 317 7th grade students from 20 schools around Melbourne Median age 13 y 144 boys, 173 girls	Self-reported amount of mobile phone use using INTERPHONE questionnaire: Primary exposure measures: log10 total reported number of voice calls (median number of calls per week: 8; median since start of use: 1.74 y) Secondary: log10 total number of SMS made and received (median number of sms per week: 8)	5 out 14 cognitive tests associated with number of calls 4 out 14 cognitive tests associated with number of SMS 1 out of 2 CSTs associated with number of calls, no association with SMS.	Linear regression models adjusted for age, gender, languages, socio-economic status and handedness. Training effect potential explanation for differences.	(Abramson et al., 2009)
Response time and accuracy of a computerised psychometric test battery (7 tests), Stroop Color Word Test (CST)	Cohort, 1 year follow-up 236 7th grade students Median age:13.8 y 45% male	For log10 number of voice calls and SMS (see Abramson): a) exposure at baseline b) change in exposure between baseline and follow-up	Change in cognition between baseline and follow-up and number of calls/SMS at baseline: 2 resp. 1 out of 16 tests associated. Change in cognition and changes in number of calls/SMS between baseline and follow-up: 2 resp. 0 out of 16 tests associated.	Linear GEE models adjusted for age, sex, ethnicity, SES as well as growth and time period between examination at baseline and follow-up. Training effect potential explanation for differences.	(Thomas et al., 2010a)

Mini Mental State Examination (MMSE)	Cohort, 4 year follow-up 871 non-demented Chinese participants of the Singapore Longitudinal Ageing Studies Mean age: 65 y	Self-reported amount of mobile phone use with three groups: "never or rarely": less than one call per week" (n=380) ''sometimes'': one call or more per week but not daily (n=222) "often": daily (n=269)	Cross-sectional analyses: global MMSE improved with increasing mobile phone use. Longitudinal analyses: no effect on MMSE and cognitive decline.	ANOVA and logistic regression adjusted for age, gender, education, hypertension, diabetes, cardiac diseases, stroke, leisure time activities, smoking, alcohol consumption, depression, and APOE-ε4 (and baseline cognitive domain scores in longitudinal analyses). Reverse causation a concern in cross-sectional analyses, since uptake of mobile phone may be related to cognitive function.	(Ng et al., 2012)

5.1.1.2 Far-field RF exposure from fixed site transmitters and other sources

Only two epidemiological studies addressed cognitive performance with respect to far field RF-EMF exposure from mobile phone base stations. An Austrian cross-sectional survey focussed on subjective symptoms, sleep quality, and cognitive performance of people living in urban and rural areas for more than one year in proximity to one of 10 selected base stations (Hutter et al., 2006). Subjects 18 years or older were randomly selected from the telephone directory or by random walk. In total, 365 individuals took part in the study (participation rate: 60% in urban and 68% in rural area). Cognitive performance was assessed by memory tasks, choice reaction tasks and perceptual speed tests. Exposure assessment was based on a spot measurement in the sleeping room taken a few days after completion of the questionnaires. Measurements yielded field values in the high frequency range from 0.01 to 0.75 V/m; 70% of the exposure was estimated to be from mobile phone base stations. No statistically significant differences were found for any of the measures of cognitive performance, but there was a tendency for faster reaction in perceptual speed with higher exposure. [The recruitment procedure may have led to preferably recruitment of subjects with health problems in the vicinity of base stations and therefore introduced selection bias. No adjustment was made for socioeconomic status.]

Studies with uncertainties related to inclusion criteria

One study briefly described below recruited subjects in a way that does not allow assessment of potential selection bias. Therefore, results are not included in the table, and are given little weight in the overall assessment.

In an Egyptian cross-sectional study (Abdel-Rassoul et al., 2007) cognitive performance of 85 exposed participants (living or working in or opposite a building where the first mobile phone base station was constructed in Shebin El-Kom City) was compared with 80 controls. Controls were employees and engineers of an agricultural administration building located 2 km away from the exposed building. They were matched to the exposed participants on age and sex distribution, education level, smoking and mobile phone use. Details of the recruitment process as well as participation rates are not reported in the paper. Cognitive performance was assessed using a neurobehavioral test battery consisting of 8 tests. The exposed participants exhibited a significantly poorer performance than the controls in an attention test, but they exhibited significantly better performance in another attention test and two visuomotor tests. [The exposure assessment is very crude and no meaningful measurements have been conducted with respect to the exposure of the study population. The recruitment process is not described and the comparison of employees (control group) with a mixed group (exposed group) is prone to bias; in particular, since no confounding was considered in the analysis.]

Table 5.1.2. Overview on studies about cognitive functions and far field environmental RF-EMF exposure					
Endpoint	**Study population**	**Exposure assessment**	**Results**		**Reference**
Short and medium term memory test, choice reaction task, perceptual speed	Cross-sectional 365 randomly selected participants living in the vicinity of mobile phone base stations Mean age: 44 y	Spot measurements in the bedroom, 3 exposure groups with approx. cut-offs at 50th and 75th percentile: <0.1 mW/m² 0.1–0.5 mW/m² <0.5 mW/m²	No associations with exposure.	ANCOVA, without adjustment. Results for perceptual speed were adjusted for concern, age, sex, mobile phone use, urban/rural.	(Hutter et al., 2006)

5.1.1.3 Occupational exposure sources

Only one study is available on occupational exposure, but it did not include sufficient information about the recruitment process. Therefore, it is only briefly described, and results are not tabulated. It is given little weight in the overall assessment.

In a cross-sectional study, 35 operators of RF sealers from nine different companies were included together with 37 control persons from the same companies (Wilén et al., 2004). All contacted companies agreed to participate, but it is not stated how subjects within the companies were selected, and no participation rates are reported. The age distribution was similar among exposed and unexposed, while fewer women were included in the exposed group (49%) compared to the control group (62%). Smoking was more common among RF operators (46%) than among controls (32%). Electric and magnetic field strengths were measured in front of each RF sealer used by any of the study subjects at seven positions; head, trunk, waist, knees, feet, and both hands. For each operator daily mean exposure was calculated and induced current in the ankles and in the wrists during ordinary work was derived. Participants carried out sensory-motor tests: a two-point discrimination test (2 PD test) on the tip of the 2nd finger of the non-dominating hand, dexterity test and the assembly test. Assessment of symptoms and ECG recording were also made, described in chapters 5.1.3 and 9.1. Multivariate regression analyses were used to assess correlations between the tests and various exposure parameters. No confounding control was made. Exposure levels were quite high and exceeded the Swedish standard limits at 15 out of 46 workplaces measured. The results of the three sensory-motor tests did not differ between RF-operators and controls. [This study is based on a highly exposed collective with well conducted exposure measurements. However, the sample size is small, and differences in the distribution of potential confounders between RF operators and controls, or between RF operators with different levels of exposure, were not considered in the analysis. The representativeness of participating subjects cannot be assessed, given the lack of information on the selection procedure and participation rates.]

5.1.2. Behaviour

5.1.2.1 Use of mobile phones or other RF devices operated close to the body

The association between children’s mobile phone use at age 7 and behavioural problems was investigated in a cross-sectional analysis based on the Danish National Birth Cohort (Divan et al., 2008). Mothers of 13,159 children born 1997–1999 participated in telephone interviews during 2005 and 2006 (65% of those originally enrolled in the cohort), during which information about the child’s mobile phone use at age 7, maternal mobile phone use during pregnancy, potential confounding factors, and the child’s behavioural problems was collected. The study is described in detail in chapter 11, where results on maternal mobile phone use during pregnancy are discussed, and chapter 6.1, presenting effects on hearing. The child’s own mobile phone use was assessed with the question “Does your child use a mobile phone? (text messages do not count)”, with answer alternatives “No, never”, “Yes, but less than one hour per week” and “Yes, more than one hour per week” (Sudan et al., 2013). The two latter categories were combined as only 1% reported using a mobile phone for more than 1 h per week. Behavioural problems were assessed using the 'Strength and Difficulties Questionnaire', from which an overall score of behavioural problems was generated, as well as specific ratings of emotional symptoms, conduct problems, hyperactivity and peer problems. Based on the scores obtained, children were classified as abnormal, borderline, or normal for each of the outcomes studied. Crude and adjusted risk estimates were presented, using an ordinal logistic regression model. Adjustment was made for sex, maternal age, smoking during pregnancy, mother’s psychiatric problems, and socio-occupational levels. Adjusted risk estimates were always lower than unadjusted. The adjusted OR for overall behavioural problems associated with the child’s own mobile phone use was 1.18 (95% CI 1.01–1.38), including adjustment for maternal mobile phone use during pregnancy. Being exposed to both maternal mobile phone use during pregnancy and mobile phone use at age 7 was associated with an OR of 1.80 (1.45–2.23). Results for specific types of behavioural problems varied between 0.98 and 1.08 for the child’s mobile phone use only, and between 1.25 and 1.49 for being exposed to both maternal mobile phone use during pregnancy and postnatal use at age 7. [Behavioural problems are strongly heritable, thus confounding from heritability is a severe problem, which is unlikely to have been completely captured by adjustment for mother’s psychiatric problems. No adjustment was made for paternal psychiatric or behavioural problems. Reduction of risk estimates after adjustment indicates that confounding may be an issue, and residual confounding from incomplete measurement of confounding variables is possible, especially as they were based on self-reports of sometimes very sensitive information, e.g. own behavioural and psychiatric problems. The cross-sectional assessment of the child’s own mobile phone use prevents conclusions about the time sequence of events. It is not unlikely that the child’s behavioural problems increase the probability that the child is a mobile phone user.]

The Danish Cohort Study was later updated with children born until 2002 (Divan et al., 2012), using the same design as in the previous study. Singleton children from the 2008 study were also included in this new study (n= 28745). Participation rates were 60–65%. Similar analyses as in the previous study were performed, and in addition, analyses with a larger number of confounders were conducted (sex, mother's age at birth, mother's and father's history of psychiatric, cognitive or behavioural problems as a child, combined socio-occupational status, gestational age, mother's prenatal stress, and child breastfed up to 6 months of age), as well as stratified analyses. The child's own mobile phone use at age 7, and no maternal mobile phone use during pregnancy, was associated with slightly weaker risk estimates for overall behavioural problems with later birth years, the OR for children born 2001 (n=9682) was 1.0 (95% CI 0.7-1.4). The corresponding overall result when combining all children (n=41541) was 1.2 (95% CI 1.0–1.3). For the combination of own mobile phone use and maternal mobile phone use there was also pattern of decreasing risk estimates with later birth years; among singletons in the first study the OR was 1.9 (95% CI 1.5–2.3), while the risk estimate for children born 2001 was 1.4 (95% CI 1.1–1.8). Extending the number of confounding factors controlled for did not affect the results. [Despite extending the confounder evaluation this updated study has the same basic limitations as the originally published study in the sense that there are some indications that early adopters of mobile phones differ from the general population. Heritability is a concern in analyses of behavioural problems, as well as the cross-sectional design with respect to the child's own mobile phone use.]

Studies with uncertainties related to inclusion criteria

In a Taiwanese cross-sectional study the association between "problematic mobile phone use", assessed through a questionnaire developed according to principles used for assessment of substance use dependence, and a series of risky behaviours and low self-esteem was investigated among 11111 randomly selected adolescents aged between 12 and 18 years (participation rate 91.0%) (Yang et al., 2010). Addressing a potential biophysical effect was not an explicit aim of this study. Data were analysed separately for young (<15 years) and older girls and boys by means of three-level hierarchical logistic regression models without adjustment for confounders. In all strata associations were found between problematic mobile phone use and low self-esteem as well as risky behaviours such as aggression, insomnia, smoking cigarettes, alcohol use, drug use, having a tattoo, criminal record, suicidal tendencies as well as other risky behaviours. [The study was not designed to address RF-EMF effects, and is therefore not tabulated. Causal inference to RF-EMF cannot be made.]

Table 5.1.3. Overview of studies on behaviour and use of mobile phones or other RF devices operated close to the body

Endpoint	Study population	Exposure	No. of cases	OR (95% CI)	Comments	Reference
Behavioural problems at age 7 assessed through telephone interview with mother, Strengths and Difficulties Questionnaire	Cross-sectional Danish National Birth Cohort, 13159 children born 1997–1999, exposure and outcome assessed at age 7 Participation rate 65%	Child never use mobile phone	Not given.	1.0	Adjusted for sex of child, maternal age, smoking during pregnancy, mother's psychiatric problems, and socio-occupational levels. Residual confounding likely, behavioural problems strongly heritable. Reverse causation possible. Crude exposure assessment.	(Divan et al., 2008)
		Child use mobile phone ("Yes, but less than one hour per week" and "Yes, more than one hour per week")		1.18 (1.01–1.38)		
		Child never use mobile phone and no maternal mobile phone use during pregnancy		1.0		
		Child use mobile phone and maternal mobile phone use during pregnancy		1.80 (1.45–2.23)		
Behavioural problems at age 7 assessed through telephone interview with mother, Strengths and Difficulties Questionnaire	Cross-sectional Danish National Birth Cohort, 28745 children born 1997-2002, exposure and outcome assessed at age 7 Participation rate 60-65%	Child never use mobile phone and no maternal mobile phone use during pregnancy	Not given.	1.0	Adjusted for sex of child, mother's age at birth, mother's and father's history of psychiatric, cognitive or behavioural problems as a child, combined socio-occupational status, gestational age, mother's prenatal stress, and child breastfed up to 6 months of age. Residual confounding likely, behavioural problems strongly heritable. Reverse causation possible Crude exposure assessment.	(Divan et al., 2012)
		Child use mobile phone, no maternal mobile phone use during pregnancy		1.2 (1.0–1.3)		
		Child never use mobile phone and no maternal mobile phone use during pregnancy		1.0		
		Child use mobile phone and maternal mobile phone use during pregnancy		1.5 (1.4–1.7)		

5.1.2.2 Far-field RF exposure from fixed site transmitters and other sources

In a German study of 1484 children (8–12 years) and 1508 adolescents (13–17 years), randomly selected from registration offices in four Bavarian cities (participation rate 52%), RF-EMF exposure was assessed based on a 24-hour measurement of field strength using the portable Maschek ESM-140 device with readings every second (Thomas et al., 2010b). The frequency range covered GSM 900, GSM 1800, UMTS 2100, DECT and WLAN signals. Exposure was categorized according to quartiles of the measured exposure reported as the percentage of the ICNIRP reference value. Behavioural problems were assessed with the Strengths and Difficulties Questionnaire, which includes 25 questions about mental health behaviour, reflecting five scales; emotional symptoms, conduct problems, hyperactivity/inattention, peer relationship problems and prosocial behaviour. Overall behaviour was classified into "normal" vs. "borderline/abnormal". In children, behavioural problems and daytime personal RF-EMF exposure were not correlated. In adolescents, prevalence of behavioural problems was increased in the highest exposure quartile compared to the lowest quartile of exposure (OR=2.2; 95% CI: 1.1–4.5). This was mainly due to the subscales conduct problems (OR=3.7; 95% CI: 1.6–8.4) and hyperactivity (OR=2.1; 95% CI: 0.9–4.8). [The cross-sectional design of this study prevents from firm conclusions. In addition, individual exposure measurements are affected by the person's own mobile phone use (Frei et al., 2010). Thus, it is unclear to what extent high levels of exposure are correlated with high levels of mobile phone use; and high level of mobile phone use may be the consequence of behavioural problems and not vice versa (reverse causality). In addition, the participation rate is quite low, and selection bias cannot be excluded.]

Table 5.1.4. Overview on studies about behaviour and far field RF-EMF sources						
Endpoint	**Study population**	**Exposure**	**No. of cases**	**Results**	**Comments**	**Reference**
Strengths and Difficulties Questionnaire Classified into "normal" vs "borderline/abnormal" behaviour	Cross sectional 1484 children (8–12 y) and 1508 adolescents (13–17 y) from Bavaria, Germany, recruited during 2006-2008 Participation rate: 52%	Personal exposure measurements, quartiles (in % of ICNIRP reference value): Children: <0.15% 0.15%, 0.17%, 0.20% Adolescents: <0.15% 0.15%, 0.17%, 0.21%	 30 21 25 31 19 17 15 29	 1.0 0.8 (0.4–1.5) 1.0 (0.5–1.9) 1.3 (0.7–2.6) 1.0 0.9 (0.5–1.9) 1.0 (0.5–2.1) 2.2 (1.1–4.5)	Logistic regression adjusted for age, sex, level of education, study town, environmental worries and the self estimated exposure to mobile phone frequencies Increased risk in adolescents due to conduct problems and hyperactivity Reverse causality a possibility – behavioral problems may cause excessive own mobile phone use which may influence measured exposure.	(Thomas et al., 2010b)[1]

5.1.3. Symptoms and well-being

A part of the population attributes non-specific symptoms to RF-EMF exposure in the everyday environment. Typically a wide range of neurasthenic or skin symptoms are mentioned in this context although sleep disorders, headache, sensation of prickling and concentration difficulties are among the most common in most of the studies (Chu et al., 2011; Eltiti et al., 2007b; Frick et al., 2006; Huss & Röösli, 2006; Kato & Johansson, 2012; Khan, 2008; Korpinen & Paakkonen, 2009b; Mortazavi, Ahmadi & Shariati, 2007; Röösli et al., 2004b; Schreier, Huss & Röösli, 2006; Szyjkowska et al., 2005). Attribution of symptoms to EMF is called electromagnetic hypersensitivity (EHS) or idiopathic environmental intolerance attributed to electromagnetic fields (IEI-EMF). The prevalence varies widely across countries and time periods, such as 1.5% in Sweden (Hillert et al., 2002), 3.2% in California (Levallois et al., 2002), 3.5% in Austria (Schröttner & Leitgeb, 2008), 4% in the UK (Eltiti et al., 2007b), 5% in Switzerland (Schreier, Huss & Röösli, 2006), approx. 10% in Germany (Blettner et al., 2009), 13.3 % in Taiwan (Meg Tseng, Lin & Cheng, 2011). Since there is a lack of validated criteria for defining and assessing EHS, previous studies have applied different criteria, which may explain part of the large differences observed between studies (Baliatsas et al., 2012). Attribution of symptoms to an RF-EMF source does not prove a causal association because of possible reporting bias and nocebo effects. In order to derive causality, data on RF-EMF exposure and outcome have to be collected. These studies are discussed in the following section.

5.1.3.1 Use of mobile phones or other RF devices operated close to the body

In a cross-sectional study of 808 randomly selected individuals aged 12 to 70 years the prevalence of ten various symptoms was compared between non-users and regular users of mobile phones, defined as making at least one call per day (Chia, Chia & Tan, 2000). The overall participation rate was 45% (if subjects who could not be contacted and those who refused were excluded, the participation rates were 66.6% on the household level and 67.4% on the individual level). The prevalence of headache was 60.3% among mobile phone users and 54% among non-users. The corresponding crude prevalence rate ratio was 1.12 (95% CI 0.99–1.26); after adjustment for age, sex, ethnic group, use of video display terminals and occupational group it was 1.31 (95% CI 1.00–1.70). The prevalence of headache was significantly associated with the duration of mobile phone use per day. The prevalence of the other symptoms was not significantly different between mobile phone users and non-users, but rate ratios were not reported. There was an indication of higher prevalence of concentration difficulties among non-users (20.9% compared to 14.9% among mobile phone users, corresponding to a crude prevalence rate ratio of 0.80; 95% CI 0.61–1.05). [The value of this study is limited due to its cross-sectional design, the crude exposure assessment based on self-reported data, and low participation rate.]

In a cross-sectional study in Sweden and Norway a questionnaire was sent to about 17000 individuals who used mobile phones during work hours (Oftedal et al., 2000; Sandström et al., 2001; Wilén, Sandström & Hansson Mild, 2003). Participants were randomly selected from subscription registers, where the company was the subscriber, but an individual was assigned to the phone. Participation rates were 57% for Norway and 65% for Sweden. The participants were asked about generally occurring symptoms (at least once a week) and about symptoms related to using a mobile phone. The primary hypothesis of the study was to investigate whether GSM mobile phone users experience more symptoms than NMT users, because more complaints had been obtained from the first group. Such an association was not found in the analyses; rather GSM users experienced less often warmth behind/on the ear and burning sensations (Sandström et al., 2001). In total, 13% of the Swedish and 31% of the Norwegian participants reported some symptom that they associated with mobile phone use. With respect to daily duration and frequency of mobile phone use a positive trend was found for all symptoms, which was most pronounced for warmth behind/on ear, burning skin, headache and dizziness. Most symptoms began during or within half an hour of the call and lasted up to two hours (Oftedal et al., 2000). In a refined analysis information about calling time per day and number of calls per day were combined with measurements of the Specific Absorption Rate (SAR) to calculate Specific Absorption per Day (SAD) and Specific Absorption per Call (SAC) (Wilén, Sandström & Hansson Mild, 2003). Some of the symptoms (dizziness, discomfort, concentration, and warmth on/behind the ear) were associated with SAD and the authors indicated that SAR values >0.5 W/kg may be an important factor for the prevalence of some of the symptoms. [The cross-sectional design is a limitation and results may be affected by reporting bias and/or confounding. The prevalence of symptoms attributed to mobile phone use among study participants is high. The comparison between GSM and NMT users is appealing since the latter system has a higher output power. The calculation of SAD and SAC is interesting but heavily affected by the self-reported amount of mobile phone use and thus vulnerable to information bias and confounding similar to the other analyses, and cannot overcome the limitation of the cross-sectional design. Adjusting for potential confounding was only done in the Sandstrom paper, although the covariables are not specified. No control was made of potential confounders. The large difference in symptom prevalence between Sweden and Norway is noteworthy. Non-participation may have introduced selection bias, which may perhaps explain some of the difference.]

In a Swedish cross-sectional study (Söderqvist, Carlberg & Hardell, 2008) a postal questionnaire comprising 8 pages of 27 questions with 75 items was sent to 2000 Swedish adolescents aged 15–19 years, who were randomly selected from the population registry using a stratified sampling scheme (200 individuals per gender and year). The participation rate was 63.5%. The questionnaire included questions on wireless phone use, wireless Internet connections at home or in school, wireless earphones and other wireless music equipment, TV-watching habits, sleep habits and physical activity. Subsequently, it was asked for 23 non-specific symptoms of ill health (e.g. allergic symptoms, asthmatic symptoms, other breathing difficulties, chest pain, palpitation, hay fever, eczema, dizziness, etc) on a four point Likert scale ('never', 'seldom', 'every week', 'every day'). Unconditional logistic regression analysis was used to estimate odds ratios, adjusted for age and sex. Regular use of mobile phone was defined as using the phone for at least 2 min per day and regular DECT phone use as 5 min per day. Out of 23 symptoms, regular mobile phone use was associated with asthmatic symptoms (OR=1.8, 95% CI 1.1–3.0), headache (OR=1.5, 95% CI 1.1–2.0) and concentration difficulties (OR=1.4, 95% CI 1.1–1.9). Asthmatic symptoms and headache were also related to DECT phone use. Self-perceived health (very good, good, fair, poor, very poor) was not related to wireless phone use after adjusting for insufficient sleep and tiredness. [The cross-sectional design does not allow determination of the time sequence of events, i.e. whether mobile phone use preceded the occurrence of the outcome. Reporting bias is of concern since both, exposure and outcome is self-reported. Analyses were not corrected for multiple comparisons. In addition, there is no biological explanation how use of mobile phone should cause asthma symptoms and confounding by socioeconomic status may be alternative explanations for the observed associations.]

The previously mentioned German population-based cross-sectional study (chapter 5.1.2.2) on 1484 children and 1508 adolescents (participation rate: 52%) asked about usual wireless phone use, as well as use of mobile and cordless phones during the time of the personal measurements of RF-EMF that was made during 24 hours. In adolescents, use of a mobile phone at least daily or cordless phone at least nearly daily was associated with increased prevalence of irritation but not with headache, nervousness, dizziness, concentration problems and fatigue (Heinrich et al., 2011). In children no associations were observed. Using a mobile phone in the morning of the measurement day for at least five minutes was associated with increased occurrence of headache, irritation and fatigue in adolescents at noon (Heinrich et al., 2010). Nervousness, dizziness and concentration problems at noon were not related to self-reported mobile phone use and in the evening, none of the symptoms of adolescents was related to exposure. In children, neither symptoms at noon nor in the evening were related to self-reported mobile phone use. [A large number of analyses were conducted, thus, a few raised effect estimates would be expected by chance alone. Maturity among adolescents will vary, and both mobile phone use and perceived health and well-being is associated with puberty, but was not controlled for in the analyses.] Milde-Bush and co-workers conducted an add-on to the original cross-sectional study where 1025 of the adolescents answered more detailed questions about headaches, where the purpose was to study headaches in relation to use of electronic media (Milde-Busch et al., 2010). An association between any type of headache and extent of listening to music was observed but no associations with other types of media, such as mobile phone use, computer use or watching TV.

In a Swiss study on health related quality of life, 1375 randomly selected individuals took part in a baseline survey (participation rate 37%) in 2008 (Frei et al., 2012). Cordless and mobile phone use was obtained from the questionnaire, and approximately 40% of the participants gave consent that their mobile phone connection data of the previous six months could be obtained from their operator. Exposure was categorized at the median and 90th percentile. In cross-sectional analyses, using linear regression models for linear outcomes, and logistic regression models for binary outcomes, and with adjustment for age, sex, body mass index, stress, physical activity, smoking habits, alcohol consumption, education, marital status, degree of urbanity, nightshift work, belief in health effects due to RF-EMF exposure, use of sleeping drugs, and general attitude towards the environment, neither von Zerssen score, Hit-6 headache score or prevalence of tinnitus was associated with cordless or mobile phone use. After excluding night shift workers and people who consume sleeping pills, 1212 participants were eligible for the analysis of sleep effects. Neither excess daytime sleepiness (OR=1.03; 95% CI 0.62–1.69) nor sleep disturbances (OR=0.64; 95% CI 0.31–1.28) occurred more often in the highest exposure decile of self-reported mobile phone use compared to the low exposure group (<median). These results were confirmed with the operator data: OR for excess daytime sleepiness was 0.91 (95% CI 0.39–2.11) and OR for sleep disturbances was 1.03 (95% CI 0.32–3.30). [The strength of this study is the exposure assessment since it is the only study in this chapter that used objective, operator recorded mobile phone data. The low participation rate at baseline is a limitation. Phone interviews with 634 non-responders did not indicate substantial selection bias in the study although, according to the authors, the exposure–response association for mobile and cordless

phone use tends to be biased downward. In any case, the cross-sectional analyses are limited in terms of deriving causality and vulnerable to confounding and reverse causality such as the "healthy communicator" effect which means that healthy people may tend to have more interactions including mobile phone use.]

One year later 1122 study participants (82% of the baseline survey) of the above mentioned Swiss study completed a follow-up investigation (Frei et al., 2012; Mohler et al., 2012). It was investigated whether a change in symptom scores were associated with exposure at baseline or with a change of the exposure situation. Again, after controlling for baseline confounders and if the participant had moved house between baseline and follow-up, amount of wireless phone use at baseline was not consistently associated with a change in symptom score, sleep disturbance score, excessive daytime sleepiness score, headache score or incidence of tinnitus. Similarly, an increase or decrease of wireless phone use between 2008 and 2009 was not accompanied with a respective change of health disturbances. The authors concluded that the few observed statistical associations (see Table 5.1.5), which did not show a consistent pattern, most likely were due to chance given the high number of health effects and exposures that were analysed. About 8% of the study participants reported to have EHS and an additional 14% of the participants attributed symptoms to RF-EMF exposure (attributers) without considering themselves as being hypersensitive to electromagnetic fields. The prevalence of symptoms was highest in the EHS persons, which is expected. However, health disturbances of EHS individuals and attributers were neither associated with environmental RF-EMF exposure levels nor with wireless phone use (Röösli, Mohler & Frei, 2010). Results did not differ between age groups (30–44 and 45–60 years). [The strength of this study is the prospective cohort design and the use of objective mobile phone use data. Exposure levels and changes between baseline and follow-up were relatively small, thus the power to find exposure effect is somewhat limited. The high participation rate follow-up indicates limited impact on the results from lost-to-follow-up.]

In a prospective cohort study of young adults (20–24 years) the association between mental health outcomes and use of mobile phones was investigated based on questionnaires at baseline and 1-year follow-up (Thomee et al., 2010). From 10000 women and 10000 men who were invited, 4347 women and 2778 men participated in the baseline survey (participation rate: 36%) and 2701 women and 1455 men participated in the follow-up (58% of baseline participants). In a cross-sectional analysis at baseline adjusted for relationship status, educational level and occupation, persons reporting a high amount of mobile phone use were more likely to also report stress, sleep disturbances, and symptoms of depression. In the prospective analysis, persons were excluded that reported symptoms at baseline, in order to assess who developed symptoms during the study period. In this analysis, a high amount of mobile phone use at baseline was associated with sleep disturbances in men only and with symptoms of depression in men and women. An increased occurrence of mental health outcomes was also observed in people with overuse of mobile phones and people who experienced accessibility via mobile phones to be stressful. In a subsequent analysis (Thomee, Harenstam & Hagberg, 2012) similar associations as for mobile phone use were also observed for computer use indicating that EMF exposure from mobile phone may not be relevant in this context. [The low participation rate may have introduced selection bias, which is of particular concern for the cross-sectional analysis but to some extent also for the longitudinal analysis because the drop-out rate was relatively high. Exposure assessment was based on self-reports and only a limited number of possibly relevant confounders have been considered in the analysis. In addition, it was not possible to differentiate between effects that are associated with using a mobile phone as such, and the exposure to EMF from a mobile phone.]

Studies with uncertainties related to inclusion criteria

The four studies below do not have sufficiently detailed descriptions of their study procedures to allow evaluation of potential biases. They are therefore only briefly described, and not included in the table or final analysis.

Cao and colleagues conducted a cross sectional study of 115 mobile phone users and 101 non-users recruited from one company in China, to study the association between mobile phone use and symptoms of neurasthenia (Cao et al., 2000). Outcome, exposure, and confounding information were assessed by self-reported questionnaire. The overall prevalence of neurasthenia did not differ significantly between mobile phone users and non-users, but some specific symptoms were more common among mobile phone users, e.g. nausea and hearing loss. [No information is provided about the procedures for selection of participants or participation rates, and it is not possible to evaluate comparability between exposed and unexposed individuals.]

In a cross-sectional study of 161 students and workers of a French engineering school prevalence of various symptoms did not differ between mobile phone users and non-users (Santini et al., 2001). Within the group of mobile phone users discomfort and tingling or warmth on ear were more prevalent in people using their phone more than two times per day. A comparison between GSM900 and GSM1800 users did not reveal any difference except concentration difficulties, which was more prevalent for the latter. [No data on selection of study participants and participation rate is given, making this study largely uninformative.]

In another cross-sectional study 193 females and 502 males were randomly selected from a town in the Eastern part of Turkey (participation rate not reported) (Balikci et al., 2005). Individuals were divided in mobile phone users and non-users and among users duration since start of mobile phone use was considered in the analysis. According to an ANOVA without adjustment for confounders six out of 10 symptoms were associated with mobile phone use. These were the following symptoms: headache, extreme irritation, increase in the carelessness, forgetfulness, decrease of the reflex and clicking sound in the ears. Six symptoms were also related to duration of mobile phone use. [No detail about the exposure assessment, symptom questions or study collective is given, making this study largely uninformative.]

In a cross-sectional study the association between mobile phone use and hearing and vision complaints in the Saudi population was investigated (Meo & Al-Drees, 2005). Approximately 700 mobile phone users participated in an interview or filled in a questionnaire. Duration of daily mobile phone use was not related to these complaints. [No detail about the exposure assessment, symptom questions and collective is given, making this study largely uninformative.]

Table 5.1.5. Overview on studies about non-specific symptoms and exposure to RF-EMF sources operating close to body					
Endpoint	**Study population**	**Exposure assessment**	**Results**	**Comments**	**Reference**
Headache, dizziness, concentration difficulties, loss of memory, unusual drowsiness or tiredness, sense of warmth behind or around the ear, burning sensation to the ear and face, tingling sensation to the face, visual disturbances	Cross-sectional 808 individuals randomly selected from one community of Singapore 12–70 y Participation rate 45%	Self-reported mobile phone use: Yes, at least once a day (n=362) vs. no (n=446)	Prevalence rate ratio for headache 1.31 (95% CI: 1.00–1.70). No associations were found for any of the other nine symptoms.	Proportional hazards model, adjusted for age, sex, ethnic group, use of video display terminals and occupational group, but only in analysis of headache. Selection bias may be a problem.	(Chia, Chia & Tan, 2000)
Dizziness, discomfort, concentration difficulties, memory loss, fatigue, headache, warmth behind or on ear, burning skin, tingling/tightness, other	Cross-sectional 2828 Norwegians and 7803 Swedes who used GSM or NMT mobile phones on their job randomly selected from subscription registers 87% males,ca.50% <50 y Participation rates 57% for Norway and 65% for Sweden	Self-reported mobile phone use: a) duration per day: <2min/day 2-15min/day 15-60min/day >60min/day b) frequency <2 calls/day 2-4 calls/day >4 calls per day c) NMT vs GSM mobile phone d) Specific Absorption per Day (SAD) and Specific Absorption per Call (SAC)	13% of Swedish and 31% of Norwegian participants attributed some kind of symptom to mobile phone use. Positive trends with respect to calling time and calling frequency for all symptoms, most pronounced for warmth, burning, headache and dizziness. No symptom difference between NMT and GSM users. SAD was related to dizziness, discomfort, concentration, and warmth on/behind the ear. No association for SAC.	No confounding control (except Sandstrom analysis). No unexposed group. Selection bias may be a problem. No explanation for the large difference in symptom prevalence between the countries.	(Oftedal et al., 2000; Sandström et al., 2001; Wilén, Sandström & Hansson Mild, 2003)

23 different non-specific symptoms of ill health - allergic symptoms, asthmatic symptoms, other breathing difficulties, chest pain, palpitation, hay fever, eczema, dizziness, headache, anxiety, concentration difficulties, depressed mood, sleep disturbances, stress, tiredness, cold sweat, skin rash, tingling/burning sensation of the skin, eye irritation, tinnitus, body pain, pricking sensation in the mouth, often catch infections	Cross-sectional 1269 adolescents from Sweden, randomly selected from population registries 15–19 y 52% females Participation rate 63.5%	Self-reported regular mobile phone use:	Allergic symptoms:	Ordinal logistic regression analysis, adjusted for age and sex. Non-participation may have introduced selection bias. Reverse causation may be a problem. Other lifestyle factors among adolescents may have affected both telephone habits and symptoms, i.e. confounding.	(Söderqvist, Carlberg & Hardell, 2008)
		≥2–15 min/day	1.2 (0.9–1.7)		
		>15 min/day	1.6 (1.1–2.4)		
			Asthmatic symptoms:		
		≥2–15 min/day	1.8 (1.0–3.0)		
		>15 min/day	2.0 (1.1–3.6)		
			Hay fever:		
		≥2–15 min/day	1.3 (0.9–2.0)		
		>15 min/day	1.6 (1.0–2.5)		
			Dizziness		
		≥2–15 min/day	1.3 (0.9–1.9)		
		>15 min/day	1.6 (1.1–2.5)		
			Headache:		
		≥2–15 min/day	1.5 (1.1–2.0)		
		>15 min/day	1.6 (1.2–2.3)		
			Concentration difficulties:		
		≥2–15 min/day	1.4 (1.0–1.8)		
		>15 min/day	1.6 (1.1–2.3)		
			Stress:		
		≥2–15 min/day	1.2 (0.9–1.6)		
		>15 min/day	1.6 (1.1–2.2)		
			Tiredness:		
		≥2–15 min/day	1.2 (0.9–1.6)		
		>15 min/day	1.5 (1.0–2.0)		
			No associations for other symptoms.		
		Self-reported regular DECT cordless phone use: ≥5-15 min/day, >15 min/day	Results for DECT phone use were very similar to those for mobile phone use. Self-perceived health was not related to wireless phone use.		

Chronic symptoms: selected items of the HBSC-survey: headache, irritation, nervousness, dizziness, fatigue, fear and sleeping problems Acute symptoms: selected items of the von Zerssen list: headache, irritation, nervousness, dizziness, fatigue and concentration problems.	Cross-sectional 1484 randomly selected children and 1508 adolescents of 4 German towns 8–12 y Participation rate 52%.	Self-reported usual mobile and DECT phone use (at least daily vs. less) Self-reported mobile and DECT phone use on the day of personal measurements (at least 5 min vs. less)	Typical self-reported mobile/DECT phone use and chronic symptoms: out of 28 models two significant effects for adolescents: OR for irritation and "at least daily" mobile phone use: 1.48 (1.13–1.93); "at least nearly daily" cordless phone use: 1.30 (1.02–1.64). No association for children. Self-reported at least 5 minute mobile phone use and acute symptoms: 3 out of 24 associations significant: OR for morning headache: 1.55 (1.05 –2.29); irritation: 1.64 (1.10 –2.44); fatigue: 1.76 (1.22 –2.56). No association for children.	Logistic regression models adjusted for age, sex, level of education of the parents, study town and environmental worries (partly distance to the next base station).	(Heinrich et al., 2010; 2011)
Sleep disturbance score, von Zerssen symptom list, Hit-6 headache scale	Cross-sectional 1375 randomly selected adults Switzerland 30–60 y 58% females Participation rate 37%	Operator recorded mobile phone use as well as self-reported mobile and cordless phone use. 3 exposure groups with cut-offs at 50^{th} and 90^{th} percentile	1 association out of 36 effect estimates: Decrease in Zerssen symptom score for medium self-reported mobile phone use exposure category in the 2009 examination	Linear regression for linear outcomes, logistic regression for binary outcomes adjusted for age, sex, body mass index, stress, physical activity, smoking habits, alcohol consumption, education, marital status, degree of urbanity, nightshift work, belief in health, effects due to RF-EMF exposure, use of sleeping drugs and general, attitude towards the environment.	(Frei et al., 2012; Mohler et al., 2010)

Excess daytime sleepiness, sleep disturbance score, von Zerssen symptom list, Hit-6 headache scale	Cohort with 1 year follow-up 1122 randomly selected adults Switzerland 30–60 y 60% females Participation rate at follow-up 82%	Operator recorded mobile phone use as well as self-reported mobile and cordless phone use. 3 exposure groups with cut-offs at 50th and 90th percentile	No consistent exposure-response association (6 significant associations in both directions out of 57 risk estimates): Decrease of day time sleepiness for decreasing self-reported use of mobile phone between baseline and follow-up Increase in sleep disturbance score with decreasing self-reported cordless phone use, increased sleep disturbance score for the medium baseline exposure categories of self-reported mobile as well as cordless phone use. Decrease in Zerssen symptom score for high baseline self-reported mobile phone use as well as increase in self-reported mobile phone use between baseline and follow-up.	Same methods and confounders as in the cross-sectional analyses, plus adjustment for moving house between the two surveys. Short follow-up time.	
Current stress, Karolinska Sleep Questionnaire, depression from Prime-MD screening form	Cross-sectional 2778 males and 4347 females, Sweden 20–24 y Participation rate 36%	Self-reported mobile phone use: various aspects (mobile phone use, availability demands, awakened at nights, accessibility stress, overuse) classified as low, medium, high	High vs. low mobile phone use was associated with stress, sleep disturbance, depression among both men and women.	Logistic regression (prevalence odds ratio) adjusted for relationship status, educational level and occupation.	(Thomee et al., 2010)
Current stress, Karolinska Sleep Questionnaire, depression from Prime-MD screening form	Cohort with 1 year follow-up 1455 males and 2701 females, Sweden 20–24 y Participation rate 58%	Self-reported mobile phone use: various aspects (mobile phone use, availability demands, awakened at nights, accessibility stress, overuse) classified as low, medium, high	High vs. low mobile phone use was associated with sleep disturbance in men and symptom of depression in both men and women. “Overuse” was associated with sleep disturbance in women. “High accessibility stress” was associated with stress, sleep disturbance, depression among both men and women.	Logistic regression (incidence odds ratio) adjusted for relationship status, educational level and occupation.	(Thomee et al., 2010)

Further various cross-sectional studies have investigated the association between symptoms and mobile phone or media use from a psychological perspective, e.g. in terms of problematic amount of use, or use during night-time. Thus, these studies were not designed to elucidate biophysical effects and are only briefly mentioned in the following. In a written cross-sectional survey of 6121 (out of 15000 selected) working-age (18–65 years) Finns the prevalence of mental symptoms (sleeping disorders/disturbances, depression, exhaustion at work, substance addiction, anxiety or fear) were analysed in relation to computer and mobile phone use (Korpinen & Paakkonen, 2009a). Symptoms were associated with the use of desktop computer but not with mobile phone use. An additional publication on a subset of the data from young adults aged 30 years or younger (n=1563) did not compare symptom occurrence with mobile phone use (Korpinen & Paakkonen, 2011). From a Norwegian written survey of 816 individuals (participation rate 34%) aged between 16 and 40 years it was concluded that the use of computers and mobile telephones in the bedroom were related to poor sleep habits, but that media use in the bedroom was unrelated to symptoms of insomnia (Brunborg et al., 2011). A Dutch prospective cohort study of 1656 school children reported that frequent use of mobile phones during the night for calling and sending text messages was related to self-reported tiredness (Van den Bulck, 2007).

5.1.3.2 Far-field RF exposure from fixed site transmitters and other sources

In the previously mentioned Austrian cross-sectional study on 365 individuals living in the vicinity of mobile phone base stations (Hutter et al., 2006) the participants also filled in a symptom questionnaire. Three out of 14 symptoms from the von Zerssen list were more common in the highest exposure category (headache, cold hands or feet, and difficulties to concentrate). Analyses were adjusted for age, sex, region, mobile phone use, and concerns about base stations. After taking into account concerns about base stations, sleep quality measures were not related to exposure, while concerns were associated with poor sleep quality. [Recruitment procedures may have led to overrepresentation of subjects with health problems and living very close to a base station. No adjustment for socioeconomic status was made.]

A panel of 54 volunteers (21 men, 33 women) living in the vicinity (mean: 1.9 km) of a short-wave radio transmitter (6–22 MHz) in Schwarzenburg (Switzerland) were followed for 1 week each before and after shut-down of the transmitter in 1998 (Altpeter et al., 2006). Effects on sleep quality, self-reported every morning in a diary using a visual analogue scale, and changes in the melatonin cycle (described in chapter 7.1) were investigated. Prior to shut down the average of measured magnetic field exposure was 1.5 mA/m. A cross-sectional analysis of the data before shut down revealed a 3.9 (95% CI: 1.7–6.0) unit decrease of sleep quality per mA/m increase in magnetic field exposure. After shutdown, sleep quality improved by 1.7 units (95% CI: 0.1–3.4) per mA/m decrease in magnetic field exposure. The authors indicated that blinding of the participants regarding their exposure status was not possible in this observational study and that this may have affected the outcome measurements in a direct or indirect (psychological) way. [Reporting bias and nocebo cannot be excluded in this study because people were aware of the operating status of the transmitter.]

A cross-sectional survey was conducted in three villages in Cyprus as a response to citizen's concern about RF exposure from nearby military antenna systems. The study focussed on non-specific symptoms, birth abnormalities and mortality in relation to RF-EMF exposure (Preece et al., 2007). Two villages were close to a short-wave military antenna and one village was further away. Average exposure levels in the villages were obtained from measurements and were 0.57 V/m in the highly exposed village (thereof 0.11 V/m from the military antenna), 0.46 V/m in the medium exposed village (0.04 V/m from military antenna) and below 0.01 V/m in the village with the lowest exposure. Questionnaires for adults and children were distributed to all households in the three villages, with an estimated total population size of 2150 persons. Response rate was estimated to be 87%. The prevalence of several symptoms (migraine, headache, dizziness, depression, heart problems, asthma and other respiratory symptoms) was significantly different between the three cities. Headache, migraine, dizziness and the SF-36 score on general health status were significantly related to RF-EMF exposure. [The number of participants is not reported, nor the age and sex distribution among participants. No data is provided to evaluate the comparability of the three villages. Possible differences between villages may affect the study results. In addition, reporting bias due to concerns and nocebo is very likely, especially considering that the survey was initiated in response to a call at a public meeting following several years of public concern about the antenna.]

In a random population-based cross-sectional study of 329 adults (participation rate 30%) living in four different Bavarian towns, personal measurements (Maschek Electronics dosimeter ESM-140) of exposure to the sum of mobile phone frequency bands, cordless phones and WLAN during waking hours was compared with the prevalence of chronic non-specific symptoms of ill health over the last six months. Symptoms were collected by a selection of items from the Freiburg symptom questionnaire (Thomas et al., 2008a). In the highest quartile of exposure (0.21–0.58% of the ICNIRP reference value) none of the chronic symptoms was increased compared to the lowest exposed quartile (<0.15% of ICNIRP reference). Furthermore, acute symptoms were obtained on the study day at noon and evening and compared with the exposure during morning or evening, respectively. Acute symptoms (headache, fatigue, concentration problems, tinnitus, numbness in hands or feet and eyelid twitch) were not found to be related to the exposure in the previous few hours. [A strength of the study is the use of personal dosimeters for exposure assessment. The low participation rate is a limitation.]

In the previously mentioned German population-based cross-sectional study (chapter 5.1.2.2) on 1484 children and 1508 adolescents (participation rate: 52%) personal exposure to RF-EMF was measured using a portable device and chronic as well as acute symptoms were assessed (Thomas et al., 2008b). The inquired symptoms were headache, irritation, nervousness, dizziness, fear (only chronic), sleeping problems (only chronic), concentration problems (only acute) and fatigue. Occurrence of the chronic symptoms headache, irritation, nervousness, dizziness, fatigue, fear, and sleeping problems over the last 6 months was assessed on a five-point Likert scale. Data were analysed by means of logistic regression models adjusted for age, sex, level of education of the parents, study town and environmental worries and stratified for children and adolescents. None of the symptoms was related to exposure except a reduced risk for sleeping problems in the third quartile of exposure among children (OR=0.63, 95% CI: 0.41–0.96) (Heinrich et al., 2011). A further, more complex data analysis approach, based on a functional exposure approach, confirmed these findings (Kuhnlein et al., 2009). Acute symptoms were assessed twice a day using a symptom diary. From a large number of investigated associations, only a few significant associations were found, which did not show a consistent exposure-response pattern (Heinrich et al., 2010): adolescents in the highest quartile of exposure during morning hours reported a statistically significant higher intensity of headache at noon (OR=1.50; 95% CI: 1.03– 2.19). Exposure in the afternoon was associated with higher intensity of irritation in the evening among adolescents (4th quartile: OR=1.79; 95% CI: 1.23–2.61) and higher levels of concentration problems in children (4th quartile: OR=1.55; 95% CI: 1.02–2.33). The authors concluded that the few observed significant associations were not to be regarded as causal but had rather occurred by chance (Heinrich et al., 2010). [As indicated by the authors some significant results can be expected in the numerous analyses that have been done. Personal exposure measurement provides an objective exposure measure. However, it is unclear how well a 24hour measurement represents long term exposure which is relevant for the chronic symptoms.]

In a German nationwide population based, multi-phase, cross-sectional study of 51444 individuals, 30047 persons answered questions on how mobile phone base stations affected their health (participation rate: 59%) (Blettner et al., 2009). Health complaints were measured with the Frick symptom list consisting of 38 symptoms rated on a four-point Likert scale. Geo-coded distance to the next base station and a summary health score was available for 26039 participants. Health worries were associated with self-reported distance (OR=1.35, 95% CI 1.25–1.45), but not with objectively geo-coded distance (OR=1.00; 95% CI 0.94–1.07). For persons living within 500 m of a mobile phone base station the Frick symptom score was 0.34 (95% CI 0.32–0.37) units higher than that of the rest of the participants. Subsequently, 4150 participants living in eight urban areas were selected for an in-depth questionnaire study about health disturbances and risk perception and were asked for home measurements (Berg-Beckhoff et al., 2009). Health complaints were recorded on five different symptoms scales (see table below) and RF-EMF exposure was measured at four different locations of the participants' beds during 5 minutes each. Out of the 3526 responders 1808 persons agreed with home measurements. Finally, for the analysis of measured RF-EMF exposure and health complaints data from 1326 individuals were available. None of the scores of the five symptom scales were increased in individuals exposed to total base station radiation levels above 0.1 V/m. However, the headache score HIT-6 and the von Zerssen symptom score were higher in participants attributing adverse health effects to mobile phone base stations compared to those who did not attribute their health complaints to EMFs emitted by mobile phone base stations. [The distance analysis demonstrates that reporting bias is a problem when using self-reported distance as an exposure measure. Using geo-coded distance is not informative in terms of EMF exposure but in the in-depth study part spot measurements in the bedroom have been used, which is more informative. Although exposure misclassification is of concern with respect to longer term exposure.]

In a small German questionnaire survey with 251 participants, numerous symptoms were more prevalent in participants living within 400 m of a base station compared to a control group living further apart. Moreover, within the 400 m radius, symptoms were more prevalent in persons living within 200 m of the base station than in those living between 200 and 400 m (Eger & Jahn, 2010). Exposure levels were determined with spot measurements that are not further described. The response rate was low (23%) and correlated with distance to the base station (36% in the closest category and 14% in the farthest category) indicating the presence of selection bias. [Given the correlation between participation rate and exposure levels selection bias is a very likely explanation for the observed associations.]

In a cross-sectional study based on a stratified random sample, 3611 adults (response rate: 37%) living in 22 Dutch residential areas completed a questionnaire about non-specific physical symptoms as well as environmental and psychological characteristics (Baliatsas et al., 2011).Various significant associations between occurrence of symptoms and psychological characteristics were observed. Most importantly, after adjustment for demographic and residential characteristics, the symptom score was positively correlated to self-reported proximity to base stations and power lines but not to calculated distance between household addresses and location of base stations or power lines. [A limitation of the study is the cross-sectional design and the fact that the survey was conducted in 2006 whereas data on the locations of transmitters were obtained for the year 2008. This is expected to result in erroneous distance assignment since the base stations might have changed between 2006 and 2008. Given that the distance to a mobile phone base station is not correlated to RF-EMF exposure (Frei et al., 2010), the observed absence of an association must not be considered as evidence for an absence of effect. However, the study demonstrates that studies relying on self-estimated distance to mobile phone bases stations are likely to be prone to bias.]

Apart from wireless phone use, exposure to far-field RF-EMF was also assessed in the above mentioned Swiss cohort study on health related quality of life (Frei et al., 2012; Mohler et al., 2010; Mohler et al., 2012; Röösli, Mohler & Frei, 2010). Exposure to fixed site transmitters at the place of residency was calculated with a geospatial computation model (Bürgi et al., 2010). In addition, a model was developed and validated which combined questionnaire data with the geospatial fixed site transmitter model to assess total far field RF-EMF exposure in the everyday environment from all types of sources (e.g. WLAN, fixed site transmitters, other people's mobile phones, cordless phone base stations) (Frei et al., 2009). No consistent exposure-response pattern was observed in a cross-sectional analysis of 1375 individuals for total RF-EMF and fixed site transmitter exposure with respect to headache and von Zerssen symptom score (Frei et al., 2012). Neither self-reported sleep disturbances nor excessive daytime sleepiness was related to far-field RF-EMF exposure after adjusting for various confounding factors in 1212 individuals without shift work or sleeping pill consumption (Mohler et al., 2010). Furthermore, estimated exposure at night including indoor sources such as DECT phone base stations was not related to sleep quality. In the longitudinal analysis, exposure to environmental RF-EMF at baseline was not consistently associated with symptoms, sleep disturbances, excessive daytime sleepiness, tinnitus or headache one year later (Frei et al., 2012; Mohler et al., 2012). Similarly, an increase or decrease of far-field RF-EMF exposure between 2008 and 2009 was not accompanied with a respective change in health disturbances. A subgroup analysis of 130 participants who claimed to be electromagnetic hypersensitive or attributed symptoms to RF-EMF exposure yielded similar results (Röösli, Mohler & Frei, 2010). The authors concluded that the two observed statistical associations out of 28 risk estimates (see Table 5.1.6) were most likely due to chance given the high number of health effects and exposures that were analysed. In a nested study sleep duration and sleep efficiency were determined objectively in 119 participants wearing an actimeter during 14 nights (Mohler et al., 2012). According to a random intercept mixed regression model with an autocorrelation term of one-day lag adjusted for relevant confounders, none of the outcomes was related to total RF-EMF. Moreover, there were no associations observed for night-time EMF levels or exposure to EMFs from fixed site transmitters that were measured in the bedroom during the first 7 days of study participation. [Comments see above.]

Studies with uncertainties related to inclusion criteria

In the above mentioned cross-sectional study from Egypt, several symptoms were more prevalent in 85 inhabitants or employees of a house near an mobile phone base station compared with 80 employees considered unexposed (Abdel-Rassoul et al., 2007). [Exposure assessment is very crude and no meaningful measurements have been conducted with respect to the exposure of the study population. Recruitment process is not described and the comparison of employees (control group) with a mixed group (exposed group) is prone to bias; in particular, since no confounding was considered in the analysis. Therefore, the results are not included in the table.]

A Polish cross-sectional study addressed subjective complaints of people living near mobile phone base stations (Bortkiewicz et al., 2012). Suitable flats with a total of 1154 inhabitants from five regions of Łódź were selected for the study according to the transmitting characteristics of base stations in the vicinity. 181 men and 319 women participated and were interviewed about their demographics, occupational and environmental exposure to EMF, health conditions and subjective complaints. Electric field measurements were performed in the buildings located closest to the azimuth of the antennas and distance was obtained from the housing estate plan. Electric fields above 0.8 V/m were recorded in 12% of the flats. Electric field strength was not correlated to the distance between flats and base stations. After adjusting for age, sex, self-reported occupational ELF- and RF-EMF exposure as well as EMF-emitting household equipment, the prevalence of headache and impaired memory was related to the distance to the next base station, although the highest prevalence was not found closest to the base station but in the distance category of 101 to 150 m for headache and more than 150 m away for impaired memory. No data about the association between symptoms and measured EMF exposure were presented but the authors concluded that they did not find a correlation between the electric field strength and the frequency of subjective symptoms. [The cross-sectional design is a limitation for assessing causality and it is unclear which analyses were adjusted for possibly relevant confounding factors. Some relevant confounding factors are missing, however. Participants were selected using a uniform procedure, but it is not clear whether it ensured a random selection, and participation rates were not reported.]

Table 5.1.6. Overview on studies about non-specific symptoms and far-field RF-EMF sources					
Endpoint	**Study population**	**Exposure assessment**	**Results**		**Reference**
14 symptoms from the von Zerssen list, Pittsburgh sleep quality index (PSQI)	Cross-sectional 365 randomly selected participants living in the vicinity of mobile phone base stations Mean age: 44 y	Spot measurements in the bedroom, 3 exposure groups with aprox. cut-offs at 50^{th} and 75^{th} percentile: <0.1 mW/m² 0.1–0.5 mW/m² >0.5 mW/m²	Risk for headache, cold hands or feet, and difficulties to concentrate were increased in the highest exposure categories, remaining 11 symptoms and PSQI were not. Concerns about base stations were associated with poor sleep quality.	Logistic regression adjusted for for age, sex, region, mobile phone use, concerns about base stations	(Hutter et al., 2006)
Self-reported morning freshness/tiredness on a 100 unit visual analogue scale	Panel: 54 volunteers (21 men, 33 women) Mean age: 53 y	Modelled 24 h average H field exposure from a short-wave radio transmitter (6–22 MHz) using Maxwell equations validated with measurements	Cross-sectional analysis: 3.9 (95% CI: 1.7–6.0) unit decrease of sleep quality per mA/m. Before-after: 1.7 (95% CI: 0.1–3.4) unit increase in sleep quality per mA/m decrease.	Cross-sectional: linear median regression model adjusted for age and gender; before-after: random effects linear regression adjusted for age and gender. Participants not blinded to exposure status.	(Altpeter et al., 2006)
Migraine, headache, dizziness, SF-36	Cross-sectional Approximately 1870 children and adults from three villages in Cyprus Participation rate: 87%	Exposure from military antennae (17.6 MHz) measured in each town (1 building) using spectrum analyser: 1) 0.57 V/m (thereof 0.11 V/m from the military antenna), 2) 0.46 V/m (0.04 V/m from military antenna) 3) <0.01 V/m	Migraine, headache, dizziness, SF-36 related to RF-EMF.	Chi square and logistic regressions without adjustment. Participation rate estimated at 87%, but the actual number of participants is not reported, nor age and sex distribution. No data is provided to evaluate the comparability of the three villages. The study was initiated in response to several years of public concern. Reporting bias and nocebo cannot be excluded.	(Preece et al., 2007)

Chronic symptoms: selected items of Freiburg symptom score: headache, neurologic symptoms, cardiovascular symptoms, sleeping disorders, fatigue. Acute symptoms: selected items from von Zerssen list (headache, fatigue, concentration problems) and neurological symptoms': either tinnitus, numbness in hands or feet and eyelid twitch	Cross-sectional 329 randomly selected residents of 4 German towns 18–65 y 53% females Participation rate 30%	Personal exposure during waking hours of one day: sum of GSM 900, GSM 1800, UMTS (up- and downlink), DECT and WLAN Reference: < 0.15% of ICNIRP limit; top quartile: 0.21 to 0.58% of ICNIRP limit	No association for chronic symptoms: OR for headache:1.2 (95% CI: 0.26.4); neurological symptoms: 0.6 (95% CI: 0.1–4.2); cardiovascular symptoms: 2.4 (95% CI: 0.6–9.9); sleeping disorders: 1.1 (95% CI: 0.5–2.1); fatigue: 0.7 (95% CI: 0.3–1.8) No associations on acute symptoms.	Logistic regression adjusted for age and sex.	(Thomas et al., 2008a)
Chronic symptoms: selected items of the HBSC-survey: headache, irritation, nervousness, dizziness, fatigue, fear and sleeping problems Acute symptoms: selected items from von Zerssen list: headache, irritation, nervousness, dizziness, fatigue and concentration problems.	Cross-sectional 1484 randomly selected children and 1508 adolescents of 4 German towns 8–12 y Participation rate 52%	Personal exposure during waking hours of one day: sum of GSM 900, GSM 1800, UMTS (up- and downlink), DECT and WLAN Quartiles (in % of ICNIRP limit): children: 0.15%, 0.17%, 0.20%; adolescents: 0.15%, 0.17%, 0.21%; Sensitivity analyses using the 90th percentile as cut-off (children: 0.25-0.92%, adolescents: 0.26-0.78%)	Personal exposure and chronic symptoms: no increased risk for any symptom but OR= 0.63 (95%: CI: 0.41–0.96) for sleeping problems among children. Personal exposure and acute symptoms: 1 out of 18 risk estimates increased in children: concentration problems in the afternoon: OR=1.55 (95%: CI: 1.02–2.33); 2 out of 18 risk estimates increased in adolescents: headache in the morning: 1.50 (1.03–2.19), irritation in the afternoon: OR=1.79 (95%: CI: 1.23–2.61)	Logistic regression models adjusted for age, sex, level of education of the parents, study town and environmental worries and functional exposure approach.	(Heinrich et al., 2010; 2011; Kuhnlein et al., 2009; Thomas et al., 2008b)

38 health complaints of the Frick symptom score	Cross-sectional 26039 German residents within a panel survey carried out regularly 14–69 y Participation rate 59%.	Geocoded distance to the closest mobile phone base station < 500m vs. > 500m	Increase in Frick score < 500 m vs > 500 m: 0.34 (95% CI: 0.32– 0.37). Health worries were associated with self-reported distance (OR=1.35, 95% CI 1.25–1.45) but not with objectively geo-coded distance (OR=1.00; 95% CI 0.94–1.07).	Multiple linear regression model adjusted for age, sex, income, education, region, city inhabitants and concerns/attribution.	(Blettner et al., 2009)
5 symptom scales: sleep quality (PSQI), headache (HIT-6), symptom score (Von Zerssen list),SF-36 mental and physical	Cross-sectional 1326 individuals from 8 urban German regions 15–71 y Participation rate 44%	Sum of GSM 900, GSM 1800 and UMTS from a spot measurement in the bedroom, dichotomized at 90th percentile (i.e. > 0.1 V/m)	No associations observed with measured fields. Headache score HIT-6 and the von Zerssen symptom score higher in participants attributing adverse health effects to mobile phone base stations.	Subset of Blettner et al. 2009 invited to in-depth questionnaire about health disturbances and risk perception and home measurements. Linear regression model adjusted for age, sex, rural/urban, education level, mobile phone use, risk perception and stress.	(Berg-Beckhoff et al., 2009)
19 symptoms with a self-developed questionnaire	Cross-section: 251 residents of a German municipality Participation rate 23%	Spot measurements of mobile phone base station exposure: high (0.7–1.17 V/m) vs. low (0.18 V/m)	11 out of 19 symptoms associated with exposure (sleep disturbances, depression, cerebral affection, joint pain, infections, skin changes, circulatory disturbances, balance disturbances, impaired vision, hormonal changes, gastrointestinal disturbances.	Student's t-test. Participation rate 23% and correlated with distance to the base station (36% closest, 14% farthest). Selection bias likely.	(Eger & Jahn, 2010)
Somatization scale of the Four-Dimensional Symptom Questionnaire (4DSQ or 4DKL)	Cross sectional Random sample of 3611 adults ≥18 y Response rate 37%	Geocoded distance to the next base station	Symptom score was related to self-estimated distance but not to geocoded distance to the next base station.	Log-linear mixed-effects regression model adjusted for gender, age, education, occupational status, ethnicity, home ownership status, house type, psychological factors (perceived environmental sensitivity, lack of perceived control, problem-solving, avoidance) and either perceived proximity to base station and power lines or actual distance to power lines and base stations.	(Baliatsas et al., 2011)
Sleep disturbance score, excess daytime sleepiness, von Zerssen symptom list, Hit-6 headache scale	Cross-sectional 1375 randomly selected adults 30–60 y 58% females Baseline participation rate 37%	Total modelled RF-EMF, night time EMF,EMF from fixed site transmitters, 3 exposure groups with cut-offs at 50th and 90th percentile	1 association out of 28 risk estimates: Reduced headache score for medium fixed site transmitter exposure category.	Linear/logistic regression adjusted for numerous confounding factors such as age, sex, body mass index, stress, physical activity, smoking habits, alcohol consumption, education, marital status, degree of urbanity, nightshift work, belief in health, effects due to RF-EMF exposure, use of sleeping drugs and general, attitude towards the environment (set of confounders varies somewhat according to model and outcome).	(Frei et al., 2012; Mohler et al., 2010)

Excess daytime sleepiness, sleep disturbance score, von Zerssen symptom list, Hit-6 headache scale	Cohort study with 1 year follow-up 1122 randomly selected adults 30–60 y 60% females Follow-up participation rate 82%	Total modelled RF-EMF, night time EMF, EMF from fixed site transmitters, 3 exposure groups with cut-offs at 50th and 90th percentile	4 associations out of 46 risk estimates: Decrease of day time sleepiness for decreasing exposure during night between baseline and follow-up as well as decreasing fixed site transmitter exposure between baseline and follow-up Increased headache score for medium fixed site transmitter exposure category at baseline Decrease of von Zerssen score with decreasing fixed site transmitter exposure between baseline and follow-up in EHS individuals only.	Same as the above plus moving house between the two surveys.	(Frei et al., 2012; Mohler et al., 2012; Röösli, Mohler & Frei, 2010)
Sleep duration and sleep efficiency measured by actimetry	Cross-sectional 119 individuals 30–60 y 61% females	Total RF-EMF, night time EMF, and EMF from fixed site measured in the bedroom during one week	No effects.	Random intercept mixed regression model with an autocorrelation term of one-day lag adjusted for age, percent fulltime equivalent, bedtime, sex, body mass index, smoking status, weekday, presence of a bed partner, alcohol intake within 4 hours before going to bed, physical activity during the day, sleeping during the day, and educational level.	(Frei et al., 2012; Mohler et al., 2010; Mohler et al., 2012; Röösli, Mohler & Frei, 2010)

5.1.3.3 Occupational exposure sources

Studies with uncertainties related to inclusion criteria

In the above mentioned cross-sectional study of 35 RF sealer operators and 37 control persons from the same companies (Wilén et al., 2004) all study participants filled in a questionnaire about how frequent various non-specific symptoms occurred. Having symptoms was defined if symptoms occurred at least once a week. RF operators reported non-significantly more fatigue, headaches, warmth sensations (hands, body, arms, feet), and sleeping disorders than controls. Cumulative exposure was significantly higher for persons reporting fatigue, headache and warm hands compared to persons without such symptoms. For the other symptoms no significant differences were observed. [This study is based on a highly exposed collective with well conducted exposure measurements. However, the sample size is small, and differences in the distribution of potential confounders between RF operators and controls, or between RF operators with different levels of exposure, were not considered in the analysis. The representativeness of participating subjects cannot be assessed, given the lack of information on selection procedure and participation rates. Therefore, the results are not included in the analysis.]

5.1.4. Blood brain barrier integrity

5.1.4.1 Use of mobile phones or other RF devices operated close to the body

A Swedish cross-sectional study aimed to investigate effects of mobile and cordless phone use on the blood-brain barrier (Söderqvist, Carlberg & Hardell, 2009b; Söderqvist et al., 2012) and the blood-cerebrospinal fluid barrier (Söderqvist, Carlberg & Hardell, 2009a). From 1000 randomly selected individuals aged between 18 and 65 years and living in Örebro, 31% participated in the study, in total 314 persons. Blood samples were taken at the hospital. As a putative marker of blood-brain barrier dysfunction serum S100B was determined and as a potential marker of the blood-cerebrospinal fluid barrier dysfunction transthyretin in the blood was measured. In addition, concentration of β-trace protein was determined. Exposure to mobile and cordless phones was obtained by a written questionnaire. Serum S100B levels were not found to be related to mobile or cordless phone use, except in one small subgroup analysis where latency of UMTS use was positively correlated with S100B levels in men (p=0.01, n=31) but not in women (Söderqvist, Carlberg & Hardell, 2009b). Transthyretin levels were not related to most of the analysed exposure proxies such as mobile phone use (yes/no, considering 0, 5, or 10 years of latency) or cumulative hours of cordless or mobile phone use (Söderqvist, Carlberg & Hardell, 2009a). Time since first use of mobile phones was positively correlated to transthyretin levels in men but not in women. In women, a short term effect was reported: the shorter the time period between blood withdrawal and the most recent phone call, the higher were the transthyretin levels. However, minutes of mobile phone use on the day of giving blood was not related to transthyretin. Concentration of β-trace protein was not associated with mobile phone use, except in a subgroup analysis of participants aged 18–30 years among whom lower concentrations were related to number of hours of use. [The low participation rate and self-reported exposure data are a limitation of this study. Furthermore, the absence of a consistent exposure-response pattern for both markers, and effects confined to subgroup analyses, does not provide strong support for a causal association.]

Table 5.1.7. Overview on studies behaviour and exposure to RF-EMF sources operating close to body.

Endpoint	Study population	Exposure assessment	Results	Comments	Reference
Serum S100B concentration dichotomized at 0.10 µg/l	Cross-sectional 314 individuals randomly selected from population registries 18–65 y 58% females Participation rate 31%	Self-reported DECT and mobile phone use: type of phone, daily duration, time since first use	OR of mobile and DECT phone: 0.8 (95% CI: 0.3–2.0) 5y latency: 0.8 (95% CI: 0.3–2.0) 10y latency: 0.7 (95% CI: 0.2–2.0)	Logistic and linear regression adjusted for sex and time for giving blood	(Söderqvist, Carlberg & Hardell, 2009b)
Serum transthyretin concentrations dichotomized at 0.31 g/l	Same study as above.	Same study as above.	OR of mobile and DECT phone: 1.2 (95% CI: 0.6–2.4) 5y latency: 1.2 (95% CI: 0.6–2.5) 10y latency: 1.5 (95% CI: 0.7–3.1)	Logistic and linear regression adjusted for age and sex.	(Söderqvist, Carlberg & Hardell, 2009a)

Serum β-trace protein concentrations	Same study as above	Same study as above.	Standardized β-coefficient: Hours of wireless phone use: -0.01 (95% CI -0.12 – 0.10) Years since first use: 0.01 (95% CI -0.11 – 0.13)	Linear regression adjusted for age, sex and BMI.	(Söderqvist et al., 2012)

5.1.5. Brain electrical activity

Studies with uncertainties related to inclusion criteria

The cross-sectional study Arns et al. included also analyses of brain electrical activity, EEG (Arns et al., 2007). As mentioned above, the study recruited subjects in a way that does not allow assessment of potential selection bias. Therefore, it is only briefly described, and results are not included in the table, and are given little weight in the overall assessment. EEG measurements were compared among 100 right-handed healthy heavy mobile phone users, 100 intermediate users and 100 non-users. Participants were selected from the Brain Resource International Database. Personality characteristics of the three exposure groups were compared. The heavy user group scored higher on Extraversion (p=0.01) and on openness (not significant) as compared to the non-user group and as a consequence these factors were considered in the data analyses. The heavy user group had more delta (p=0.007 for eyes closed and 0.011 for eyes open) and theta (p=0.023) power than the naïve user group in eyes open and eyes closed situation. Beta activity did not differ between groups. During open eyes condition alpha peak frequency was higher in the naïve group compared to the intermediate group (p=0.001), but did not significantly differ from the heavy user group (p=0.106). No difference in the alpha activity between the groups was noted when the eyes were closed. [The amount of mobile phone use was obtained by multiplying the answers of various questions and not expressed in interpretable units. Recruitment process is unclear and subsequently the comparability of the groups is difficult to judge.]

Excluded studies

(Al-Khlaiwi & Meo, 2004; Navarro et al., 2003; Santini et al., 2002; 2003)

5.2 Volunteer studies

5.2.1 Cognitive performance (adults and children)

Over the last 20 years the exponential increase in mobile phone availability has given rise to questions about possible effects on users. Indeed, since a notable amount of RF EMF emitted by mobile phones is transmitted through the skull and reaches the brain, it is possible to hypothesize a physiological influence of these low level RF EMF on human cerebral activity, with a consequent potential influence on human cognitive performance. A number of studies have assessed several aspects of human cognitive and behavioural performance, such as memory and working memory, attention (divided, selective, focused), spatial and verbal recognition, vigilance, learning, decision making or perception. Each of these functions can be tested by means of different tests and tasks, managed by a computer or simply administered in a paper-and-pencil way. Usually dependent variables are measures of speed (i.e., the time needed to accomplish the requested activity) or accuracy (i.e., the number or percentage of correct responses to the task or, conversely, the number or percentage of errors or absence of response to a task).

The WHO (WHO, 1993) report on effects of RF EMF exposure reported only one study published before 1992. It was focused on changes in visual perception thresholds with 2450 MHz exposure at 5 and 10 W/m^2 (Meister et al., 1989). Changes in visual perception thresholds were reported with both power densities, but the authors themselves admitted that the study was very preliminary and replication studies would be needed to validate these findings. No studies were concerned with other effects on cognitive performance.

The present literature search resulted in 70 papers relevant for these endpoints (including three meta-analyses that will be described later). Of these, 59 completely complied with the inclusion criteria. The remaining 11 papers had uncertainties related to the inclusion criteria; these are briefly discussed at the end of the section and not included in the tables.

In most of the reported studies signals and localised exposures typical of those that occur when using mobile phones have been used. A few of the studies with base station-like exposures have applied local exposures and exposure levels that are comparable to those caused by exposure when talking with mobile phones and therefore these are included under mobile phone handset related studies.

Several studies reported in this section were primarily aimed at investigating brain neurophysiology (EEG, event-related potentials or evoked potentials, event-related synchronization/desynchronization, magnetoencephalography) or brain metabolism (positron emission tomography, functional magnetic resonance imaging), but also assessed cognitive function and performance. In this section only those endpoints will be presented, while the other endpoints are dealt with in other sections.

The tables at the end of each section summarize the results of each study and provide information about their methods. Similar and further details are included in the following text, with the exception that the use of a double-blind design, meaning that neither participant or researcher was aware of the exposure conditions, is usually not reported in the text. Comments about particularly small samples sizes are made since the smallest samples are attached with highest uncertainties provided other study details are similar. Exposure was controlled in all studies that are included in the analysis. If SAR values were provided, it is specified in both the tables and text, otherwise other exposure measures are provided, or at least output power along with other details of exposure setup.

5.2.1.1 Mobile phone handset related studies

The basic design, exposure details and results of the 59 studies included in the analysis which are related to mobile phone handset exposures are summarised in Table 5.2.1.

Studies with healthy adults

In the first study investigating the effects of microwave emissions on preparatory slow brain potentials, the authors also recorded performance in both a simple finger movement task and a complex and cognitive demanding task, the visual monitoring task, administered in a fixed order (Freude et al., 1998). The participants were 16 healthy males exposed to both real and sham conditions (for about 13 min) in the same session. The study was conducted single blind and used a counterbalanced cross-over design. The GSM 916.2 MHz signal was emitted by a GSM phone with an extended antenna and the phone was positioned against the left ear. This exposure resulted in a maximum SAR averaged over 10 g of 0.88 W/kg. The loudspeaker of the phone was switched off during the whole experiment. No significant effects were reported on performance measures.

The same group (Freude et al., 2000) two years later replicated and extended the study, by conducting two separate experiments including respectively 20 and 19 volunteers; due to artefacts in electrophysiological registration the final analyses were carried out with data from 16 participants for each group. In the first experiment participants completed a visual monitoring task, while in the latter the visual monitoring task was followed by a simple finger movement task and a two-stimulus task, administered in a fixed order. Using a single blind, counterbalanced cross-over design, the participants were exposed in the same session to both a GSM 916.2 MHz signal emitted by a phone with extended antenna placed against the left ear (SAR_{10g} = 0.88 W/kg) and to a sham condition. No significant effects were reported on performance measures.

Preece et al. (1999) were interested in the effects of a simulated mobile phone signal at 915 MHz on cognitive functioning in healthy adults. The study consisted of two training sessions and then three test sessions separated by 48 h, in which 36 healthy participants were involved. Each testing session lasted about 25-30 min and allowed assessment of some cognitive functions, by means of 10 different tasks administered in a fixed order. In each experimental session subjects were exposed unilaterally (left side of the head) to an analogue signal, a GSM-like signal at 915 MHz or sham for the whole duration of the session. The RF signals were emitted from a quarter-wave antenna mounted on a physical copy of an analogue phone which was held against the ear. The mean output power was 1 W for the analogue signal and 0.125 W for the GSM-like signal. [No information about SAR was provided.] A randomized, double-blind, three-way cross-over design was used. The authors reported a single significant effect of a reduction in choice reaction times ($p < 0.003$); this speeding up of performance was observed more strongly during analogue (gain of 14.5 ms) than digital (gain of 3.5 ms) RF exposure. No effects arose in the other nine tasks testing for other dependent variables (vigilance accuracy, memory speed and/or accuracy, attention speed and accuracy). The researchers controlled for systematic errors which might have been introduced as a result of consumption of substances and sleep habits. [No adjustment for multiple comparisons was applied to the results despite the high number of statistical tests.]

One of the first contributions in a series of studies carried out by the same research group, aimed at investigating effects of cellular phones on EEG during a visual working memory task (Krause et al., 2000a). In this study, a visual sequential letter memory task with three different working memory load conditions (i.e. levels of difficulty: 0-, 1-, and 2-back) was administered to the participants in a single-blind, counterbalanced, cross-over design. The 24 volunteers were tested under a 30-min exposure to a GSM 902 MHz signal emitted by a digital phone and 30 min to a sham exposure with about 5 min break between the conditions. The phone was positioned at the right side of head comparable to normal use position and was set to transmit at the maximum output power, which resulted in an average power of 0.25 W. No significant effects were reported on accuracy or speed measures. [SAR was not specified, beyond stating "According to the manufacturer (Nokia) the SAR was well below 2 W /kg".]

The same group carried out another study similar to the previous one, using the same exposure (C. Krause, e-mail correspondence with G. Curcio, 31.01.2013), with the only exception that the investigated output was the EEG changes during an auditory working memory task (Krause et al., 2000b). In this study, 16 participants were asked to complete an auditory verbal memory task lasting about 60 min, 30 under GSM and 30 under sham condition, in a single-blind, counterbalanced cross-over design. Also in this case, no significant effect was observed on performance.

The study previously discussed (Krause et al., 2000b) was replicated, except for using a double-blind design, exposing the left side of the head instead of the right and using a larger sample size (Krause et al., 2004). The 24 participants were asked to complete an auditory verbal memory task lasting about 60 min, of which 30 min was under real (GSM 902 MHz signal, SAR_{10g} = 0.648 W/kg) and 30 min under sham exposure. An increased mean percentage of incorrect answers was observed in real compared to sham exposure (respectively 19.1 ± 4.2 and 6.3 ± 3.1; $p < 0.001$), which was not observed in the previous study.

A subsequent study from the same research group (Krause et al., 2007) aimed to further investigate the effects of exposure to a GSM 902 MHz signal on cognitive functioning. In this study the main aims were to assess the effects of continuous wave and pulse modulated EMF on brain functioning, and the possible presence of differences between left and right side EMF exposure. Exposure setup was improved in this study with respect to blinding by applying a signal generator and linear power amplifier that fed the signals directly to the antenna of a mobile phone handset placed about 20 mm from the exposed side. The authors carried out two different experiments, each one on a sample of 36 healthy males: one with the auditory verbal memory task and one with the visual sequential letter memory task with four different memory loads. Each experiment included six exposure conditions: sham, continuous wave, and pulse modulated during both left- and right-side exposures. SAR_{10g} was 0.74 W/kg in all RF exposure conditions. The study followed a double blind, fully counterbalanced, cross-over design with the three sessions separated by a week. Each session included exposures to both sides, first one then the other, during which the participants performed the tasks. No significant effects were reported on accuracy or speed measures for either cognitive task.

In a single-blind, counterbalanced, cross-over design, Koivisto et al. (2000b), investigated the effects of mobile phone exposure on response times to a complex battery of twelve different tasks. While performing the tasks, 48 participants were exposed to a GSM 902 MHz signal and to a sham signal for 60 minutes; the two sessions were separated by 24 hours. The phone was placed against the left ear and had its loudspeaker removed to avoid acoustic cues that may reveal the exposure condition. The mean output power was set to 0.25 W. [No SAR was provided.] The results indicated an increased speed in the simple reaction time task ($p = 0.026$, reduction of 9 ms), vigilance task ($p < 0.001$, reduction of 25 ms) and mental arithmetic task ($p = 0.044$, reduction of 29 ms) during exposure, while no indication of effect of exposure was observed in the remaining tasks. Also percentage of errors in the different tasks was analysed. While the error levels were generally low, in one test a significant difference was observed. Fewer errors were made under RF exposure (2.5%) than under sham exposure (3.6%) in the vigilance task ($p = 0.022$). [No correction for multiple tests was reported.]

Haarala et al. (2003b) replicated partially by testing the same endpoints in a similar study to that of Koivisto et al. (2000b), but applied some methodological improvements. With RF signal and experimental protocol similar to the Koivisto et al.'s study, the authors extended and methodologically improved the experiment by using a double blind design, larger sample size, multicentre testing and some additional tasks. The complete battery included simple and choice reaction times, subtraction task, sentence verification task, vigilance task, and three versions of the Stroop task. The 64 participants (32 in Finland and 32 in Sweden) were exposed to a GSM 902 MHz signal (SAR_{10g} = 0.99 W/kg) and to a sham signal for about 65 minutes. The authors controlled for the temperature between skin and phone in addition to removing the earphone. No significant effects were reported on accuracy or speed measures, in any of the administered tasks.

Another study that aimed at investigating the effects of mobile phones on working memory performance was conducted by Koivisto et al. (2000a). In a single blind, counterbalanced, cross-over design, 48 participants were exposed for 30 minutes to a GSM signal (SAR_{10g} = 0.68 (Haarala et al., 2004)) and a sham signal. Also in this study the phone was positioned at the left side and the loudspeaker was removed. Performance was assessed during exposure by means of a sequential letter memory task with different working memory load (0-, 1-, 2-, and 3-back). The authors reported again a speed up of response times limited to target responses when the memory load was highest (3-back; $p < 0.05$, reduction of 36 ms) but not in the other conditions; no effects were observed on accuracy measures. [No correction for multiple comparisons was reported and with correction the reported decrease in response time would most likely not have been significant. No information is provided concerning time of day of the different exposures.]

Again, the study by Koivisto et al. (2000a) was subsequently methodologically improved by Haarala et al. (2004). Also in this case, improvements included double blind design, larger sample size, multicentre testing, more comfortable method of holding the phone, use of some additional tasks, rigorous control of the temperature between skin and phone and of the distance between phone and ear. While the mobile phone battery was used as the power source, the loudspeaker was removed. The 64 participants (32 in Finland and 32 in Sweden) were exposed to a GSM 902 MHz (SAR_{10g} = 0.99 W/kg) signal and to a sham signal for about 65 minutes in counterbalanced order in separate sessions about 24 hours apart. Under this kind of exposure the participants were asked to complete a short term memory task with varying memory load (0-, 1-, 2- and 3-back). No significant effect was observed on memory performance as a function of exposure to the GSM signal.

Haarala et al. (2003a) conducted a study on the effects of a GSM exposure on cerebral blood flow (see Section 5.2.3) during a working memory task, similar to the one used in previous studies (Koivisto et al., 2000a; Krause et al., 2000a). Fourteen healthy right-handed male volunteers participated in the study but due to missing behavioural data the final analysis was carried out on only 10 participants. Each participant was exposed to both a GSM 902 MHz signal and to a sham signal for about 45 minutes from a mobile phone placed against the left ear. Participants were exposed to both conditions at the same day [no information about the interval between the exposures was provided]. Since the exposure and behavioural testing were done during and concurrently with PET scans, it was found that PET signals increased the SAR_{10g} intensity of 0.99 W/kg by about 22% and changed the location of peak SAR by < 1 mm. Even after the removal of the loudspeaker from the mobile phone, an acoustic signal was recorded during GSM exposure; at a frequency of 16 kHz the signal was 19.3 dB higher than in the sham condition. Due to this, two pilot studies were conducted on independent participants to test whether a sound from the battery of the mobile phone or the heating during GSM exposure could reveal the exposure condition. There was no indication that the participants became aware of the exposure condition based on any of these cues. No significant effects were reported on accuracy or speed measures. [The number of participants included in the analyses was low in this study, making it less likely to detect small effects, if any. It is not clear whether including only 10 of the 14 exposed participants in the analyses influenced the designed counterbalance.]

Some years later, the same research group (Aalto et al., 2006) carried out a new study on the effects of mobile phone exposure on cerebral blood flow (see Section 5.2.3), with the aim to methodologically improve the study of Haarala et al. (Haarala et al., 2003a). In the present study, the authors employed a more sensitive experimental design removing the noise from the mobile phone by removing the battery in addition to the loudspeaker, by applying a silent external power source and by inserting an earplug in the participants' left ear against which the phone was positioned. Behavioural data on a simple working memory task (1-back task) were recorded in 12 participants during a 51-minute exposure to signals from the modified GSM mobile handset (SAR_{10g} = 0.74 W/kg) and sham signal. For this study the authors informed that the participants underwent the sham and the real exposures with an interval of 15 minutes, in counterbalanced order. As in the previous study, no effects were seen on reaction times or accuracy of responses. [The number of participants was low.]

More recently the Finnish group carried out a similar study by using high-resolution PET to measure relative cerebral metabolic rate of glucose (see Section 5.2.3) as a consequence of exposure to a GSM 902 MHz signal (Kwon et al., 2011). To control the vigilance status during the exposure, a simple visual 0-back task was administered to the 13 male participants. The whole exposure lasted 33 minutes, gave a SAR_{10g} of about 0.7 W/kg and was done following a counterbalanced paradigm [as far as possible given the odd number of participants] with an interval of at least 6 days between the two conditions. The mobile phone was modified to avoid temperature increase, by feeding the antenna with signals via a coaxial cable from a distant identical mobile phone. Furthermore, the battery and the loudspeaker of the phone used for exposure was removed. No effect of exposure was observed on reaction time and error rate of the visual task. [Also in this study the number of participants was low.]

Furthermore, Kwon et al. (2012b) also investigated the potential influence of short-term GSM handset-like 902 MHz exposure on cerebral blood flow assessed by means of PET (see Section 5.2.3). Fifteen male participants underwent four different exposure conditions (left: SAR_{10g} = 1.0 W/kg, right: 0.7 W/kg, forehead: 0.7 W/kg, and sham), each lasting for 5 minutes. This procedure was performed three times with 10-minute intervals between the exposures. The phones and the exposure system was as described in the previous study (Kwon et al., 2011). During exposure, the participants performed a simple visual vigilance task. Exposure was not found to have any influence on any measure of task performance. [The repeated exposures in the latter study would make it more likely that a potentially small effect would be detected. However, the short intervals between exposures increased the risk for carry-over effects, unless effects, if any, lasted very shortly. Also in this study the authors strived to achieve a balanced design but due to the number of participants and the number of repeated sequences of exposures, complete counterbalancing was not possible.]

Curcio et al. (2004) investigated the time-course of RF-induced effects on cognitive performance in four different tasks. Twenty volunteers (10 females and 10 males) were randomly assigned to one of two groups of which one received the exposure before and one during the testing session. All participants were exposed to a GSM 902.4 MHz signal (SAR_{10g} 0.5 W/kg) and to a sham signal, each for 45 minutes with the phone positioned 1.5 cm from the left ear. The exposure conditions were given in counterbalanced order with at least 48 hours between the conditions. Results indicated an improvement of performance speed in real exposure as indicated by decrease of simple ($p = 0.005$, reduction of 47 ms vs. sham) and choice-reaction times ($p = 0.002$, reduction of 40 ms vs. sham). Moreover, participants exposed before the testing showed a faster performance than those exposed during the testing itself ($p = 0.02$, reduction of 85 ms) indicating that a time-window seems necessary to induce cognitive effects provided that this difference was caused by the RF EMF exposure. An alternative explanation may be that the exposure situation (having the mobile phone close to the head, knowing that exposure may occur) might have influenced performance. No other effects on attention and mental arithmetic performance were observed, neither between real and sham exposure nor between different time of exposure (before, during). [No corrections for multiple comparisons were applied and these effects were observed on very small groups. No information was provided whether the tests were performed on the same time of day.]

Effects of mobile phone exposure on performance during an auditory task were investigated by Hamblin et al. (2004). Twelve volunteers were exposed to a GSM 895 MHz signal and a sham signal, each for a total duration of 60 minutes and in different session with an interval of 1 week. In the real exposure condition a GSM phone was set to transmit at maximum output power, with a mean value of 0.25 W. The exposure setup minimized the risk of auditory cues and heat from the mobile phone to reveal the exposure condition used and this was confirmed in a pilot test. The task required participants to answer as fast as possible to target auditory stimuli by pressing the mouse button. A statistically significant difference in reaction times between real and sham conditions was observed, indicating a reduced performance speed under real exposure ($p = 0.024$, increase of 53 ms), while no effect was seen on accuracy measures. [The study was performed single blind, the sample size was low and information about time of day for the different exposure conditions was not provided. The SAR of the commercial mobile phone used was indicated to be 0.87 W/kg, but the provided source of information might not have been reliable. In the following study (Hamblin et al., 2006) an identical exposure setup seemed to be used with a significantly lower SAR.]

An extension of the previous study was subsequently performed (Hamblin et al., 2006). In this case, the authors aimed at overcoming some of the common methodological limitations by using a double blind design, providing results based on a large sample size, including sensory and cognitive performance endpoints. Furthermore, the authors informed that the design was both randomized and counterbalanced. To this extent, 120 volunteers were exposed 1 week apart to a sham/sham and to a sham/active session during which they were exposed to a GSM signal at 895 MHz (SAR_{10g} 0.11 W/kg) over temporal regions: half of the participants received exposure to the left side of the head, with the other half received right side exposure. As in the previous study the exposure setup minimized the risk of auditory cues and heat from the mobile phone to reveal the exposure condition used. In both sessions they were asked to complete an auditory and a visual odd-ball paradigm. Bonferroni correction was applied only to EEG data, while the whole experiment was designed to detect differences of 1/4 of a standard deviation (80% power). No significant differences were reported on reaction times at visual and auditory tasks.

Possible effects of exposure to GSM signals on episodic memory were investigated by means of an encoding-retrieval paradigm (Hinrichs & Heinze, 2004). Following a double-blind, counterbalanced cross-over design, 12 participants were exposed for 30 minutes to a 1840 MHz GSM-like electromagnetic field and to a sham condition with the exposure conditions on separate days at the same time of day. The phone was placed close to the left ear of the participants. The electronics of the phone were removed to prevent thermal sensation. After 20 minutes of exposure, the phase of encoding of words visually presented on a computer screen started and lasted for the remaining period of exposure. Subsequently, in the retrieval phase and after a 15-minute break performance measures were collected. No significant differences were reported for any indices of performance speed and accuracy. [The low number of participants should be noted.]

Besset et al. (2005) attempted to emulate real-life exposure by using a more complex and long protocol of exposure. In a double blind study 55 volunteers were assigned (matched for age, gender and general intelligence as measured by IQ) to an EMF-on or EMF-off group. Each of the volunteers participated in the study lasting 45 days (3 of baseline, 28 of exposure period, 14 of recovery): during this period they were exposed 2 hours per day (18.00–20.00), 5 days per week (from Monday to Friday). Each participant was asked to hold a GSM 900 MHz phone with the preferred hand over the preferred ear for the whole 2-hour period. SAR_{10g} was measured to be 0.54 W/kg, the average value for four mobile phone positions, left/right side contact/tilt position, and with the phone transmitting at maximum output power similar to exposures during the blinded tests (R. de Seze e-mail correspondence with G. Curcio, 12.06.2014). Cognitive assessment by means of 22 different tasks covering four broad categories (information processing speed, attention capacity, memory and executive function) were carried out at 4 time points: one during baseline (day 2), two during the exposure period (day 17 and 32, pooled in the statistical analyses) and one in the recovery phase (day 45). No effect of exposure was reported. [Since the cognitive assessments were done 13 hours after the previous exposure (testing from 9 to 11 in the morning), including a whole sleep night, any potential acute and short-term effects would not have been detected. Thus, even if there was no indication of any lasting effects of the exposure, short-term effects cannot be excluded and no comparison can be done with other studies.]

A study that also tried to emulate real life exposure, attempting to test the possible cumulative effects of brief (15 min) repeated exposures limited to one day, was carried out by Curcio et al. (2008). Using an exposure setting identical to the previous work (Curcio et al., 2004), here 24 volunteers were exposed to a GSM at 902.4 MHz with a SAR_{10g} of 0.5 W/kg, or a sham signal. Each exposure lasted 15 minutes and was repeated 3 times for each condition during a period of 85 minutes. The two conditions were on separate days at the same time of day. The order of conditions was counterbalanced across the participants. Immediately after each 15-minute exposure, participants were asked to complete two psychomotor tasks, lasting 10 min. Neither measures of speed nor indices of accuracy showed a statistically significant difference as a result of exposure to the EMF.

Schmid et al. (2005) investigated the effects of the exposure to a third generation mobile phone (UMTS) on visual perception as assessed by means of four different perceptual-attention tasks. In a randomized crossover design, the tasks were administered under three different exposure conditions: “High” (SAR_{10g} = 0.37 W/kg) or “Low” (SAR_{10g} = 0.037 W/kg) exposure conditions at 1970 MHz and sham condition (50 dB below Low exposure), each lasting for about 50–60 minutes (C. Sauter, e-mail correspondence with G. Curcio, 14.03.2013). For each of the 58 participants, all exposures and tests were on the same day. The exposure was managed by a generator producing randomly sham exposure or a UMTS generic signal that was emitted by helical antennas mounted at the left side of a headset such that mobile phone handset exposure was mimicked. Bonferroni correction was applied because of multiple testing (significance criterion: $p < 0.004$). No significant differences (p-values: 0.19–0.98) were reported on indices of both speed and accuracy in any of the four tasks used.

The same authors (Unterlechner et al., 2008) carried out a study with the same exposure system and conditions assessing the effects of UMTS Low and High exposure compared to sham condition, on attention and reaction time tasks. The tasks were administered to 40 volunteers during 90-min exposure sessions (C. Sauter, e-mail correspondence with G. Curcio, 14.03.2013). The exposure conditions were chosen pseudo-randomly by software. Applying crossover design, for each participant the exposure conditions were administered at separate days with 10 – 12 days intervals and always at the same time of day. Also in this case, no significant differences were reported on indices of both speed and accuracy in any of the four tasks used.

A different approach to the study of mobile phone-related effects on cognitive functions was provided by Eliyahu et al. (Eliyahu et al., 2006). They attempted to establish a link between the exposure of a particular brain region and cognitive functions associated with the specific area. To this extent, four tasks were used on the basis of their hemispheric specificity: verbal recognition task (activating left side), spatial recognition task (activating right side) and two spatial compatibility tasks (activating the left or right side depending on stimuli characteristics). These tasks were administered to 36 participants under exposure on the left-side and right-side to a GSM 890.2 MHz signal and under a sham condition. The mean output power was set to 0.25 W. Each exposure condition was performed in two 60-minute sessions separated with a 5-minute break. Exposure conditions, sessions and hand used for responding were included as factors in the analyses. No main effect of exposure was observed for any of the tasks. In one of the four tasks (spatial recognition) an interaction was observed between exposure, session (first and second) and hand used, for response time ($p = 0.037$). Response times were lower in the second than in the first session for all conditions except for left hand responses to left side exposure, where response times increased. Therefore, a further analysis was done for left-hand response times compared to the combined results for right side and sham exposures, revealing that the increase from first to the second session was significant ($p = 0.02$). For the other three tasks, no significant main effects of exposure or interactions were found. [No correction for multiple comparisons was applied. The paper provides no indication that the additional analyses only for left hand responses was planned a priori.]

Some years later, the same group (Luria et al., 2009) aimed at replicating and extending the study by Eliyahu et al. (2006). They assigned 48 participants to three different groups: left-side and right-side exposure to GSM 890.2 MHz signals (SAR = 0.54–1.09 W/kg) and sham exposure. Each of them was exposed to the signal in 12 consecutive blocks separated with a few seconds, for about 60 min in total. During this period they completed the only task that in the previous study appeared to be sensitive to RF exposure, i.e. the spatial working memory test. For response time as well as for accuracy, the results showed no significant main effect of exposure and no significant interaction between groups (with different exposures), blocks (time) and hand used for response. However, there was a trend toward longer reaction times under left-side exposure. This brought the authors to average right-side and sham exposures considering them as a single condition and run further analyses. In these analyses, the planned comparisons showed longer reaction times in the group exposed at left side in the first ($p < 0.05$; 146 ms) and the second block ($p < 0.05$; 139 ms longer) for responses with the right hand. No differences were significant for left hand responses. [Although the authors informed that the results provided above were not significant when Bonferroni post-hoc criteria were applied, they did conclude about an effect of exposure. In addition to a relatively high likelihood that the positive findings happened by chance, the findings in the study deviated from those in the first one by Eliyahu et al. (2006). Only Eliyahu et al. found a time dependent difference in response times between exposure conditions, and the suggested effects were for left side responses in the first study, and for right-sided in the second one. The interpretation of the latter study is also hampered because no pre-exposure response data was provided and no demographic information about the two groups were provided. In this study, as well as the previous one (Eliyahu et al., 2006), the participants were not able distinguish the RF and the sham exposures, indicating that the blinding was successful even though both studies were conducted single blind.]

Keetley et al. (2006) aimed at investigating the effect of exposure to a GSM 900 MHz signal on neuropsychological performance at eight different validated tasks administered in counterbalanced order, providing 18 dependent variables. The cognitive tasks were administered to a sample of 120 volunteers who were exposed to a GSM signal (phone set to transmit at the mean output power 0.23 W; [no SAR provided]) and to a sham one (phone set on stand-by). During exposures the phones was placed next to the left ear. Since the phone emitted a “just-perceptible buzzing sound” when transmitting at full power (even though the loudspeaker was removed), the phone was covered with soundproofing material, and heat insulation between the phone and the head was applied to prevent the participants from sensing the difference in temperature in the two conditions. The exposures lasted 90 minutes, while the tests started after 30 minutes of exposure. Comparing real and sham exposure, the data indicated mixed results, with an unexpected impairment of simple- and choice-reaction times (respectively $p = 0.005$ and $p = 0.011$), verbal memory (Rey’s Audio Visual Learning Test; $0.005 < p < 0.043$) and of sustained attention (Trial Making Task A; $p = 0.019$), and a hypothesized improvement of task switching/divided attention function as measured by Trail Making Task B ($p = 0.02$) and Trail Making Task difference ($p = 0.004$). No other tests indicated any effect of exposure. [In the statistical analysis, the authors did not apply any correction for multiple comparisons, but adjusted for different known covariates to specific tasks (i.e., age, education, gender). Moreover, a question could be raised whether stand-by mode can be used as a sham condition. During the 30-minute sham exposure period, the participants were most likely exposed to no or at most one burst of signal lasting only for approximately 2 seconds (Mild, Andersen & Pedersen, 2012). Therefore, the contrast to the RF EMF exposure condition with a continuous signal lasting for 30 minutes is in any case significant. While it was informed that the sham and RF EMF sessions were performed separately, a week apart, no information is provided concerning the time of the day for the tests.]

Terao et al. (2006) investigated motor preparation performance assessed by means of visuo-motor choice reaction time and movement time. In this task participants were asked to react to visual stimuli and received information about the type of answer a few seconds before the presentation of stimuli. Sixteen volunteers were asked to complete such tasks both before and after an exposure to an 800 MHz pulse modulated mobile phone EMF and to a sham signal in two sessions, each lasting 30 minutes, and separated by at least 7 days. Under the antenna and 30 mm below the scull SAR averaged over 10 g was about 0.05 W/kg according to results from tests with a phantom. To avoid sound cues that could reveal the exposure condition, the audio circuitry of the handset was disabled. In this double blind, randomized and counterbalanced, crossover study, no effects were observed on measures of accuracy, reaction time or speed as a function of exposure to the EMF.

Terao et al. (2007) carried out a companion study with the same exposure and experimental characteristics to the previous one (Terao et al., 2006). In the present study the effects of 30-min exposure to mobile phone on saccades (quick and simultaneous movements of both eyes in the same direction, aimed to assure visual fixation) recorded with electrodes (electrooculography) in three different tasks before and after the 30-minute exposure. For each task the mean saccade latency, peak velocity and amplitude of the first saccade were calculated. In addition reaction times to visual signals (visual detection task) were investigated. Ten volunteers participated. Also in this case no effects of exposure were reported.

In 2010, the same research group (Okano et al., 2010) performed another study aimed at investigating the possible effect on the inhibitory control of saccades. In a double blind, counterbalanced, crossover study, 10 participants were exposed to a pulse modulated mobile phone signal at 1950 MHz and a sham condition. Except for the exposure frequency used, the exposure characteristics and setup, including prevention of acoustic cues, were the same as in the two previous studies (Terao et al., 2006; Terao et al., 2007). Before and after the exposure each volunteer completed four different oculomotor paradigms and latencies, reaction times and speeds of the eye movements were analysed. In addition frequency of prosaccades towards the target was recorded in one task (antisaccade), frequency of saccades in response to cue in another (cued saccade), and in yet another task (one of two overlap saccade tasks) frequency of saccades prematurely initiated were recorded. Again, no statistically significant differences between RF and sham exposures were reported as a function of exposure.

Russo et al. (2006), aiming at overcoming some methodological limitations (small sample size, single blind design, type of exposure signal) of several previous studies (Curcio et al., 2004; Edelstyn & Oldershaw, 2002; Koivisto et al., 2000b; Krause et al., 2000b; Lee et al., 2003; Preece et al., 1999; Smythe & Costall, 2003) to investigate the effect of GSM and continuous wave exposures on attention. In total 168 participated. They were randomly assigned to the two types of signals (84 to each) and all were exposed to a sham condition. The exposures were emitted by a mobile phone positioned so that the antenna touched or was close to the left side of head for half of the participants (n=42) for each type of exposure and similar for right side exposure (n=42). Both signals were at 888 MHz and resulted in SAR_{10g} of about 1.4 W/kg [averaging volume was provided by the same group (Cinel et al., 2007) in another study]. The study was performed double-blind and the order of RF EMF exposure and sham exposure was counterbalanced across participants. For each participant the two sessions were at the same time of day and separated with a week. Attention was assessed by simple- and choice-reaction time task, subtraction task and vigilance task during exposures. No effects of exposure were reported on measures of speed or accuracy.

Cinel et al. (2007) carried out a study which was a partial replication of the one by Maier et al. (2004) (see below) by employing a similar auditory threshold task, but with a much larger sample of participants (n=168). The task was performed before and after 40 minutes of exposure. Exactly the same exposures and allocation of participants were used as in the study by Russo et al. (2006): a GSM signal (84 participants), a continuous wave signal (84 participants), and a sham signal (the whole sample), and for each group with the right ear exposed for half of the participants (n=42) and the left ear for the other half (n=42). Both RF EMF conditions applied 888 MHz and the maximum SAR averaged over 10 g was 1.4 W/kg. The design was a double-blind, counterbalanced crossover study with the two exposure sessions about a week apart. The tasks were performed immediately before and after the 40-minutes exposure. No effects of exposure were reported on accuracy measures.

A concurrent but independent study to the one by Russo et al. (2006) was carried out by Haarala et al. (2007), with a similar set-up and methodology. Here all 36 participants were exposed to three different conditions: a pulsed (GSM), a continuous wave (both at 902 MHz and with SAR_{10g} = 0.74 W/kg), and a sham signal for 45 minutes. The conditions were in separate sessions at the same time of day a week apart and in counterbalanced order. In this study, the mobile phone battery was disconnected and the phone received signals from an external generator while placed in the normal use position. Exposures were directed to both the left (45 min) and right side of the head (45 min) in the same session. Dependent variables were attention, assessed in four tasks, and short-term memory, assessed in four tasks with different memory loads. Also, a control study was carried out without exposure equipment to assess the possible influence of equipment itself on performance. No effects of exposure, including left side versus right side exposures, were reported on measures of speed or accuracy.

Fritzer et al. (2007) conducted a single-blind study investigating short- and long-term effects of RF EMF exposure on sleep and cognitive functions. To this extent, the 20 participants were exposed for six nights (8 h per night); 10 to a GSM signal at 900 MHz generated by three antennas positioned at 30 cm from the head vertex (SAR_{1g} = 0.875 W/kg); 10 to a sham signal. The groups were randomized and matched with respect to age and educational level. Before the first exposure night there was one habituation night and then one night for collecting baseline data. Before and after the baseline night and the first and second nights of exposure, participants were submitted to a cognitive evaluation, consisting of seven different tasks assessing attention, learning and memory. No effects on neuropsychological tests were reported as a function of exposure to the field. [No adjustments for multiple comparisons were made. This experiment was based on a between group comparison, and for each group only a small sample was studied. However, based on data from the literature, a statistical power of 0.80 was estimated for an effect size larger than 1.32.]

Irlenbusch et al. (2007) aimed at investigating the effect of a 30-min exposure to GSM 902.4 MHz and sham signals on visual discrimination threshold. To this extent, a spiral antenna, connected to a phone and to an amplifier was positioned in front of the subjects at a distance of 0.8 m so that a measurable SAR (0.007 W/kg averaged over 1 g) would be reached at the level of the retina. The RF EMF and sham sessions were performed at the same time of day, separated by two weeks, and preceded with a 30-min sham exposure as an adaptation period. In a single blind, randomized, crossover study, 33 participants were asked to detect luminance thresholds. No effects on performance were reported as a function of exposure to RF.

In a study by Regel et al. (2007a) both waking EEG and cognitive performance were assessed. Twenty-four participants were exposed for 30 min to three different conditions: pulsed GSM, continuous wave, and sham signal. The two RF signals used the same frequency (900 MHz) and SAR (1 W/kg averaged over 10 g). EMF was emitted by a planar patch antenna placed 11.5 cm from the left side of the head. In a double-blind, randomized, counterbalanced cross-over design attention and working memory were assessed in five different tasks all presented in two consecutive sessions (one in the first 15 min and one in the second 15 min) in fixed order during each exposure. The repetition of the tasks was done to include the time factor in the analyses. Each exposure was applied at separate days, but at the same time of day for each participant. The results indicated significant effects of exposure on reaction speed in the 2-back and the 3-back tasks ($p < 0.002$) with slower responses to 2-back tasks during both RF exposures (sham: 1.95 1/s, CW: 1.87 1/s, PM: 1.81 1/s), and to 3-back tasks during PM exposure only (sham: 1.70 1/s, CW: 1.70 1/s, PM: 1.58 1/s). For accuracy, analyses showed a significant interaction between exposure condition and session for the 3-back task ($p < 0.004$). Here diagrams suggested that this interaction was due to higher accuracy for the pulsed exposure in the second session (last haft of exposure) but not in the first session. These effects were confirmed also after adjusting for multiple comparisons with Bonferroni-like correction. No significant differences were observed when applying the simplest (1-back) condition for working memory or for any of the two tasks used to test attention. [No post hoc analyses were provided to test which of the RF exposures conditions that differed significantly from sham (if any)]

A subsequent study by the same group (Regel et al., 2007b) aimed at investigating possible dose dependent effects of 900 MHz GSM signals on attention and memory tasks. Here signals at two different levels (SARs averaged over 10 g: 0.2 W/kg and 5 W/kg) were compared to sham exposure. Also in this study the signals were emitted by a planar antenna positioned 11.5 cm from the left ear. Fifteen participants were exposed for 30 min, and simultaneously they completed a simple reaction time task, a two-choice reaction time task and an n-back task with varying cognitive load (1-, 2- and 3-back). This study followed a double-blind, randomized, cross-over design with each exposure condition at separate nights before sleep. As in the previous study (Regel et al., 2007a), the series of tests was presented twice during the 30- min exposure period. Results showed a significant reduction in response speed only to the 1-back task with increasing field intensity ($p < 0.004$). Accuracy was not found to change with exposure intensity in any task. In the first half part of the 2-back task accuracy was higher under the 0.2 W/kg exposure (96%) compared to sham (93%) ($p < 0.003$), but no such significant difference was observed for the 5 W/kg exposure. The two reaction time tasks and the 2- and 3-back tasks did not reach statistical significance on speed measures, and the reaction time tasks and the 1- and 3-back tasks did not differ between exposures on measures of accuracy. The two positive findings were significant also after Bonferroni-like correction was applied to the statistical analyses.

In this same track and in the same laboratory, some years later Schmid et al. (2012a; 2012b) carried out two studies to better evaluate the effects of different signal features on sleep macrostructure, sleep EEG, and cognitive performance. Also in these studies RF exposures were emitted by a planar antenna positioned 11.5 cm from the left side of the head. In the first study (Schmid et al., 2012a) 30 participants were exposed to two differently modulated GSM signals (14 and 217 Hz, respectively) both with SAR 2.0 W/kg and to a sham condition for 30 min before going to sleep. Acoustic noise was used to mask any sound that might accompany the RF EMF exposure. The order of exposures was randomized and “partially balanced”. For each participant the three exposure sessions were given at the same time of night before sleep at weekly intervals. During the exposure period, they were asked to complete two tasks for assessing attention and three for working-memory performance, with all tasks performed in fixed order in the first session (15 min) and the second session (15 min) of each exposure period. By applying a Bonferroni-like adjustment for multiple tests, the significance level was $p < 0.015$ for individual tests. There were significant differences between exposure conditions for speed in the 1-back ($p = 0.002$) and the 2-back tasks ($p = 0.0008$) while “post hoc analyses showed that there was only a trend level decrease in speed in the first session of the 2-back task for the 217-Hz pulse modulated condition” ($p = 0.035$). A decrease in accuracy was limited to the first of the two 3-back task sessions under 14 Hz pulse-modulated condition ($p = 0.013$). There was no evidence that any of the exposures influenced attention. [Since there was a lack of consistency in results, a clear exposure-related effect on cognition could not be concluded.]

In the second study (Schmid et al., 2012b) 25 volunteers were exposed weekly to three different conditions for 30 minutes prior to a full night’s sleep: a 900 MHz RF signal pulse-modulated at 2 Hz (SAR = 2 W/kg), a 2 Hz pulsed magnetic field (peak magnetic flux density = 0.70 mT), and a sham condition, with random order of exposure conditions. As in the previous study, during the exposure period each participant was asked to complete attention and working-memory tasks twice: in the first 15 minutes and in the last 15 minutes. No significant effects were observed for RF EMF exposure. Out of five tasks, only the simple reaction time task showed an increased reaction speed under magnetic field exposure ($p < 0.015$) [0.015 was the significance level after adjustment for multiple tests]. Also in this case it could not be concluded that there was a clear exposure-related effect on cognition.

The first study that directly compared the possible effects of GSM and UMTS signals was done by Kleinlogel et al. (2008b). Following a double-blind, randomized, crossover design 15 participants were exposed to four different conditions: sham, 900 MHz GSM base station-like signal (SAR: 1.0 W/kg), 1950 MHz UMTS handset-like signal “Low” (0.1 W/kg) and 1950 MHz UMTS handset-like signal “High” (1.0 W/kg). The RF EMF signals were emitted by a small antenna mounted at the normal mobile phone position. The exposure conditions were in sessions a week apart and at the same time of day. Under the exposure to each of these conditions, participants completed a continuous performance test, a measure of selective and sustained attention, between 6.5 and 17.5 min of exposure. No significant effects were observed for reaction time. A borderline significant difference between the exposure conditions was reported on performance errors ($p = 0.05$) for one of two testing conditions. A post hoc analysis showed that the participants committed more errors under UMTS “Low” exposure (1.60) than under Sham (0.73; post hoc $p = 0.02$). It should be stressed that no similar trends were observed with UMTS “High” or GSM conditions, both with 10 times higher SAR. [Such borderline effect would disappear if any type of correction for multiple comparisons was applied.]

Sauter et al. (2011) aimed to compare possible cognitive effects of 900 MHz GSM and 1966 MHz WCDMA (3G UMTS) signals (both with SAR approaching 2 W/kg). In this 9-day study (7 h 15 min per day), exposure was directed to the head from a head-worn antenna. Of the 9 days, 3 were dedicated to GSM, 3 to WCDMA/3G UMTS, and 3 to sham conditions; consecutive experimental days were separated by two weeks. The exposure conditions were randomly assigned and in counterbalanced order. As cognitive outcomes three tasks measuring attention (one of them with two types of stimuli analysed separately and in total) and two working memory (0-back and 2-back) were administered twice every experimental day during the exposure. For all tests, reaction time as well as correct responses were analysed separately for each time of day. Out of a high number of comparisons, a few resulted in p-values slightly below 0.05. No effect of exposure reached statistical significance after the application of Bonferroni correction for multiple comparisons (significance criterion $p < 0.0014$).

In a study mainly aimed at investigating EEG features during an auditory oddball paradigm, Stefanics et al. (2008) exposed 36 participants to a UMTS ($SAR_{1g} = 1.75$ W/kg) and sham signal for 20 minutes. The signals were generated by an UMTS mobile phone connected to a patch antenna placed next to the right ear. The exposure conditions were provided in separate sessions a week apart and in counterbalanced order. Performance (accuracy index) was tested before and after exposure. No statistically significant effects of exposure were reported.

To test the impact of TETRA signals on cognitive function of emergency service personnel who regularly use TETRA handsets, Riddervold et al. (2010) tested 53 emergency service workers. Each of them was exposed to both a 420 MHz TETRA signal and a sham signal for 45 minutes. The signals were generated by a TETRA handset connected to an external antenna placed in the “cheek position”. To achieve a high exposure scenario, the phone was running in a 1-minute sequence with the TETRA transmitter (talk button) on for 54 seconds and off for 6 seconds. SAR_{10g} was determined to be 2.0 W/kg. The two sessions were at least 24 hours apart and the order was randomized. [Complete counterbalancing could not be achieved because 3 of the 56 included participants did not complete both sessions]. In each session they completed four different tasks assessing vigilance, attention, working memory and executive functioning reaction times. No effects of exposure were reported as a consequence of TETRA exposure. [The authors had calculated that 55 participants were required to ensure a 95% likelihood of detecting an effect if it existed.]

Curcio et al. (2012) investigated the effects of GSM 902.4 MHz mobile phone emissions (SAR_{10g} = 0.5 W/kg at 2 cm depth) on measures of attention as assessed by a somatosensory Go-No Go task, where the participants were instructed to react to double electric pulses, but not to single pulses. Cognitive data was acquired in 12 healthy volunteers, both before and after a 45-minute exposure to a GSM handset or sham condition. The mobile phone was placed 1.5 cm from the right ear so that no heating of the phone could be sensed. The two exposure conditions were separated by a week and the order was counterbalanced. No exposure-related effects on cognitive performance, accuracy or reaction times, were reported. [The low number of participants reduced the ability to detect potentially small effects of exposure.]

Studies with healthy adults with uncertainties related to the inclusion criteria

In this paragraph are some studies that failed to meet all of the inclusion criteria, presenting some methodological or statistical weaknesses. More specifically, in some cases no SAR and/or output power was stated (Lee et al., 2003; Mortazavi et al., 2012; Smythe & Costall, 2003), no clear control of exposure or of blinding procedure was provided (Croft et al., 2002; Edelstyn & Oldershaw, 2002; Hladky et al., 1999; Papageorgiou et al., 2004), or no direct statistical comparison between sham and real conditions were done (Eibert et al., 1997; Vecchio et al., 2012a). Therefore they are only briefly discussed and are not tabulated, and will not be given any weight in the overall assessment.

Eibert et al. (1997) investigated whether a GSM mobile phone signal may influence cognitive performance, specifically attention and verbal learning. Using a between-subjects design, 52 participants were exposed to a GSM mobile phone signal (900 MHz), positioned at a distance of approximately 45 cm from the head with an E-field of approximately 40 V/m. Exposure was intermittent across a 30-minute period (10 minutes off, 10 minutes on, 10 minutes off). No effects of exposure were reported. [The results of the study cannot be further evaluated since no numerical data were provided, including no results from the statistical analysis beyond the statement of no significant differences].

Hladky et al. (1999) used a commercial 900 MHz GSM mobile phone to expose 20 healthy participants. Each of them underwent three different sessions of visual evoked potentials and performance recordings, separated by 14 days (sham, mobile phone, “normal wireless telephone”) during which both a subtraction test and a test of switching attention were administered before and during a 6-min exposure to the signal. The exposure was done while the participants held the phone with their own hand to the right ear. No significant differences were reported on both indices of performance and errors. [Not all performance measures were provided and no clear blinding was reported. It was stated that a peak output power of 1.5 W was prioritised, but there is no information about how the exposure level was controlled. No information was provided about the wireless phone.]

Edelstyn and Oldershaw (2002) aimed at investigating the effects of exposure to a mobile phone on attention assessed by means of four attention capacity tasks and two processing speed tasks, administered in counterbalanced order across participants. In a single blind study, 38 participants were randomly assigned to the exposed (GSM) or sham exposed group. The whole exposure lasted 30 minutes. An improvement of immediate verbal memory capacity, immediate visuospatial memory capacity, and sustained attention were reported. [No correction for multiple testing was reported. No procedures were reported to control for potential cues (acoustic of thermal) which is in particular important when holding the mobile phone in the hand and towards the ear. Furthermore, no information was provided about the mobile phone used and whether or how the output power was controlled. The provided SAR referred to a newspaper article.]

Croft et al. (2002) investigated the influence of mobile phone exposure on neural functioning including performance of an auditory discrimination task. In a single blind, counterbalanced, cross-over design, 24 participants were exposed to a 900 MHz GSM signal and a sham signal. During the 20-minutes exposure, participants were asked to complete the discrimination task four times. Of note, the exposure was delivered between parietal and occipital lobes, with the phone placed 5 cm radial to the head and the estimated average power was 3–4 mW. [However no measurements of the actual emissions during experiments were performed.] No significant differences were observed on both reaction times and errors.

Lee and colleagues (Lee et al., 2003) carried out an experiment to assess the effect of exposure to a 1900 MHz GMS mobile phone on attention measures in a single-blind study. Seventy-eight volunteers were randomly assigned to the experimental or control group, and the total exposure lasted 25 minutes. Participants were asked to complete two tasks: the first assessing sustained attention, and the other selective and switched attention. Results showed an improvement of reaction times in the sustained attention task between the two groups, while no significant differences were found for the other tests. [It was informed that the mobile phone was switched on or off, but no information was provided about the mode of operation the phone (stand-by mode or talking mode) or about the control of exposure level.]

A study by Smythe and Costall (2003) aimed at investigating the possible effects of RF EMF exposure. Sixty-two healthy volunteers (33 males and 29 females) were randomly assigned to one of three test conditions: no phone, sham condition, and GSM 1800 MHz signal. The exposure lasted for a total of 15 minutes, during which they completed a semantic and spatial memory task, followed by a distraction task. Their recall was tested immediately after the end of the exposure (short-term memory) and 8 days later (long-term memory). Males exposed to an active phone made fewer spatial errors than those exposed to an inactive phone in the short-term session while there was no significant difference for the semantic memory. No effects of exposure were observed in females. [No information was provided that indicate that the level of exposure was controlled, although a SAR value was provided for the commercial mobile phone used, but again, with no information about how it was obtained. Furthermore, blinding could easily have been compromised since the participants held the operating phone with their hands.]

Maier et al. (2004) published a pilot study on perceptual-attention processes of auditory function. Here, using a weaker field than in the other study and an exposure period of 50 min, they exposed 11 individuals to the Order Threshold task. Also in this study performance preceding and following exposure phase was compared. Results showed worse performance after the exposure to the GSM 900 MHz signal in nine of the 11 participants (~82%); statistical analysis indicated a significant decline of group performance. [The GSM phone was placed 4 cm from left ear, but beyond providing information about the phone used, there was no information about applied output power or recorded exposure level.]

In an attempt to verify the gender specific results obtained by Smythe and Costall (2003) (discussed above), Papageorgiou et al. (2004) exposed their participants to RF fields (900 MHz) emitted by a dipole antenna close to the ear and to a sham signal for 45 min each. The emitting antenna was driven by a signal generator and the RF fields were described as "similar to that emitted by mobile phones". The mean output power was reported to be 64 mW [SAR not provided]. Under the exposure, the subjects were asked to complete a short task (Wechsler test) to assess memory performance. The effect on memory performance of RF exposure compared to the condition without exposure was analysed separately for the two genders and showed no significant differences. [Since no information about blinding was provided, in addition to the uncertainty about the exposure level, no weight can be attached to this study.]

In a similar study, with the same exposures as used by Papageorgiou et al. (2004), the same group (Papageorgiou et al., 2006) exposed 19 participants for 45 minutes while they performed an auditory working memory task with a low frequency auditory warning signal before one memory task and with a high frequency signal before another memory task. No effects on performance were observed. [Also in this study no information was provided that indicated that the participants were blinded to the exposure conditions.]

In a study mainly aimed at studying event-related desynchronization of EEG alpha rhythms, Vecchio et al. (2012a) administered a visual Go-No Go task. In a double blind, cross-over study 11 participants were exposed for 45 min to a 900 MHz GSM (SAR = 0.5 W/kg) and sham condition. Results showed that only in the GSM exposure condition reaction times to the Go stimuli were significantly faster after exposure than before it. [No statistical analysis was performed to compare results from GSM and sham sessions, since only separate analyses were carried out on GSM and sham conditions. Therefore, no conclusion can be drawn based on these results.]

Mortazavi et al. (2012) exposed 160 university students in a single blind study in which each participant underwent both GSM and sham conditions. The mobile phone was continuously receiving a call from another phone that was transmitting a steady level of noise (S.M.J. Mortazavi, e-mail correspondence with G. Curcio, 19.05.2013), and thus no control for the exposure level was done. In the sham condition, the phone was in stand-by mode. Exposure lasted 10 min and performance was assessed before and after the exposure, by means of a visual reaction time task. The authors claimed to be interested to assess acute and chronic effects, the latter by creating three groups of different frequency of use (low, moderate, frequent). Results showed a significant decrease of reaction times after GSM compared to sham exposure, independent of frequency of use. [No explanation of the control of exposure level was given; therefore no weight can be attached to this study.]Studies including children and adolescents

Preece et al. (2005) carried out a provocation study on children with the aim to replicate their previous results on adults (Preece et al., 1999). Participants were tested after the full consent of both parents, and in general particular attention was paid to ethical issues. In this study the cognitive dimensions of attention and memory were studied by means of the same tasks used in the previous study. The participants (18 children: nine boys, nine girls; age range: 10.2–12.2 years) underwent three experimental conditions: sham, GSM-900 exposure at "Full power" (mean average output power 0.25 W giving a SAR of 0.28 W/kg) and "Low power" (output power = 0.025 W). The conditions were at consecutive days and with the order randomized-With a few exceptions the tests were performed at approximately the same time of day. During exposure the phone was positioned against the left ear. The audio transducer of the phone was removed to avoid acoustic cues. Of the 22 outcomes, the simple reaction time task was closest to reaching statistical significance ($p = 0.02$), but after Bonferroni correction for multiple comparisons (with criterion for statistical significance: $\alpha = 0.0023$) this effect disappeared. No other endpoint resulted in p-values less than 0.05 when the EMF (both Full and Low power) and sham conditions were compared.

Another study was aimed at investigating the effects of mobile phone exposure on cognitive performance in 32 children (10–14 years old) (Haarala et al., 2005). Based on previous studies (Koivisto et al., 2000b; Krause et al., 2000b), four different tasks were selected for assessing attention-vigilance and four tasks with different complexity for assessing memory under the exposure to a 902 MHz GSM signal (SAR10g = 0.99 W/kg) and sham at consecutive days at the same time of day and with order of conditions counterbalanced. Also in this study the phone was placed against the left ear, while the loudspeaker of the phone was removed to reduce the sound generations, the phone was placed in a case and measurements of temperatures indicated that no difference could be sensed between the real and the sham exposure. No statistically significant differences between GSM and sham exposures were observed on both speed and accuracy measures of cognitive functioning.

Leung et al. (2011) also investigated the differential effects of RF EMF emitted by mobile phones of second (2G: GSM, 894.6 MHz, SAR10g = 0.7 W/kg) and third generation (3G: UMTS, 1900 MHz, SAR10g = 1.7 W/kg) on three groups of participants: 41 adolescents (13–15 years), 42 young adults and 20 elderly. Each participant was exposed to three exposure conditions (sham, 2G, 3G) in sessions separated by at least 4 days and with the same timing. Order of exposure conditions as well as side of exposure was randomly assigned and partially counterbalanced across participants. For 2G exposure the signals were emitted by a test phone, while for the 3G exposure the signals were fed to and emitted by a monopole antenna that were incorporated in a dummy 3G phone. The mobile phones were placed in the ordinary use position during exposure. In each session an auditory 3-stimulus oddball paradigm and an n-back task at varying cognitive load (1-, 2-, 3-back) were administered. The authors balanced the difficulty of the tasks according to participants' performance that accounted for individual differences in cognitive ability. Accuracy and reaction time were analysed for both tasks. The only significant effect was observed on accuracy in the n-back task, where participants did better under sham than the 3G condition ($p = 0.04$); post hoc analysis showed that this effect was significant in the adolescents' group ($p = 0.002$). [No correction for multiple comparisons was applied. The participants were not able to distinguish between sham and the RF EMF exposure conditions.]

Studies including patients and IEI-EMF volunteers

Jech et al. (2001) investigated the cognitive effects of mobile phone exposure in a sample of 22 patients with narcolepsy-cataplexy, all (but five) treated with different drugs or a mix of drugs. They were allowed to sleep for 20 min prior to the start of the study, and subsequently were exposed to a 900 MHz GSM signal (SAR10g = 0.06 W/kg) and a sham signal for 45 min on consecutive days in counterbalanced order. The mobile phone did not touch the head and was thermally insulated. In each session after 5 min of exposure they were asked to complete a visual odd-ball paradigm for the evaluation of vigilance and sustained attention.

During the task, EEG and evoked response potentials were also recorded (see Section 5.2.2). Statistical analyses controlled for the type of stimulus (target, standard), the order of examination days and the interested hemifield of sight. A facilitating trend was observed on reaction times. More specifically, under exposure to RF signal, participants' performance was faster than under sham condition, with an average reduction of 20 ms ($p < 0.05$ after Bonferroni's correction). No effects of exposure were observed for missing or wrong behavioural responses. Potential influence of other factors, such as sleep prior to the session and coffee intake were tested without finding any significant difference between days with sham and RF EMF exposures. [The author stated that it was impossible to hear whether the mobile phone was on. It is not explained how this was assessed.]

In a single-blind experiment, Wilén et al. (2006) tested 20 individuals with IEI-EMF who reported symptoms in connection with mobile phones only. These participants were also compared with a matched control group of 20 volunteers. All were exposed for 30 min to a 900 MHz GSM signal (SAR10g 0.8 W/kg) and a sham condition at separate days in random order. The signals, generated by a mobile phone, were emitted by an antenna positioned 8.5 cm from the right ear. Each participant was tested at the same time of day in both sessions and the order of sessions was randomized. Exposure occurred in a room that had been specially designed to ensure a low background level of power frequency and radiofrequency fields. They were asked to complete an arousal/vigilance task and a short-term memory task before and after the exposures. No significant effects of exposure were found on the memory function by applying repeated-measures analysis of variance. [No numerical results of the cognitive tests were provided. However, the authors informed that Bonferroni correction for multiple outcomes was applied.]

Wiholm et al. (2009) investigated the effects of a prolonged exposure (2.5 h) on spatial memory of 23 individuals attributing symptoms to mobile phone exposure and 19 non-symptomatic individuals. Performance of the cognitive task was assessed before and after exposure to GSM 884 MHz (SAR10g = 1.4 W/kg) and sham signals. The signals were emitted by a patch antenna placed some centimetres from the left side of the head. Testing occurred in unshielded rooms, but assessment of low frequency and radiofrequency fields revealed low background levels (< 0.05 V/m) (Hillert et al., 2008). In this crossover designed study, the different exposure sessions were on separate days but always at the same time of day. No differences were observed between the groups or the exposure conditions for test performed before exposure, whereas results showed a significant reduction of distance travelled in the virtual maze (an improved performance) after real exposure compared to sham ($p < 0.026$); this effect was only evident in the symptomatic group indicated by an RF by group effect ($p < 0.025$). [No correction for multiple comparisons was applied to the analyses.]

Table 5.2.1. Mobile phone handset related studies assessing cognitive performance effects

Endpoint and Participants[a]	Exposure[b]	Response	Comment	Reference
Studies with healthy adults				
Visual monitoring task (VMT) and simple finger movement task assessed during exposure 16 male volunteers (21–26 years)	GSM phone with extended antenna against the left ear, 916.2 MHz SAR_{10g} 0.88 W/kg About 13 min[c]	No effect of exposure.	Single-blind, counterbalanced for order of conditions, cross-over. Short duration of exposure. For event related potentials see Section 5.2.2.1.	Freude et al. (1998)
1st experiment:, VMT assessed during exposure 16 male volunteers (21–30 years, mean 25.3 years) 2nd experiment: VMT, simple finger movement task and two-stimulus task assessed during exposure 16 male volunteers (21–26 years, mean 25.7 years)	GSM phone with extended antenna against the left ear, 916.2 MHz SAR_{10g} 0.88 W/kg About 6 min in the first and about 15 min in the second experiment[c]	No effect of exposure.	Single-blind, counterbalanced for order of conditions, cross-over. Short duration of exposure. For event related potentials see Section 5.2.2.1.	Freude et al. (2000)

Attention and memory performance in ten different tasks assessed during exposure 36 volunteers (20–60 years; 18 males, 18 females)	Mobile phone copy with quarter-wave antenna against right ear Simulated GSM signal, 915 MHz, mean output power 0.125 W Analogue signal, 915 MHz, output power about 1 W About 25–30 min	Decrease in choice reaction times (stronger in the analogue condition). No effect of exposure on other endpoints.	Double-blind, randomized, three-way cross-over. Substantial difference in emitted power between the two RF EMF conditions. No correction for multiple tests.	Preece et al. (1999)
Visual sequential letter memory task performance with varying working memory load (0-,1-, and 2-back) assessed during exposure 24 volunteers (20–30 years; 12 males, 12 females)	GSM phone over the right posterior temporal region, 902 MHz Mean output power 0.25 W, SAR < 2 W/kg according to data from manufacturer About 30 min	No effect of exposure.	Single-blind, counterbalanced for order of conditions, cross-over. For event related potentials see Section 5.2.2.1.	Krause et al. (2000a)
Auditory verbal memory task performance in encoding and retrieval activity assessed during exposure 16 volunteers (mean 23.2 years; 8 males, 8 females)	GSM phone over the right posterior temporal region, 902 MHz Mean output power 0.25 W, SAR < 2 W/kg according to data from manufacturer 30 min	No effect of exposure.	Single-blind, counterbalanced for order of conditions, cross-over. For event related potentials see Section 5.2.2.1.	Krause et al. (2000b)
Auditory verbal memory task performance in encoding and retrieval activity assessed during exposure 24 volunteers (24.3 ± 8.1 years; 12 males, 12 females)	GSM phone over the left posterior temporal region and antenna 4 cm from head, 902 MHz SAR_{10g} 0.648 W/kg About 30 min	Increased mean percentage of incorrect answers.	Replication of Krause et al. (2000b). Double-blind, counterbalanced for order of conditions, cross-over. Larger sample than in previous study. Task blocks order partially balanced. For event related potentials see Section 5.2.2.1.	Krause et al. (2004)
1st experiment: auditory verbs memory task performance assessed during exposure 36 male volunteers (23.6 ± 2.38 years) 2nd experiment: visual sequential letter memory task with varying working memory load (0-,1-, 2- and 3-back) assessed during exposure 36 male volunteers (22.9 ± 2.4 years)	GSM phone antenna ~20 mm from right and left posterior temporal region, GSM-like and CW signals, 902 MHz SAR_{10g} 0.74 W/kg About 27 min for each side (auditory task) and about 40 min for each side (visual task)	No effect of exposure.	Partial replication of Krause et al. (2000a; b; 2004). Double-blind, fully counterbalanced, cross-over. Larger sample than in previous studies. Evaluation of possible hemispheric effects. For event related potentials see Section 5.2.2.1.	Krause et al. (2007)
Reaction time performance assessed in 12 tasks during exposure 48 volunteers (18–49 years; 24 males, 24 females)	GSM phone against left ear with antenna ~ 4 cm from head, 902 MHz Average output power 0.25 W About 60 min	Decrease of response times in simple reaction time and vigilance tasks; decrease of time needed in a mental arithmetic task. Fewer errors in vigilance task. No effect of exposure on other endpoints.	Single-blind, counterbalanced for order of conditions, cross-over. Task order not completely balanced. No correction for multiple comparisons.	Koivisto et al. (2000b)

Cognitive functioning assessed in 9 tasks during exposure 64 volunteers: (Finland: 20–42 years;16 males, 16 females; Sweden: 20–42 years; 16 males, 16 females)	GSM phone against left ear, 902 MHz SAR_{1g} 0.88 W/kg, peak value 1.2 W/kg About 65 min	No effect of exposure.	Partial replication of Koivisto et al. (2000b) Double blind, counterbalanced for order of conditions, cross-over. Large sample, multicentre testing.	Haarala et al. (2003b)
Sequential letter memory task with varying working memory load (0-, 1-, 2-, and 3-back) assessed during exposure 48 volunteers (18–34 years; 24 males, 24 females)	GSM phone against left ear with antenna ~ 4 cm from head, 902 MHz Average output power 0.25 W, SAR 0.68 W/kg, peak value 1.39 (Haarala et al., 2004) About 30 min	Decrease of response times with highest memory load for “targets”; no effect for non-targets. No effect of exposure on other endpoints.	Single-blind, counterbalanced for order of conditions, cross-over. Real and sham conditions in a same session. Task versions order completely balanced. No correction for multiple comparisons.	Koivisto et al. (2000a)
Memory tasks with varying working memory load (0-,1-, 2- and 3-back) assessed during exposure 64 volunteers: (Finland: 20–42 years; 16 males, 16 females; Sweden: 20–42 years; 16 males, 16 females)	GSM phone against left ear, 902 MHz SAR_{10g} 0.99 W/kg, peak value 2.07 W/kg About 65 min	No effect of exposure.	Partial replication of Koivisto et al. (2000a) Double blind, counterbalanced for order of conditions, cross-over. Large sample, multicentre testing.	Haarala et al. (2004)
Memory task with varying working memory load (0-, 1-, 2- and 3-back) assessed during exposure 10 male volunteers (21–35 years; 25.36 ± 4.57 years)	GSM phone against left ear, 902 MHz SAR_{10g} 0.99 W/kg About 45 min	No effect of exposure.	Double-blind, counterbalanced, cross-over. Small sample. For brain blood flow see Section 5.2.3.	Haarala et al. (2003a)
Simple working memory (1-back task) assessed during exposure 12 male right-handed volunteers (25 ± 2 years)	GSM phone against left ear, 902 MHz SAR_{10g} 0.74 W/kg About 51 min	No effect of exposure.	Improvement of Haarala et al. (2003a). Double-blind, counterbalanced, cross-over. Small sample. For brain blood flow see Section 5.2.3.	Aalto et al. (2006)
Simple visual vigilance task (0-back task) assessed during exposure 13 male right-handed volunteers (21–29 years; 24.5 ± 2.8 years)	GSM phone against right ear, 902.4 MHz SAR_{10g} 0.7 W/kg 33 min	No effect of exposure.	Double-blind, nearly counterbalanced, cross-over. Small sample. For brain glucose metabolism see Section 5.2.3.	Kwon et al. (2011)
Visual vigilance task (match-to sample 0-back task) assessed during exposure 15 male volunteers (20–28 years)[d]	GSM phone against right ear, left ear and forehead, 902.4 MHz SAR_{10g} 0.7 W/kg (right exposure), 1.0 W/kg (left exposure), 0.7 W/kg (front exposure) 5 min, 3 times for each condition	No effect of exposure.	Double blind, nearly counterbalanced, cross-over. Different exposure in the same session day. For brain regional blood flow see Section 5.2.3.	Kwon et al. (2012b)

Vigilance, attention and mental arithmetic functioning (acoustic simple- and choice-reaction tasks, visual search task, and arithmetic descending subtraction task), assessed as speed and accuracy before, during (50% of volunteers) or after exposure (50% of volunteers) 20 volunteers (22–31 years; 10 males, 10 females).	GSM phone 1.5 cm from left ear, 902.4 MHz SAR_{10g} 0.5 W/kg 45 min	Decrease of both simple- and choice-reaction times. No effect of exposure in other tasks.	Double-blind, counterbalanced. Tasks during and after exposure in different groups, randomly formed. Tasks administered in the same (fixed) order. Small groups. No corrections for multiple comparisons.	Curcio et al. (2004)
Sustained attention task (auditory odd-ball paradigm), assessed during exposure 12 right-handed volunteers (19–44 years; 4 males, 8 females)	GSM phone over the right temporal region, 894.6 MHz Mean output power 0.25 W 60 min	Increase of reaction time. No effect on accuracy.	Single-blind, counterbalanced, cross-over. Small groups. No corrections for multiple comparisons. For event related potentials see Section 5.2.2.1.	Hamblin et al. (2004)
Sustained attention tasks (auditory and visual odd-ball paradigm) assessed after exposure 120 volunteers (18–69 years; 46 males, 74 females)	GSM phone against right (n=60) or left (n=60) ear, 895 MHz SAR_{10g} 0.11 W/kg 30 min	No effect of exposure.	Double-blind, pseudo-randomized, counterbalanced, cross-over. Exposure on both sides of the head. Different cognitive tasks administered in pseudo-random counterbalanced design over each session. Large sample. Statistical power of 0.80. For event related potentials see Section 5.2.2.1.	Hamblin et al. (2006)
Episodic memory task (encoding-retrieval paradigm), exposure during encoding phase 12 right-handed volunteers (18–30 years; 2 males, 10 females)	Mobile phone antenna emitting GSM like signal over left ear, 1870 MHz SAR_{10g} 0.61 W/kg 30 min	No effect of exposure.	Double-blind, counterbalanced, cross-over design. Small group. No corrections for multiple comparisons. Small sample. For magnetic brain activity see Section 5.2.2.	Hinrichs & Heinze (2004)
Information processing speed, attention capacity memory and executive function assessed by 22 tasks 4 times in a 45-day period 55 volunteers (EMF-on:18–40 years, 24 ± 0.8 years;14 males, 14 females; EMF-off: 18–33 years, 24.6 ± 0.7 years; 13 males, 14 females)	GSM phone against the preferred ear, 900 MHz SAR_{10g} 0.54 W/kg 120 min/day 5 d/week in 4 weeks	No effect of exposure.	Double-blind. Participants assigned to groups after matching for age, gender and IQ. Cognitive assessment done 13 hours after the previous exposure. Emulation of a real-life situation.	Besset et al. (2005)
Psychomotor performance (acoustic simple reaction time task and sequential finger tapping task) assessed after exposure 24 volunteers (19–36 years; 12 males, 12 females)	GSM phone 1.5 cm from right ear, 902.40 MHz SAR_{10g} 0.5 W/kg 15 min x 3 times	No effect of exposure.	Double-blind, counterbalanced. Tasks administered in the same (fixed) order. No corrections for multiple comparisons.	Curcio et al. (2008)

Visual perception (Critical Flicker and Fusion Frequency Test, Visual Pursuit Test, Tachistoscopic Traffic Test Mannheim, and Contrast Sensitivity Threshold) assessed during exposure 58 volunteers (20–40 years; 29 males, 29 females)	UMTS generic signal emitted by helical antenna close to left side of the head, 1970 MHz SAR_{10g} 0.037, 0.37 W/kg ~ 60 min	No effect of exposure.	Double-blind, randomized, crossover. Participants exposed to High, Low and Sham exposure in the same day. Perceptual tests administered in the same (fixed) order. Bonferroni adjustment for multiple tests (significance criterion: $p < 0.004$).	Schmid et al. (2005)
Attention (simple-reaction time, vigilance and determination tasks, and Flicker and Fusion Frequency test) assessed during exposure 40 volunteers (21–30 years; 20 males, 20 females)	UMTS generic signal emitted by a helical antenna close to left side of the head, 1970 MHz SAR_{10g} 0.037, 0.37 W/kg 90 min	No effect of exposure.	Double-blind, pseudo-randomized, crossover. Tests and exposure conditions presented pseudo-randomly. Bonferroni adjustment for multiple tests.	Unterlechner et al. (2008)
Spatial and verbal recognition tasks, two spatial compatibility tasks assessed during exposure 36 right-handed male volunteers (19–27 years)	GSM phone over right and left ears, 890.2 MHz Average output power 0.25 W Two ~ 60 min exposures separated with 5 min break for each exposure condition.	Increase in reaction time with left side exposure and left hand responses when compared to combined results for sham and right side exposures, limited to one task out of four.	Single-blind, counterbalanced, cross-over. Hand of response considered as factor. No correction for multiple comparisons. For discrimination see Section 5.2.4.	Eliyahu et al. (2006)
Working memory assessed by spatial task during exposure 48 right-handed male volunteers (age not provided)	GSM phone over right and left ears, 890.2 MHz SAR 0.54–1.09 W/kg About 50-60 min	No effect of exposure.	Partial replication of Eliyahu et al. (2006). Single-blind; right-, left-side and sham exposures in different groups, randomly formed. Bonferroni correction for post-hoc analysis. For discrimination see Section 5.2.4.	Luria et al. (2009)
Neuropsychological performance (8 tasks testing: learning, memory, attention, language, decision making, perception) assessed during exposure 120 volunteers (18–/0 years; 58 males, 62 females)	GSM phone against left ear with antenna 1.5 ± 0.5 cm from head, 900 MHz Mean output power 0.23 W About 90 min	Impairment of simple- and choice-reaction times, of verbal memory task and of sustained attention task. Improvement of task switching/divided attention. No effect of exposure in other tasks.	Double-blind, counterbalanced, cross-over. Pilot study to control for detection of field based on noise and/or heating. Large sample. MP set on stand-by during sham exposure. Use of different covariates for specific tasks. No correction for multiple comparisons.	Keetley et al. (2006)
Motor preparation (visuo-motor choice reaction time, movement time and accuracy) assessed before and after exposure 16 volunteers (23–52 years; 9 males, 7 females)	Pulsed EMF signal emitted by mobile phone over right ear, 800 MHz; 20 ms time division multiple access frame, 6.7 ms time slots 30 mm under the scull: SAR_{10g} 0.05 ± 0.02 W/kg 30 min	No effect of exposure.	Double-blind, randomized, counterbalanced crossover. Subjects held the phone with their own hand. No correction for multiple tests.	Terao et al. (2006)

3 saccade tasks (eye movement latency, speed, amplitude and task accuracy) and perceptual-attention performance assessed by reaction time to visual detection task before and after exposure 10 volunteers (23–52 years; 4 males, 6 females)	Pulsed EMF signal emitted by mobile phone over right ear, 800 MHz; 20 ms time division multiple access frame, 6.7 ms time slots 30 mm under the scull: SAR_{10g} 0.05 ± 0.02 W/kg 30 min	No effect of exposure.	Double-blind, randomized, counterbalanced crossover. Subjects held the phone with their own hand. Small sample. No correction for multiple tests.	Terao et al. (2007)
Inhibitory cortical performance assessed by 4 oculomotor paradigms (eye movement latency, speed, amplitude, task accuracy of and partly frequency of saccades) before and after exposure 10 volunteers (24–47 years; 3 males, 7 females)	Pulsed EMF signal emitted by mobile phone over left ear, 1950 MHz; 20 ms time division multiple access frame, 6.7 ms time slots Mean output power 250 mW 30 min	No effect of exposure.	Double-blind, randomized, counterbalanced crossover. Small sample. No correction for multiple tests.	Okano et al. (2010)
Attention (simple- and choice-reaction time task, subtraction task and vigilant task) assessed during exposure 168 volunteers (17–41 years; 69 males, 99 females) half exposed to GSM and half to CW signal	GMS and CW signal emitted by a phone over right (n = 42) or left (n=42) ear, 888 MHz SAR_{10g} 1.4 W/kg ~ 35-40 min per side	No effect of exposure, including no difference between results with GSM PM and CW exposure.	Double-blind, participants randomly assigned to type of EMF exposure, counterbalanced and crossover for order of EMF and sham for each EMF conditions. Assessment of effect on both left and right side. For symptoms see Cinel et al. (2008) in Section 5.2.4.	Russo et al. (2006)
Perceptual-attention (auditory order threshold task) assessed before and after exposure 168 volunteers (18–42 years; 54 males, 114 females) half exposed to GSM and half to CW signal	GSM and CW signals emitted by a phone over right (n=42) or left (n=42) ear, 888 MHz SAR_{10g} 1.4 W/kg 40 min per side	No effect of exposure.	Partial replication of Maier et al. (2004). Double-blind, counterbalanced, crossover. Assessment of effect on both left and right side. For symptoms see Cinel et al. (2008) in Section 5.2.4.	Cincel et al. (2007)
Attention (simple reaction times, 10-choice reaction time, subtraction, verification and vigilance tasks) and short term memory tasks with varying load (0-,1-,2- and 3-back) assessed during exposure 36 male volunteers (23.81 ± 2.44 years)	Pulsed and CW signal emitted by GSM phone against right or left ear, 902 MHz SAR_{10g} 0.74 W/kg, peak 1.18 W/kg ~ 45 min per side	No effect of exposure, including no difference between results with GSM PM and CW exposure.	Double blind, counterbalanced, crossover. Assessment of effect on both left and right side.	Haarala et al. (2007)
Seven tests evaluating attention, learning and memory assessed before and after exposure RF EMF: 10 male volunteers (22–36 years) Sham: 10 male volunteers (23-37 years)	GSM signal emitted by 3 antennas 30 cm from the vertex of the head, 900 MHz, SAR_{1g} 0.875 W/kg 8 h x 6 nights	No effect of exposure.	Single-blind, randomized, between-participants comparison. Tasks administered in the same (fixed) order. Small groups, but statistical power of 0.80 estimated for effect size larger than 1.32. No adjustment for multiple comparisons.	Fritzer et al. (2007)
Perceptual performance assessed by visual discrimination threshold under exposure 33 volunteers (19–27 years; 21 males, 12 females)	GSM signal emitted by spiral antenna connected to a phone positioned 0.8 m in front of subject, 902.4 MHz SAR_{1g} 0.007 W/kg in retina 30 min	No effect of exposure.	Single-blind, randomized, crossover. Experimental control for circadian rhythms.	Irlenbusch et al. (2007)

Attention (simple- and choice-reaction times tasks) and working memory (n-back task) assessed during exposure 24 male volunteers (19–25 years)	GSM PM and CW signal emitted by planar patch antennas 115 mm from head at left side, 900 MHz SAR_{10g} 1 W/kg 30 min	Reduced reaction speed in the two working memory tasks (2- and 3-back) mainly with PM); increased accuracy in the one working memory task (3-back) for PM in last part of exposure. No effect of exposure on working memory in the 1-back task and on attention.	Double-blind, randomized, counterbalanced cross-over design. Tasks administered in fixed order. Adjustment for multiple endpoints (Bonferroni-like). For sleep EEG see Section 5.2.2.3.	Regel et al. (2007a)
Attention (simple- and choice-reaction times tasks) and working memory (n-back task) assessed during exposure 15 male volunteers (20–6 years)	GSM signal emitted by planar antennas 115 mm from left ear[e], 900 MHz SAR_{10g} 0.2, 5 W/kg 30 min	Dose-dependent reduced reaction speed for one working memory task (1-back). No effects on speed in other tasks. No dose-dependent effect on accuracy, increased accuracy in the first part of exposure to 0.2 W/kg for one working memory task (2-back). No other effects on accuracy.	Double-blind, randomized, cross-over design. Tasks administered in fixed order. Adjustment for multiple endpoints (Bonferroni-like). For sleep EEG see Section 5.2.2.3.	Regel et al. (2007b)
Attention (simple reaction time task, 2-choice reaction time task) and memory (1-, 2-, 3-back tasks) assessed during exposure 30 male volunteers (20–26 years)[d]	PM signal emitted by planar antenna 115 mm from left side of head, 900 MHz PM at 14 Hz with pulse width 2.3 ms, and at 217 Hz with pulse width 0.577 ms, respectively SAR_{10g} 2 W/kg 30 min	No effect with 217 Hz modulation. Decreased accuracy with 3-back memory task only with 14 Hz in the first part of exposure. No effect of exposure in other tasks.	Double-blind, randomized, partially balanced, cross-over. Tasks administered in fixed order. Adjustment for multiple endpoints (Bonferroni-like). For sleep EEG see Section 5.2.2.3; for subjective endpoints see Section 5.2.4; for cardiovascular system see Section 9.2.	Schmid et al. (2012a)
Attention (simple reaction time task, 2-choice reaction time task), and memory (1-, 2-, 3-back tasks), assessed during exposure 25 male volunteers (20–26 years)	PM RF signal emitted by patch antenna 115 mm from left side of head, 900 MHz PM at 2 Hz SAR 2 W/kg Pulsed magnetic field from Helmholtz coils at both sides of head, pulse frequency 2 Hz Peak magnetic flux density 0.70 mT 30 min	PM RF exposure: no effects. Pulsed magnetic fields: improved speed in one attention task; no effects in other tasks.	Double-blind, randomized, cross-over. For sleep EEG see Section 5.2.2.3; for subjective endpoints see Section 5.2.4; for cardiovascular system see Section 9.2. Tasks administered in fixed order. Adjustment for multiple endpoints (Bonferroni-like).	Schmid et al. (2012b)

Attention assessed by continuous performance test during exposure 15 male volunteers (20–35 years)	GSM base station-like signal emitted by broadband antenna against the left ear, 900 MHz SAR_{10g} 1.0 W/kg UMTS handset-like signal, 1950 MHz SAR_{10g} 0.1, 1.0 W/kg Both 30 min	No effects on reaction time, Increased errors in UMTS lowest level in one of two task conditions.	Double-blind, randomized, cross-over. Tasks administered in fixed order. No adjustment for multiple test. For event related potentials see Section 5.2.2.1; for awake EEG and symptoms see Kleinlogel et al. (2008a) in Sections 5.2.2.2 and 5.2.4.	Kleinlogel et al. (2008b)
Attention (divided attention, vigilance task, and selective attention) and working memory (0- and 2-back tasks) assessed during exposure 30 male volunteers (18–30 years)	Head mounted antenna emitting GSM signal, 900 MHz or UMTS signal, 1966 MHz SAR_{10g} 2 W/kg About 7 h 15 min per day, each condition on 3 days	No effect of exposure.	Double-blind, counterbalanced, randomized, cross-over. Bonferroni adjustment for multiple tests (significance criterion: $p < 0.0014$).	Sauter et al. (2011)
Attention assessed by auditory oddball paradigm before and after exposure 36 volunteers (19–28 years; 16 males, 20 females)	Signals from UMTS mobile phone emitted by patch antenna over right ear, [frequency not specified] SAR_{1g} 0.39 (1.75 W/kg in brain 30 mm from the surface) 20 min	No effect of exposure.	Double-blind, counterbalanced, cross-over. For event related potentials see Section 5.2.2.1; for auditory system see Section .	Stefanics et al. (2008)
Vigilance, attention, working memory and executive functioning (Reaction Times, Corsi Span test, Digit Span test and Traill Making Test-B) assessed during exposure 53 emergency service males (25–49 years)	TETRA handset against left side of the head, 420 MHz SAR_{10g} 2.0 W/kg 45 min	No effects of exposure.	Double blind, randomized, cross-over design. Statistical power with 55 volunteers was estimated to be 95%. For subjective endpoints see Section 5.2.4.	Riddervold et al. (2010)
Attention assessed by somatosensory Go-No Go task before and after exposure 12 male volunteers (19–25 years)	GSM phone 1.5 cm from right ear, 902.40 MHz SAR_{10g} at 2 cm depth 0.5 W/kg 45 min	No effect of exposure.	Double blind, counterbalanced, cross-over. Small sample. No correction for multiple comparisons. For blood oxygen dependent response see Section 5.2.3.	Curcio et al. (2012)
Studies including children and adolescents				
Attention and memory performance in 10 different tasks, assessed during exposure 18 children (10.2–12.2 years; 9 boys, 9 girls)	GSM phone against left ear, 902 MHz Average output power 0.25 W giving brain maximum SAR 0.28 W/kg, and 0.025 W ~ 30-35 min	No effect of exposure.	Double-blind, randomized, three-way cross-over. Substantial difference in emitted power between the two conditions. Bonferroni correction for multiple tests. Tasks administered in the same (fixed) order.	Preece et al. (2005)

Attention-vigilance and memory performance in eight tasks, assessed during exposure 32 children (10–14 years; 16 boys, 16 girls)	GSM phone against left ear, 902 MHz SAR_{10g} 0.99 W/kg ~ 50 min	No effect of exposure.	Double-blind, counterbalanced, cross-over. Incomplete balancing of tasks order. Experimental control of possible auditory or thermal cues from mobile phone. For detection see Section 5.2.4.	Haarala et al. (2005)
Sensory processing and working memory (auditory 3-stimulus oddball task and n-back task at varying cognitive load) assessed during exposure 41 adolescents (13–15 years; 21 males, 20 females) 42 young adults (19–40 years; 21 males, 21 females) 20 elderly (55–70 years; 10 males, 10 females)[d]	GSM (2G) handset against left and right ear, 894.6 MHz SAR_{10g} 0.7 W/kg UMTS (3G) standard handset against left and right ear, 1900 MHz SAR_{10g} 1.7 W/kg ~ 55 min	Reduced accuracy in n-back under 3G exposure, more evident in adolescents. No effect of 2G exposure.	Double-blind, randomized, partially counterbalanced, cross-over. No correction for multiple comparisons. For event related potentials see Section 5.2.2.1.	Leung et al. (2011)
Studies including patients or IEI-EMF individuals				
Sustained attention task (visual odd-ball paradigm), assessed during exposure 22 patients with narcolepsy-cataplexy (48 ± 11.7 years; 9 males, 13 females)	GSM signal emitted by a phone close to the right ear, 900 MHz SAR_{10g} 0.06 W/kg 45 min	Decrease in reaction times. No effects on missing or wrong behavioural responses.	Double-blind, counterbalanced, cross-over. Bonferroni corrections for multiple comparisons. All patients (but five) were treated with different drugs. For event related potentials see Section 5.2.2.1.	Jech et al. (2001)
Arousal/vigilance (critical flicker fusion threshold) and short-term memory (modified version of Sternberg test) assessed during exposure 20 volunteers with IEI-EMF (32–64 years, 45.4 ± 9.6 years; 16 males, 4 females) 20 healthy controls (29–65 years, 44.9 ± 10.5 years; 16 males, 4 females)	Signals from GSM test mobile phone emitted by a base station antenna 8.5 cm from right side of the head, 900 MHz SAR_{10g} 0.8 W/kg 30 min	No effects of exposure.	Single-blind, randomized, cross-over. Low background exposure levels. For subjective endpoints see Section 5.2.4; for autonomic nervous system see Section 9.2.1.	Wilén et al. (2006)
Spatial memory and learning by Virtual Morris Water Task assessed before and after exposure 23 volunteers with IEI-EMF (28.8 ± 7 years; 9 males, 14 females) 19 healthy controls (29.4 ± 6 years; 12 males, 7 females)	GSM signal emitted by "patch antenna on left side of the head", 884 MHz SAR_{10g} 1.4 W/kg 150 min	Improvement in performance in IEI-EMF group. No effect of exposure in controls.	Double-blind, cross-over design. Incomplete balancing of conditions sequence. Low background exposure levels. No correction for multiple comparisons. For sleep EEG see Lowden et al. (2011) in Section 5.2.2.3; for subjective endpoints see Hillert et al. (2008) in Section 5.2.4.	Wiholm et al. (2009)

Abbreviations: 2G: second-generation wireless telephone technology; 3G: third-generation wireless telephone technology; CW: continuous wave; EEG: Electroencephalogram; GSM: Global System For Mobile Communication; IEI-EMF: Idiopathic environmental intolerance attributed to EMF; PM: pulse modulated; TETRA: Terrestrial Trunked Radio; UMTS: The Universal Mobile Telecommunications System; VMT: visual monitoring task.

[a] If not otherwise stated, only healthy volunteers participated. The maximal number of volunteers participating in analyses is provided.

[b] SAR with relevant averaging volume (e.g. SAR_{10g}) is specified if included in the paper.

[c] Duration of exposure is estimated on the basis of info provided in the paper.

[d] In some analyses a lower number of participants were included.

5.2.1.2 Mobile phone base station related studies

The basic design and results of the six studies included in the analysis which related to mobile phone base station exposures are summarised in Table 5.2.2. Two of these studies assessed healthy adults only and one assessed children and adolescents. Three other studies included a sample of participants with IEI-EMF.

Studies with healthy adults

A study regarding perceptual-attention processes of auditory function was carried out by Maier et al. (2004). It was published after a pilot study conducted the same year that is reported in the “Studies not included in the analysis”. They exposed 33 individuals to a discrimination task (order threshold task), a test requiring participants to determine whether two successive stimuli are temporally separate and from which side they were delivered. A pulsed modulated 900 MHz RF signal (217 Hz pulse frequency, similar to the GSM 900 system) was emitted by an antenna 2 m over the head of the participants, resulting in a power density of 10 mW/m^2. The test was performed on two separate days, one day with RF EMF exposure and one with sham exposure, and for each participant at the same time of day. Each day, after a first testing phase (serving as baseline) participants rested for a period of 30 min during which they received the GSM-like or sham exposure. A second phase of testing followed the exposure. For analyses, the change in performance from before to after RF EMF exposure was compared to the corresponding change from before to after sham exposure. Results indicated that the exposure to pulsed fields resulted in reduced performance (increase of order threshold) in 23 of the 33 participants (69.7%). Statistical analyses were carried out using three different statistical tests (t-test, Wilcoxon test and Sign test), and two of them (Wilcoxon and Sign test) indicated significant differences ($p = 0.04$ and $p = 0.01$, respectively). [Interestingly, the t-test that uses the magnitude and direction of each individual result as basis for the analysis did not indicate a relation. As also explained by the authors, a plot of individual results suggested that this was due to the weight of outliers, which have less influence in the Wilcoxon test and least in the Sign test. The different findings by different tests make the results difficult to interpret. More important, however, is the fact that five of the participants were exposed to the pulsed RF signal in the first session and 28 in the second (no information is provided about how the allocation to order was done), and order or exposures was not adjusted for in the analyses. Therefore, potential effects of exposure and of order cannot be distinguished. Also children were included in the group (from the age of eight), but no separate results were provided.]

Studies including children and adolescents

Riddervold et al. (2008) exposed 40 adolescents (15–16 years) and 40 adults to four conditions: sham condition, a CW (2140 MHz) condition, a signal at 2140 MHz modulated as UMTS and a UMTS 2140 MHz signal including all control features. Each exposure lasted for 45 minutes and was given in a separate session. The sessions were separated by at least 24 h. The order of sessions was randomized and balanced. The RF signals were emitted by an UMTS base station antenna placed 2.8 m from the participants, resulting in electric field strengths between 0.9 and 2.2 V/m, which should simulate exposure of those living 20 meters or more from a base station. The background RF-field between 10 MHz and 6 GHz was less than 0.001 V/m. Also the 50 Hz magnetic field strength was low. Binding was ensured by having the same acoustic as well as electric noise level during all conditions. During the exposure, participants were asked to complete a cognitive battery assessing attention, vigilance and memory, with Trail Making Task-B (divided attention) as a main outcome. No effects of exposure were reported on any of the cognitive tasks. [Although all exposure conditions were included in the statistical analyses, only the UMTS signal that included all control features was compared with sham. The authors noted that they had lodged their analytic plan with an independent organisation prior to initiating their investigation.]

Studies with patients and IEI-EMF volunteers

In the following studies, individuals with IEI-EMF were included to test their sensitivity to exposures from base stations. From information in the papers, some of the participants may have self-reported sensitivity to base station exposures, but that was not required to be included in the IEI-EMF groups. Therefore, the exposure used in these studies was most likely relevant to only some of those in these groups, and for some of the IEI-EMF participants the exposure was presumable much weaker than the signals they believed being reasons for their symptoms. However, not sufficient information is provided in any of the papers to evaluate this completely.

Regel et al. (2006) tested the effect of 45-minute exposures to two different levels of UMTS (2140 MHz) base station signals (1 or 10 V/m) and to sham in 117 participants of which 33 with IEI-EMF who reported sensitivity to RF fields emitted from mobile phones, cordless phones and antennas and 84 healthy controls. The signals were emitted by antenna 2 m from and targeting the left back side of the participants. The testing took place within a chamber shielded from outside exposures and background levels between 80 MHz and 5 GHz were less than 1 mV/m. Exposure conditions order was random and the sessions were conducted weekly at approximately the same time of day. Several cognitive tasks were used to evaluate attention (three tasks) and short-term memory (three tasks with increasing load), and were administered in a fixed order at the beginning of exposure and then again during the last minutes of exposure. Of 44 statistical tests done, the authors reported three marginal effects. In one of the attention tasks and for the sensitive group only there was a difference in speed between the three exposure conditions ($p=0.03$) with the 1 V/m condition resulting in a slightly lower speed averaged over both test sessions compared to the other conditions and the changed from the first to the second test session also differed ($p=0.007$); here a decrease in speed was observed under the sham and the 1 V/m conditions but not under the 10 V/m condition A decrease in accuracy ($p = 0.05$) in the least demanding task (1-back) was observed only in healthy controls. After applying a Tukey-type correction for multiple tests (significance criterion $p < 0.0051$) both effects disappeared. [It can be reasonably concluded that in this study no consistent effect of exposure was observed.]

Eltiti et al. (2009) included a group of 44 IEI-EMF individuals who associated heath problems with exposure from mobile phones or base stations, and an age-matched control group (selected from an initial sample of 115 individuals). They were exposed to GSM and UMTS base station signals and to a sham condition, following a randomized, crossover design with the exposure conditions separated with at least a week (see (Eltiti et al., 2007a) for details concerning design). The GSM like signal was a combination of the 900 and the 1800 MHz bands and the UMTS signal used the 2020 MHz band and they were emitted by a base station antenna placed 5 meters from the participant. Power density was 10 mW/m^2 with both types of RF signal. The tests were conducted in a shielded room, with shielding effectiveness greater than 60 dB at the tested frequency range (Eltiti et al., 2007a). Cognitive performance was assessed through three tests of attention and working memory. The total duration of exposure for each condition was 50 minutes, during which cognitive tasks were administered. No effects of exposure were reported on any of the cognitive tasks. Bonferroni correction for multiple comparisons was used with significance criterion $p < 0.017$.

Furubayashi et al. (2009) assessed the effects of a 2140 MHz W-CDMA signal (brain SAR_{10g} = 0.0078 W/kg) in 11 females with IEI-EMF and 43 healthy female volunteers. All IEI-EMF participants reported that their symptoms were related to the use of mobile phones and/or to exposure from base stations. W-CDMA signals were emitted by a horn antenna placed 3 meters behind the participants, resulting in whole body averaged SAR of 0.0015 and maximum brain tissue SAR averaged over 10 g of 0.0078 W/kg. The tests were performed in a shielded room. The participants were exposed to four 30-minute conditions: continuous exposure to the signal, intermittent exposure with the source turned on and off at random over 5-minute intervals, a sham condition involving noise (65 dB) and a sham condition without noise. The four sessions were conducted on two consecutive days, each day with two sessions separated by at least 2 hours. The order of the different conditions was determined randomly. Attention performance was assessed through a precued choice reaction time task, with the task administered both before and after exposure periods. Four different conditions of the task were included and each analysed separately. No effects of the exposure were found on cognitive measures for any of the groups. [The number of volunteers with IEI-EMF was low.]

Wallace et al. (2012) examined the effects of acute exposure (50 min) to a TETRA base station signal on attention, short-term memory and working memory. The same study design was applied as in the previous study by the same group (Eltiti et al., 2009). Forty-eight IEI-EMF and 132 healthy controls were exposed double-blind to both a TETRA (420 MHz, 10 mW/m^2) and sham condition emitted by antenna positioned 4.95 m in front of participants. The tests took place in a shielded room and the shielding effectiveness was between

55 and 60 dB at 420 MHz. The IEI-EMF participants were included if they reported to be sensitive to EMF fields from “such as those produced from base stations and mobile handsets”. Participants that did not reach specified task performance criteria for a task were excluded from analysis. This left 36–48 IEI-EMF participants and 107–129 controls to be included in the respective analyses. Results from the working memory task and three versions of the short-term memory task were provided. No evidence was found in either group to suggest that an acute exposure to a TETRA base station signal has an impact on cognitive functions. [Results from the attention task were not presented in the paper because performance varied unexpectedly between the three different versions.]

Table 5.2.2. Base station related studies assessing cognitive performance effects

Endpoint and Participants[a]	Exposure[b]	Response	Comment	Reference
Studies with healthy adults				
Perceptual-attention assessed by auditory order threshold task before and after exposure 33 volunteers (8–70 years; 17 males, 16 females)	GSM signal emitted by patch antenna 2 m over the head, 900 MHz Power density 10 mW/m^2 30 min	Decrease in performance (higher order threshold).	Double-blind, crossover; 5 volunteers exposed to GSM signal in the first session and 28 in the second, and order of exposure not included in analyses. Application of different statistical tests. Children included in the group, without separate analyses.	Maier et al. (2004)
Studies including children and adolescents				
Attention, vigilance and memory (simple- and complex-reaction times tasks, Paired Associated Learning and Trail Making Test-B) during exposure 40 adolescents (15-16 years; 17 males, 23 females) 40 adults (25–40 years; 24 males, 16 females)	Three types of signals emitted by antenna 2.8 m from the participant: CW, signal modulated as UMTS, UMTS signal including all control features; all: 2140 MHz Electrical field strength 0.9-2.2 V/m 45 min	No effect of exposure.	Double-blind, randomized, balanced, cross-over design. Sham was only compared with the UMTS signal that included all control features. Low background exposure levels. For subjective endpoints see Section 5.2.4.	Riddervold et al. (2008)
Studies including patients and/or IEI-EMF individuals				
Attention (simple- and choice-reaction times tasks, and visual selective attention task) and short-term memory (n-back task) assessed twice during exposure 33 volunteers with IEI-EMF (20–60 years; 14 males, 19 females) 84 healthy controls (20–60 years; 41 males, 43 females)	UMTS base station-like signal emitted by antenna 2 m from and targeting left back side of participants, 2140 MHz Electric field strength 1 and 10 V/m; brain SAR_{10g} 0.45 mW/kg at 1 V/m, 0.045 mW/kg at 0.1 V/m 45 min	No effect of exposure.	Double-blind, randomised, cross-over design. Tasks administered in fixed order. Large sample of healthy controls. Low background exposure levels. For subjective endpoints see Section 5.2.4. Turkey adjustment for multiple end points.	Regel et al. (2006)

Attention and memory (digit symbol substitution, digit span and mental arithmetic tasks) assessed during exposure 44 volunteers with IEI-EMF (46.14 ± 13.2 years; 26 males, 18 females) 44 healthy controls (46.1 ± 13.3 years; 24 males, 20 females)	Base station antenna 5 m from participant emitting GSM like signal (combination of 900 and 1800 MHz frequency bands) and UMTS like signal (2020 MHz) Power density 10 mW/m^2 50 min	No effect of exposure.	Double blind, randomized, cross-over. Fewer participants than planned caused unbalanced design. Low background exposure levels. Bonferroni correction for multiple comparisons (significance criterion 0.017). For subjective endpoints see Eltiti et al. (2007a) in Section 5.2.4; for autonomic nervous system see Section 9.2.1.	Eltiti et al. (2009)
Working memory (Operation Span task), short term memory (Digit Span backward and forward), and attention (Letter Cancellation task) during exposure 48 volunteers with IEI-EMF (18–73 years; 19 males, 29 females) 132 healthy controls (18–80 years; 65 males, 67 females)	TETRA signals emitted by antenna 4.95 m in front of participant, irradiating upper legs and upwards, 420 MHz Power density 10 mW/m^2, mean SAR appr. 0.27 mW/kg 50 min	No effect of exposure.	Double blind, randomized, counterbalanced cross-over. Bonferroni correction for the 3 short term memory tests (significance criterion 0.01). Results from the attention task not provided. For subjective endpoints see Wallace et al. (2010) in Section 5.2.4; for autonomic nervous system see Section 9.2.1.	Wallace et al. (2012)
Attention (choice reaction times) assessed after exposure 11 female volunteers with IEI-EMF (27–57 years; 37.27 ± 9.67 years) 43 female healthy controls (21–51 years, 37.98 ± 8.22 years)	W-CDMA base station like signals emitted by horn antenna 3 m behind participant, 2140 MHz Electrical field strength 10 V/m, brain SAR_{10g} 0.0078 W/kg 30 min continuous and intermittent (randomly on and off at 5 min intervals)	No effect of exposure.	Double blind, randomized, counterbalanced cross-over. Small sample for IEI-EMF. Testing room was shielded. For subjective endpoints see Section 5.2.4; for autonomic nervous system see Section 9.2.1.	Furubayashi et al. (2009)

Abbreviations: CW: continuous wave; GSM: Global System For Mobile Communication; IEI-EMF: Idiopathic environmental intolerance attributed to EMF; TETRA: Terrestrial Trunked Radio; UMTS: The Universal Mobile Telecommunications System; VMT: visual monitoring task; W-CDMA: Wideband Code Division Multiple Access.

[a] If not otherwise stated, only healthy volunteers participated. The maximal number of volunteers participating in analyses is provided.

[b] SAR with relevant averaging volume (e.g. SAR_{10g}) is specified if included in the paper.

[c] Duration of exposure is estimated on the basis of info provided in the paper.

[d] In some analyses a lower number of participants were included.

[e] Exposure setup explained in Huber et al. (2003).

5.2.1.3 Studies with other types of exposure

The basic design and results of the only study included in the analysis which related to other than mobile phone-related type of exposure are summarised in Table 5.2.3.

Studies with healthy adults

Lass and colleagues (Lass et al., 2002) investigated the effect of exposure to a 450 MHz signal (pulsed modulated at 7 Hz) and to a sham condition, on the performance in three cognitive tests. EMF signals were emitted by quarter wave antenna positioned 10 cm from right side of the head. The study was carried out on 100 students randomly assigned to each exposure condition, following a single blind paradigm. The participants in the two groups were similar in age, educational background and computer skills. Between collected indices of accuracy and speed in terms of mean values, only a significant increase of accuracy (fewer errors) in the memory recognition task as a function of exposure to the field ($p = 0.032$) was reported. [The main methodological problem of this study is related to the total duration of exposure to the field that varied between participants, based on their ability to complete the tasks. No correction for multiple analyses was applied. SAR estimates provided in this paper were not accurate. However, in later studies applying exactly the same exposure system, signal frequency and duty circle, calculations according to standardized methods were applied resulting in maximum SAR averaged over 1 g to be 0.30 W/kg (Hinrikus et al., 2008a).]

Table 5.2.3. Other forms of exposure studies assessing cognitive performance effects

Endpoint and Participants[a]	Exposure	Response	Comment	Reference
Studies with healthy adults				
Attention, divided attention, and short-term memory tasks, assessed during exposure EMF exposure: 50 volunteers (20.7 ± 2.1 years; 31 males, 19 females)[b] Sham exposure: 50 volunteers (21.7 ± 3.3 years; 32 males, 18 females)[b]	EMF signal emitted by quarter wave antenna 10 cm from right side of the head, 450 MHz PM at 7 Hz (duty cycle 50%) Power density 1.58 W/m^2 SAR_{1g} 0.30 W/kg (Hinrikus et al., 2008a) 10-20 min (varied between participants)	Increase of accuracy only in the visual short-term memory task. No effect on speed.	Single-blind, randomized, between group comparisons. Tasks administered in the same (fixed) order. No correction for multiple analyses.	Lass et al. (2002)

Abbreviation: SAR_{1g}: SAR averaged over 1 g.

[a] If not otherwise stated, only healthy volunteers participated. The maximal number of volunteers participating in analyses is provided.

[b] In some analyses a lower number of participants were included.

5.2.2 Brain electrical activity

The WHO Environmental Health Criteria (1993) did not include any studies relevant for this section. The current literature search for volunteer studies on effects of RF exposure on brain electrical activity resulted in 62 relevant papers, of which one was excluded because the study did not include a blinded sham condition; the study is listed at the end of this section. Of the 61 papers that met the initial inclusion criteria, 55 were included in the overall review section, and six papers with missing information about blinding of participants or specific design issues were reported on briefly at the end of the section under the headline “Papers with uncertainties related to inclusion criteria”. These are not included in the tables. All included studies explored effects of RF exposures on brain electrical activity using the electroencephalogram, or EEG, with the exception of one study that used magnetoencephalography (MEG). In almost all these studies signals and localised exposures typical of those that occur when using mobile phones have been used. A few of the studies with base station-like exposures have applied local exposures and exposure levels that are comparable to those caused by exposure when talking with mobile phones and therefore these are included under mobile phone handset related studies. Only one study has been conducted applying typical base station exposure with regards to exposure levels and whole body exposures.

Of note, several studies included in this chapter involved multiple outcomes, including behavioural, cognitive, metabolic, wellbeing and other measures as specified with cross-references in the tables. In the current section only results related to EEG data will be reviewed and discussed.

The EEG is a non-invasive neurophysiologic measurement that is recorded from electrodes placed on the scalp and reflects synchronous activity in relatively large populations of cortical neurons. It is a particularly useful measure of behavioural state (i.e. sleep vs. wakefulness) and variations in activity are also routinely used to observe changes in cognitive state or response to various types of stimuli. Commonly, the EEG is divided into discrete frequency ranges which are generally designated as delta (< 4 Hz), theta (4–8 Hz), alpha (8–12 Hz), and beta (12–30 Hz). Within the alpha range there is wide variability between individuals, and therefore individual alpha frequency (IAF) is also commonly used and reflects the dominant EEG alpha frequency of an individual. A measure of brain function closely related to the EEG is the "evoked" or "event-related" potential (ERP). ERPs are obtained by sampling the EEG time-locked to a reference event such as the presentation of a stimulus or the onset of a motor response, and averaging the samples together in order to obtain an electrical waveform that represents brain activity associated with a specific sensory, cognitive, or motor event. The waveform appears as positive and negative deflections in the recorded electrical potentials and these deflections are recorded at different latencies after the onset of a stimulus or event that evokes them. Typically it is assessed whether the amplitudes or the latencies of these deflections are influenced by the exposure. In regards to sleep, EEG patterns are well characterized and routinely used as indices of the different sleep stages that a typical healthy individual will move between during the night. Normal human sleep consists of two distinct phases – non-rapid eye movement (NREM) and rapid eye movement (REM) sleep – that are defined by distinct differences in EEG activity and other physiological activity and that alternate throughout the night. NREM sleep is further subdivided into four stages (stage 1, 2, 3, and 4) that reflect the depth of sleep, and the pattern and distribution of these stages across the night is referred to as sleep architecture. There is also activity in the EEG that is specific to sleep and occurs predominantly during stage 2 NREM sleep, known as sleep spindles, which are bursts of oscillatory brain activity that occur approximately between 12 and 14 Hz. The EEG during resting/waking, sleep, and ERPs have all been used to help determine whether RF EMF influences brain activity.

Tables at the end of each section summarize results and provide information about study details including study design. Similar details as well as more details about results are included in the text in the narrative. As one of the inclusion criteria for volunteer studies, the exposure conditions should not be known to the volunteers (single blind design) and ideally not known to both volunteer and research personnel (double blind design). When no info about blinding of a study is included in the description of the study in the text, a double blind design was used. Additionally, when information about measures to ensure blinding was given in the paper, this has been included in the text. In EEG studies, the recorded signals undergo artefact rejection, which can be either done manually or automatically. It is usually not specifically stated whether this part of the analysis is performed blinded, however, no specific information about blinding does not necessarily mean that the inspection was done unblinded. (For sleep EEG studies, see more details in the introduction to Section 5.2.2.3. Tables as well as the narrative of the studies include information about estimates of statistical power if given in the paper. When there was no such information, comments about particularly small samples sizes are made since the smallest samples are attached with the highest uncertainties provided other study details are similar. Exposure was controlled in all studies that are included in the analysis as a basis for the health risk assessment. If SAR values are provided it is specified in both the tables and text, otherwise power density or electric field strength is given. If none of these quantities are provided, output power along with other details of exposure setup are described. In general, study design and methodology are commented on if they were assessed to be of importance for the interpretation of the study results.

5.2.2.1 Event-related potentials

Mobile phone related studies with healthy adults

In order to look at possible effects of EMF on preparatory slow brain potentials, Freude et al. (1998) recorded the EEG in 16 male participants during performance of a simple finger movement task and a complex and cognitive demanding task, the visual monitoring task. During recording, participants were exposed to a GSM mobile phone handset (916.2 MHz) positioned next to the left ear for about 13 minutes. The exposure resulted in a maximum SAR averaged over 10 g of 0.88 W/kg. The study was conducted single blind. The antenna of the phone was fed with signals from an external signal generator and the microphone and loudspeaker of the phone was switched off during the whole experiment. Each participant was exposed to the GSM and the sham conditions in the same session, with order of exposure counterbalanced. No effects were observed during the finger movement task. Significant decreases in slow brain potentials were observed at the central and temporo-parieto-occipital regions during the visual monitoring task only ($p < 0.05$). There also was a significant interaction between exposure and hemisphere ($p < 0.05$), with a more pronounced difference between real and sham exposure at the right hemisphere. [The more pronounced effect on the right side is unexpected since exposure was at the left side. There is no information in the paper that interference of RF EMF exposure with recorded EEG was controlled.]

In order to replicate and extend their initial study, Freude et al. (2000) performed two similar additional experiments in young male volunteers, both conducted single blind. In the first experiment 16 participants performed a visual monitoring task, and in the second experiment the same tasks plus two additional cognitive tasks were performed by 16 participants. During the cognitive tasks EEG was recorded and exposure was applied to the left side of the head with the same exposure setup as in the first study, using a GSM mobile phone handset (916.2 MHz, SAR_{10g} = 0.88 W/kg) for an unspecified duration while participants performed tasks (about 6 minutes in the first and about 15 minutes in the second experiment). Results from both experiments showed a decrease in slow brain potential amplitude in central and temporo-parieto-occipital regions during the visual monitoring task when the EMF was on compared to the EMF off condition ($p < 0.05$). In the second experiment a significant interaction was found between exposure and hemisphere ($p < 0.05$), with the most pronounced difference for the right hemisphere. No effects of exposure were observed during the performance of the other tasks. [These findings complied with those in the previous study (Freude et al., 1998).]

In a series of studies, Krause et al. (2000a; b; 2004) investigated the effects of a GSM mobile phone signal on event-related desynchronisation (ERD) and synchronization (ERS) EEG responses during cognitive processing. ERD is the relative amplitude decrease in a given EEG frequency band that occurs in response to an event, and ERS is the similar relative increase in amplitude. In a single blind study, Krause et al. (2000a) firstly explored effects on the EEG during a visual working memory task. The 24 participants underwent two exposure conditions (EMF on and EMF off) which were applied sequentially in a counterbalanced order and lasted approximately 30 minutes each, during which a visual working memory task was completed. Exposure was provided by a standard GSM mobile phone (902 MHz) placed at the right side of the head and was set to emit at an average output power of 0.25 W. Four EEG frequency bands were analysed separately (4–6 Hz, 6–8 Hz, 8–10 Hz and 10–12 Hz). In the presence of EMF, ERD and ERS responses were altered in the 6–8 Hz (differences between ERS and ERD responses were reduced in the EMF exposure condition) and 8–10 Hz (ERD responses were enhanced and delayed in the EMF exposure condition) frequency bands but for both frequency ranges only when examined as a function of memory load and also depending on whether the presented stimulus was a target or not ($p < 0.05$). [SAR was not specified, beyond stating “According to the manufacturer (Nokia) that SAR was well below 2 W /kg”.] Using the same exposure regime, Krause et al. (2000b) also investigated effects on 16 participants (14 included in the analysis), replacing the visual task with an auditory memory task, which consisted of an encoding and a recognition phase. The same four frequency bands were analysed separately as in Krause et al. (2000a). No effects of exposure were observed for any frequency band for the encoding phase. During the recognition phase an increase in EEG power in the alpha frequency range (8–10 Hz) was seen in the exposure condition ($p = 0.022$). In addition, in all four frequency bands the time course of ERD and ERS over the exposure period differed between the GSM and the sham conditions (p-values in the range 0.0001–0.003) and provided results indicated that the difference in time course also depended on phase (encoding and retrieval phase) for the three frequency bands (4–6 Hz, 8–10 Hz and 10–12 Hz, p-values in the range 0.0037 – 0.017). In order to improve on these initial studies, Krause et al. (2004) performed a double blind replication study using the auditory memory task. Again using the same protocols, 24 participants underwent the two exposure conditions, only differing from their previous studies by applying exposure to the left side, and SAR_{10g} was measured to be 0.648 W/kg. During exposure, decreased ERS in the 4–6 Hz frequency band was observed during both encoding and retrieval ($p = 0.03$) and for the 6–8 Hz band a four-way interaction ($p=0.048$) suggested that “exposure to EMF decreased the magnitude of the initial ERS responses, especially during memory retrieval and over the left hemisphere”. No effects were found in the higher frequency bands (8–10 and 10–12 Hz). [The authors were unable to replicate their initial findings, with results suggesting that effects on the EEG are somewhat variable and not easily replicated, or may even be due to chance, particularly when no correction for multiple comparisons has been applied in any of these studies. It should also be noted that no information was provided about measures to prevent heat sensations or acoustic cues from the mobile phones when operating or to prevent interferences of the RF signals with the recorded EEG signals.]

In a partial replication of their earlier studies, Krause et al. (2007) aimed to further investigate the possible effects of pulse modulated (PM) and continuous wave (CW) RF EMF on ERD and ERS EEG responses during cognitive processing. Two groups, both consisting of 36 male volunteers, were recruited. Both groups underwent 6 exposure conditions (PM EMF, CW EMF, and sham conditions, with each condition applied to first one side and then the other) while performing either a visual memory task or auditory memory task. PM EMF, CW EMF, and sham conditions were in separate sessions and in a counterbalanced order separated by a week. The exposure setup was improved in this study with respect to blinding by applying a signal generator and linear power amplifier that fed the signals directly to the antenna of a mobile phone handset placed about 20 mm from the exposed side. In all RF exposure conditions the carrier frequency was 902 MHz and SAR_{10g} was 0.74 W/kg. For the visual memory task group, exposure lasted for approximately 80 minutes (40 minutes for each side of exposure), and for the auditory memory task exposure lasted approximately 54 minutes (27 minutes for each side of exposure). Analysis of the EEG signals was done for frequencies between 1 and 20 Hz. When averaged over both exposure sides, results showed slightly greater alpha (approximately 8 Hz) ERS responses during encoding and smaller alpha ERD responses during recognition for the auditory memory task during PM exposure when compared with CW exposure ($p < 0.05$). Similarly, greater magnitude alpha (approximately 8–12 Hz) ERD responses were seen for the visual memory task during PM exposure ($p < 0.05$). When looking at exposure side separately, the only effects seen were during the CW exposure in the auditory memory task, with greater alpha (10-15 Hz) ERS during encoding when exposure was on the right side, and greater alpha (approximately 10 Hz) ERD during recognition when exposure was on the left side ($p < 0.05$). [Despite the presence of some small effects on the EEG during the exposure conditions, it should be noted that differences in exposure side were also seen during the sham condition, which brings in the possibility of the reported results being due to chance, particularly also given the large number of comparisons performed in this study without correction. No information was provided concerning time of day for the different sessions and about steps to prevent interferences of the RF signals with the recorded EEG signals.]

Hamblin et al. (2004) performed a single blind pilot study in 12 participants to explore the sensitivity of ERPs to the RF EMF emitted by a GSM mobile phone handset. Attending two separate sessions in counterbalanced order with a one week interval, participants were exposed to both an EMF-emitting (895 MHz, 0.25 W average output power) and sham mobile phone at the right side of the head for 60 minutes while performing auditory and visual oddball tasks and having their EEG recorded. The exposure setup minimized the risk of auditory cues and heat from the mobile phone that could potentially reveal the exposure condition, and the effectiveness of this was confirmed in a pilot test. Several exposure-related results were reported, with reduced N100 (an early sensory component) amplitude ($p = 0.029$) and latency ($p = 0.018$) and delayed P300 (a later cognitive component) latency ($p = 0.025$) being observed. No significant changes were obtained for the other two analysed components. [The SAR of the commercial mobile phone used was indicated to be 0.87 W/kg, but the provided source of information might not have been reliable. In a follow-up of this pilot study the same group (Hamblin et al., 2006) used an exposure setup that seems to be identical and in this case SAR averaged over 10 g was measured to be 0.11 W/kg.] In this latter double blind study, Hamblin et al. (Hamblin et al., 2006) investigated the effects of a GSM handset exposure (895 MHz) on both visual and auditory ERPs using a randomised and counterbalanced design. The sample comprised 120 participants who underwent 30 minutes exposure (EMF and sham) while visual and auditory oddball tasks were performed and the EEG was recorded. Half of the participants received exposure to the left side of the head, with the other half receiving right side exposure. In contrast to their original pilot study (Hamblin et al., 2004) no differences between the EMF and sham exposure conditions were observed for any auditory or visual ERP components. [It should also be noted that this second study was much larger (120 vs. 12 participants in the original pilot) and the whole experiment was designed to detect differences of 1/4 of a standard deviation (80% power). The authors provided a more detailed dosimetry of the applied exposure. As in the previous study, the exposure setup minimized the risk of auditory cues and heat from the mobile phone to reveal the exposure conditions. For none of the studies the authors informed about controlling whether RF EMF influenced the recorded EEG.]

Using a different approach, Hinrichs and Heinze (2004) used magnetoencephalography (MEG) to investigate potential effects of an 1800 MHz GSM-like signal (SAR_{10g} = 0.61 W/kg) on brain activity. In contrast to EEG, which measures voltage differences on the scalp, MEG is a non-invasive technique that measures the resultant magnetic fields of the brains electrical activity. Twelve participants were exposed at the left hemisphere to real and sham conditions for 30 minutes in counterbalanced order on separate days at the same time of day. The phone was placed close to the left ear of the participants, while the electronics of the phone were removed to prevent thermal sensation. During the last 10 minutes of exposure, the learning or encoding phase of a memory test was conducted. MEG was subsequently recorded during memory retrieval with a differentiation made between signals recorded during identification of words that were earlier encoded (old words) and for detection of new words. Statistical analyses were done separately for different brain regions and for two latency periods after the presentation of the old and new words, respectively. In regards to brain activity, an interaction between exposure and new versus encoded words was observed in some occipito-temporal areas of the left hemisphere (the exposed side) in the earliest latency period ($p = 0.025$). However it is not clear whether these differences were increases or decreases in activity, and post hoc analyses did not reveal significant differences between real and sham exposures for either type of words even though no correction for multiple comparisons was made. There was no indication of any effects of exposure in other brain regions. [The lack of information regarding direction of change makes interpretation and comparison with other EEG studies difficult. Furthermore, the number of participants was low in this study.]

Yuasa et al. (2006) investigated whether exposure from a GSM mobile phone influenced somatosensory evoked potentials (SEPs) and in particular recovery functions after exposure. Twelve participants underwent two 30-minute exposures (real and sham), delivered to the right side of the head by a standard mobile phone handset. The handset was controlled by a mobile phone simulator to emit 800 MHz at maximum output power and held by the participant (therefore resulting in a variable SAR averaged over 10 g between 0.054 and 0.02 W/kg in the brain at 3 cm from skull, as the participant would not be able to hold the phone in the exact same position for the entire exposure duration). SEPs were recorded both before and after exposure from the hand sensory area of the right hemisphere following left median nerve stimulation. No effect of exposure was seen on SEPs in terms of changes in amplitudes or latencies, or on their recovery function. [Explicit information about blinding is not provided, but it is stated that participants were not able to distinguish between real and sham, suggesting that it at least was single blind. No information was provided about randomization, counterbalancing or about time difference between real and sham exposures. A low number of volunteers participated.]

Using transcranial magnetic stimulation (TMS), Ferreri et al. (2006) investigated the excitability of the brain before and after real and sham exposures to a GSM mobile phone handset (902.4 MHz). Under the real condition the mobile phone was set to transmit at maximum power (0.25 W average output power) and SAR was measured to be 0.5 W/kg, [but the averaging volume was specified]. The phone was positioned 15 mm from the left side of the head and the space was chosen “to avoid subjects having any heating or buzzing effects produced by the device”. Fifteen participants underwent two recording sessions, (real and sham) comprising 45-minute exposures, separated by a week. The recording of motor evoked potentials (MEPs) was done using a paired-pulse paradigm before, immediately after, and again 1 hour after exposure. By applying two magnetic pulses (a conditioning and a test stimulus) applied with 1–17 ms inter-pulse intervals, it was of interest to see whether nerve excitation would be different between the RF exposure and sham conditions. The effect of main interest was the triple interaction of time (baseline, immediately and 1 hour after exposure], exposure condition and hemisphere exposed. Although not significant ($p = 0.07$), the trend level interaction observed indicated a potential transient decrease in intracortical inhibition (SICI) and increase in intracortical facilitation (ICF) (both measures of cortical excitability) in the exposed hemisphere, which remains to be tested by other studies. [No information was provided about randomization, counterbalancing or time of day for the different exposure conditions.]

Using an auditory oddball paradigm, Stefanics et al. (2008) investigated the effects of 3G mobile phone (UMTS) exposure on event related potentials in 36 volunteers. The signal was emitted by a planar antenna at the right side of the head resulting in brain SAR_{1g} of 0.39 W/kg 30 mm from skull. In a cross-over design, participants underwent real and sham exposures in separate sessions a week apart and were presented with random series of tone bursts both before and after exposure. No significant effects of mobile phone exposure were found on the amplitude or latency of the ERP components analysed. Evoked gamma activity was also analysed but no exposure-related changes were observed. [The study was designed to be counterbalanced, but this could not have been completely achieved since data from only 29 volunteers were included in the final analysis. Data from seven volunteers were rejected because the minimum number of accepted trials were not reached.]

Kleinlogel et al. (2008b) investigated the effects of both GSM and UMTS mobile phone technologies on visual and auditory evoked potentials, as well as cognitive performance, using an auditory oddball paradigm and continuous performance test during exposure. Fifteen participants underwent four different 30-minute exposure conditions in random order at weekly intervals with all conditions at the same time of day (plus an initial training session): a GSM base station-like signal (900 MHz, SAR_{10g} = 1 W/kg), a weak UMTS handset-like signal (1950 MHz, SAR_{10g} = 0.1 W/kg), a high UMTS handset-like signal (1950 MHz, SAR_{10g} = 1 W/kg), and sham. Both RF EMF signals were emitted by a small antenna mounted at the normal position for mobile phone use. EEG wires were configured to prevent the EMF signals from interfering with the recorded EEG signals, and testing confirmed no interference. Overall, no significant effects were found for visual or auditory evoked potentials for any of the exposure conditions. For the visually evoked potentials, a tendency for a more anterior position for the topographical centroid during the GSM exposure ($p < 0.06$) was observed. [The same study assessed effects on resting EEG (Kleinlogel et al., 2008a) (see Section 5.2.2.2).]

A European multicentre project (Parazzini et al., 2009; Parazzini et al., 2010) aimed to test effects of UMTS mobile phone exposure on the auditory system, including central nervous system processing of auditory information. In both studies participants were exposed for 20 minutes to UMTS 1947 MHz mobile phone signals and to a sham condition. In the first study, Parazzini et al. (2009) positioned a UMTS mobile phone against the ear that was tested for hearing functions. SAR_{1g} measured approximately at the position of cochlea (2 cm under the surface) was 0.069 W/kg. The study was performed with sham and RF exposure sessions on separate days and the order of exposures were designed to be counterbalanced, which was not always completely achieved for all analyses due to the odd number of participants. Before and after exposures the participants underwent an auditory oddball regime during which ERPs where recoded. Middle latency components (N1 and P2) were examined from non-target responses, whereas late potentials (N2 and P3) were examined from responses to targets only. Latencies were analysed for all components and for the P3 component amplitude was also analysed. The number of participants included for the various components ranged from 33 to 59. Shift in responses from before to after exposure was compared between the UMTS and the sham condition without resulting in any significant finding. Parazzini et al. (2010) conducted a similar study but with a higher exposure level (SAR_{1g} 20 mm from the surface: 1.75 W/kg) obtained by amplifying the signals from the UMTS phone and emitting them via a patch antenna positioned against the test ear. The same study design, tests and analyses were used as in the previous study but in this study both latencies and amplitudes of all recorded ERP components were analysed. Fifty-two volunteers were included in the analyses. Also in this study, no effect of exposure was observed.

Using a less common measure of event related potentials, de Tommaso et al. (2009) investigated the effects of GSM handset exposure (900 MHz) on initial contingent negative variation (iCNV) in the EEG, a measure thought to be associated with attention and expectancy stimulus processing. Ten volunteers underwent three exposure conditions (real exposure to a mobile phone with SAR_{10g} 0.5 W/kg, exposure to a mobile phone with the output power signal connected to an internal load rather than the antenna and resulting in negligible SAR, and sham) lasting 10 minutes each, during which they performed a simple auditory detection task. Each exposure session was separated by a 10-minute time interval and the order of exposure conditions was randomized. EMF interference was earlier tested with a commercial EEG instrumentation without showing any effect. When compared with sham, the iCNV amplitude and habituation index were both significantly reduced in both exposure conditions ($p < 0.001$). [The condition applying the internal load and the sham condition differed concerning heating of the phone, but were almost identical to the sham condition with respect to RF exposure, thus making it unlikely that the observed difference between these conditions was due to RF exposure. Furthermore, if there was an effect of the RF signals, we also would have expected a difference between the condition with 0.5 W/kg and the one with negligible SAR, which was not observed. The number of participants was low.]

Kwon et al. (2009) explored potential effects of GSM mobile phone emissions on brain activity using mismatch negativity (MMN). MMN is an ERP component and a sensitive measure for stimulus feature discrimination at the level of cortex. Using a mobile phone handset, transmitting at 902 MHz (SAR_{10g} 0.82 W/kg), 17 participants were exposed in three 6-minute blocks at each side of the head (one block of sham and two blocks of exposure) while MMN responses to changes in acoustic stimuli (four deviant types: duration, intensity, frequency, and gap) were recorded. The MMN variables analysed were mean amplitude, peak amplitude, and peak latency of the signal. Analysis of variance indicated an effect of exposure ($p = 0.045$) with peak amplitude being slightly higher in the sham condition. However, pairwise analyses did not result in significant differences between sham and respectively ipsilateral and contralateral exposures. No other exposure-related effects were observed. [The order of exposures (sham and real) and side of exposure was meant to be counterbalanced. However, since results from one of the 18 participants had to be excluded due to extensive artefacts, complete counterbalancing was not achieved. The authors referred to other studies in which interference between EMF and recorded EEG had been tested, and no interference found.]

Vecchio et al. (2012a) investigated whether mobile phone emissions modulate event-related desynchronization (ERD) of alpha rhythms in the EEG and whether this in turn may lead to changes in cognitive–motor performance. EEG was recorded in 11 volunteers both prior to and following a 45-minute exposure to a mobile phone handset (902.4 MHz, $SAR_{10g} = 0.5$ W/kg) at the left side of head. Real and sham exposure sessions were one week apart and the order was random. During recordings participants performed a visual go/no-go task as a measure of cognitive motor performance. In the analysis the EEG frequency bands of interest ranged from the individual alpha frequency (the dominating frequency between 6 and 13 Hz) to 2 Hz below this frequency (low frequency alpha band) and to 2 Hz above (high frequency alpha band), respectively. No effects of exposure were observed in the low frequency band. In the high frequency alpha band an interaction was found between exposure condition and time (prior to and following exposure) ($p < 0.01$). Post hoc comparisons showed that ERD amplitude was lower in the post- than pre- EMF exposure ($p < 0.005$) and also lower in the post-exposure session when compared with sham ($p < 0.0005$). A trend ($p < 0.09$) towards a decrease of EEG power desynchronisation in the post-exposure session was also observed in the high frequency alpha range. [Few participants were included in this study. No information was provided whether the two sessions were conducted at the same time of day.]

Mobile phone related studies in healthy adults with uncertainties related to inclusion criteria

In a single blind study, Croft et al. (2002) exposed 24 participants to a mobile phone handset for 20 minutes (either turned on or off) while resting EEG (reported in Section 2.2.2.2) and phase-locked neural responses to auditory stimuli were recorded. Early phase-locked neural responses were altered, with an attenuation of the normal response decrement over time in the theta (4–8 Hz) band, decreased response in the 12–30 Hz band, and increasing midline frontal and lateral posterior responses in the 30–45 Hz band. [Despite these findings, the study is not included in the analyses because of lack of verification of exposure level, which was subsequently pointed out by Croft et al. (2008)].

Specifically looking at the P50 component of ERPs during a working memory task, Papageorgiou et al. (2006) exposed 19 participants to two exposure conditions (RF exposure on and off) while they performed an auditory working memory task. Each exposure condition was approximately 45 minutes. Among a high number of analyses, only two findings were reported to be statistical significant: increased P50 amplitude at the location of two of the 15 electrodes evoked by low frequency auditory stimuli and decreased P50 amplitude at the same location. [Adjustments were made for multiple comparisons, but the method was not specified. No information was provided that the participants were blinded to the exposure condition.]

Bak et al. (2010) aimed to investigate the effect of GSM 935 MHz mobile phone exposure on event related potentials, specifically the P300. The amplitude of the P300 was reported to be lower during exposure. [It appears that the RF EMF exposure session was consequently conducted before the sham session, and no p-values were provided for any of the results, which makes interpretation difficult.]

Mobile phone related studies including patients

Following early reports of EMF-related effects on sleep, Jech et al. (2001) investigated whether a GSM mobile phone signal (900 MHz) would have an even larger influence on patients with narcolepsy, who suffer from hypersomnia and fall asleep suddenly or unexpectedly. Twenty-two patients were exposed on two consecutive days to a real and sham exposure for 45 minutes. The mobile phone placed at the right side of the head was thermally insulated so that the participants should not sense the heat from the phone and the authors reported that “it was impossible to see or hear whether the phone was on or off”. In each session, after 5 minutes of exposure the participants were asked to complete a visual discrimination task during which visual ERPs were recorded. The target stimuli were presented in three variants: the whole field of the screen was filled with the target, or it was presented to the left or the right hemifields only. Exposure-related effects were reported for ERP amplitudes (increased P3a amplitude and decreased N2 amplitude, $p < 0.05$) but only for targets in the right hemifield. No effects were observed for latency of the ERP. [Results from only 17 of the participants were included in the analyses (three excluded due to artefacts and one could not complete the task. It should also be noted that the SAR reported for this study (SAR_{10g} = 0.06 W/kg) is extremely low and therefore the detection of potential effects may have been difficult. Potential influence of other factors, such as sleep prior to the session and coffee intake, was tested without finding any significant difference between days with sham and RF EMF exposures. No information was provided about randomization or counterbalancing order of exposures or about control of possible EMF interference with the recorded brain potentials.]

In two papers, the same group Maby et al. (2005; 2006) published results which appear to originate from the same study (e.g. identical samples). They investigated the effects of GSM mobile phone exposure (900 MHz, SAR_{10g} = 1.4 W/kg) on auditory ERPs induced by two different sound stimuli in both normal and epileptic participants. In both studies, nine healthy volunteers and six patients suffering from temporal lobe epilepsy were exposed (single-blind) to real or sham exposure from a GSM mobile phone handset at the right side of the head while auditory ERPs were recorded. Each participant took part in two sessions, one “experimental” and one “control” separated by some days. The experimental session included first a control exposure and later a real exposure. The control session was similar to the experimental one, but consisted only of sham exposures. The duration of exposure was not specified. To avoid EMF interaction with the evoked potentials, the recorded signals were low pass filtered. In both studies correlations between ERPs in the first and second exposure in the same sessions were compared in the time and frequency domains, and then it was tested whether these correlations differed between the experimental and the control sessions. In the second study (Maby, Le Bouquin Jeannes & Faucon, 2006), amplitudes and latencies of two selected evoked potentials, including their relative amplitudes and time differences, were also tested for differences between the two sessions. Variable modifications to AEPs were observed in the exposure condition in both the healthy and epileptic participants (changes in correlation coefficients, latencies, and amplitudes, p values ranging between 0.041 and < 0.001) [No clear explanation of how these observations may relate to brain function or health were provided. Despite a high number of statistical comparisons, no adjustment of p-values was applied, and the low number of participants in each group may be one reason for variable results. No information was provided concerning randomization or counterbalancing the order of sessions.]

Using a different approach, Inomata-Terada et al. (2007) investigated whether TDMA mobile phone emissions have short-term effects on motor cortex activity. Ten healthy volunteers and two patients with multiple sclerosis who had weakness after taking a hot bath were recruited for the study. Exposure was delivered to the left side of the head as in Yuasa et al. (2006). Both prior to and following the real (TDMA 800 MHz, SAR_{10g} 3 cm from scull was around 0.05 W/kg) and sham exposures, single pulse TMS was performed (stimulating the motor cortex, brainstem, and spinal nerve) and motor evoked potentials were measured using electromyogram (EMG) in both groups. For the healthy participants only, the same procedure was repeated applying paired pulses with various intervals to test potential effects on the short interval intracortical inhibition (SICI) of the motor cortex. Separate analyses were performed for the group of healthy participants. For the two patients results for each one of them were deemed significant if they deviated from the mean result for the healthy group by more than two standard deviations. No effects of exposure were found on any measures (EMG latency or amplitude) in any of the participants. [The low number of participants, in particular of patients, making it less likely to detect potentially small effects, should be noticed. No information about randomization or counterbalancing order of exposures was provided.]

Mobile phone related studies in patients with uncertainties related to inclusion criteria

Maby et al. (2004) studied auditory ERPs in healthy volunteers and epileptic patients. EEG was recorded in two sessions, one “experimental” session (with sham and real exposures) and one “control” session (with only sham exposures) similar to the ones applied by the same group in a later published study (Maby et al., 2005). Exposure-related differences in both amplitude and latency of ERPs was reported, with observations suggesting that effects of exposure were different for the healthy volunteers when compared with the epileptic patients. [This study is not included in the final analyses due to uncertainties regarding exposure level. A SAR value was provided, but without any specification of how it was determined. Furthermore, the experimental design was not clearly described. It also appears that the same order of the session with RF EMF and the control session was used for all participants. Therefore interpretation of the reported results is difficult.]

Mobile phone related studies including children or adolescents

In a similar study to some that have been performed on adults, Krause et al. (2006) assessed the effects of a GSM mobile phone handset signal (902 MHz, SAR_{1g} = 1.4 W/kg) on event related brain oscillatory EEG responses(ERD and ERS), frequency range 1–20 Hz, in children (10 – 14 years). To prevent sound cues from the phone placed next to the ear, the loudspeaker was removed, and the battery was changed to a model that did not produce a perceptible noise. Data was collected from 15 children, who underwent an EEG recording subdivided into two 30-minute blocks, one for real exposure of the left side, and the other for sham exposure. The order of exposure conditions was partially counterbalanced. During both blocks, children were required to perform an auditory memory task. Separate analyses were done for the encoding and recognition phases and for each of five cortical regions. Results showed exposure-related increased ERD and ERS responses during encoding (4–8 Hz) in frontal, occipital and left temporal regions, as well as increased ERD and ERS responses during recognition (4–8 Hz in occipital and left temporal regions, and 15 Hz in the right temporal region) ($p < 0.05$). [However, effects were of a small magnitude (~5–10 %) and no correction for multiple comparisons was made.]

Kwon et al. (2010a) investigated the effects of mobile phone exposure on auditory event related potentials (ERPs) in children, with the aim to test the potential effect on mismatch negativity (MMN) responses to changes in acoustic stimuli with respect to duration, intensity, frequency, and gap in signal (similar to the study with adults (Kwon et al., 2009)). In addition four other ERPs were analysed. In a single-blind experiment, 17 children (11–12 years) were exposed to a GSM handset-like signal (902 MHz, SAR_{10g} = 0.82 W/kg) in a one-hour testing block in which the phone was placed at one ear for the first half and the other ear for the second half. For each ear, EEG was recorded in three 6-minute blocks, with one block having the exposure turned off, and the other two blocks having the exposure turned on (order partially counterbalanced). The loudspeaker, microphone, and buzzer of the phone were removed. Amplitudes and latencies were analysed for the different potentials. The only finding that resulted in a p-value less than 0.05 was a change in latency of one of the potentials (P3a) ($p = 0.049$). This was not significant after Bonferroni correction for multiple comparisons with significance criterion 0.0083. [However, the authors themselves noted that a subsequent power analysis revealed that with the sample size of this study only large effects would have been possible to detect. The authors referred to other studies in which interference between EMF and recorded EEG had been tested, and stated that there was no interference.]

As part of the same study and using the same sample as Croft et al. (2010) (see Section 5.2.2.2), Leung et al. (2011) examined sensory and cognitive processing. The 103 participants (separated into 41 adolescents, 42 young adults, and 20 elderly) were exposed for 55 minutes to 2G (GSM; 894.6 MHz, SAR_{10g} = 0.7 W/kg) and 3G (UMTS; (1900 MHz, SAR_{10g} 1.7 W/kg) mobile phone emissions as well as a sham condition. The three conditions were on separate days at least 4 days apart. The order of exposure conditions and side of exposure were counterbalanced across participants and exposures were randomly assigned. For each individual, side of exposure and time of day were consistent. The phones were positioned against the side of the head, but none of the phones produced any audible sound during operation. During the exposures two different cognitive tasks (auditory 3-stimulus oddball task and N-back task) were performed while EEG was recorded. Results showed larger N1 amplitude (the first event related potential peak) in the 2G exposure condition ($p < 0.04$) during one of the 3-stimulus oddball tasks, and delayed event-related desynchronization (ERD) and event-related synchronization (ERS) responses of alpha power in both the 2G ($p < 0.001$) and 3G ($p < 0.04$) exposure conditions during the n-back task. Also three time-domain ERP components were analysed for both tasks, but no effects of exposure were observed. All significant differences seen were independent of age group, suggesting that children and other potentially sensitive groups such as the elderly were affected in a similar manner and therefore are not necessarily more sensitive to mobile phone exposure than adults. [The authors did not report about any measures taken to control for interference between the EMF signal and the EEG signal.]

Table 5.2.4. Studies assessing effects on event-related potentials

Endpoint and Participants[a]	Exposure[b]	Response	Comment	Reference
Mobile phone related studies with healthy adults				
EEG (slow wave potentials, visual) recorded during exposure 16 male volunteers (21–26 years)	GSM phone with extended antenna (fed by external generator) against the left ear, 916.2 MHz SAR_{10g} 0.88 W/kg about 13 min	Decrease in slow brain potential in central and temporo-parieto-occipital regions during visual monitoring task, most prominent on right side. No effect of exposure during a simple finger movement task.	Single blind, counterbalanced for order of conditions, cross-over. Short duration of exposure. No information about steps to prevent EMF interference with recorded EEG. For cognitive function see Section 5.2.1.	Freude et al. (1998)
EEG (slow wave potentials, visual) recorded during task and during exposure Experiment 1: 16 male volunteers (21–30 years) Experiment 2: 16 male volunteers (21–26 year)	GSM phone with extended antenna (fed by external generator) against the left ear, 916.2 MHz SAR_{10g} 0.88 W/kg About 6 min in the first and about 15 min in the second experiment	Decrease in slow brain potential amplitude in central and temporo-parieto-occipital regions during visual monitoring task in both experiments, most prominent at right side in the second experiment. No effect of exposure during a simple finger movement task and another task.	Replication of Freude et al. (1998) Single blind, counterbalanced for order of conditions, cross-over. No information about steps to prevent EMF interference with recorded EEG. No correction for multiple comparisons. For cognitive function see Section 5.2.1.	Freude et al. (2000)

EEG (event related desynchronisation (ERD) and synchronisation (ERS) in four bands between 4 and12 Hz, visual) recorded during exposure 24 volunteers (20–30 years; 12 males, 12 females)	GSM phone over the right posterior temporal region, 902 MHz Peak output power 2 W, SAR<2 W/kg [according to data from manufacturer] About 30 min	ERD and ERS responses altered in the 6–8 and 8–10 Hz frequency bands. No effects in other bands.	Single blind, counterbalanced, cross-over No information about steps to prevent EMF interference with recorded EEG. No correction for multiple comparisons. For cognitive function see Section 5.2.1.	Krause et al. (2000a)
EEG (ERD and ERS in 4 bands between 4 and12 Hz, auditory) recorded during exposure 16 volunteers (mean age 23.2 year; 8 males, 8 females) [n=14 in the analyses]	GSM phone over the right posterior temporal region, 902 MHz Peak output power 2 W, SAR<2 W/kg [according to data from manufacturer] 30 min	Increased EEG power in alpha range (8–10 Hz). In all frequency bands time course of ERD and ERS differed.	Single blind, counterbalanced, cross-over No information about steps to prevent EMF interference with recorded EEG. No correction for multiple comparisons. For cognitive function see Section 5.2.1.	Krause et al. (2000b)
EEG (ERD and ERS in 4 bands between 4 and12 Hz, auditory) recorded during exposure 24 volunteers (24.3 ± 8.1 years; 12 males, 12 females)	GSM phone over the left posterior temporal region (902 MHz, pulsed at 217 Hz SAR_{10g} 0.648 W/kg About 30 min	Decreased ERS in the 4–6 Hz frequency band during encoding and retrieval. No effects in the higher frequency bands.	Replication of Krause et al. (2000b). Double blind, counterbalanced, cross-over No information about steps to prevent EMF interference with recorded EEG. No correction for multiple comparisons. For cognitive function see Section 5.2.1.	Krause et al. (2004)
EEG (ERD and ERS in a frequency (0–30 Hz) – time (0–1.5 s) matrix, auditory and visual) recorded during exposure 72 male volunteers Auditory task (n=36, 23.6 ± 2.38 year) Visual task (n=36, 22.9 ± 2.4 years)	GSM-like and CW signal emitted by mobile phone antenna ~ 20 mm from right and left posterior temporal region, 902 MHz SAR_{10g} 0.74 W/kg About 27 min (auditory task) and about 40 min (visual task) for each side	Auditory: increased ERS (encoding) and decreased ERD (recognition) during GSM exposure; increased ERS (encoding) and ERD (recognition) during right- and left- side CW exposure, respectively. Visual: increased ERD during GSM exposure. All effects observed in the alpha band.	Double blind, counterbalanced, cross-over. No information about steps to prevent EMF interference with recorded EEG. No correction for multiple comparisons. For cognitive function see Section 5.2.1.	Krause et al. (2007)

EEG (event-related potentials (ERPs), visual and auditory) recorded during exposure 12 volunteers (19–44 years; 4 males, 8 females)	GSM phone over the right temporal region, 894.6 MHz Mean output power 0.25 W 60 min	Reduced N100 amplitude and latency and delayed P300 latency. No effect on the N200 and P200.	Single blind, counterbalanced, cross-over. Small sample. No information about steps to prevent EMF interference with recorded EEG. Bonferroni correction for multiple comparisons in post hoc analyses. For cognitive function see Section 5.2.1.	Hamblin et al. (2004)
Magneto-encephalography (MEG) (1–50 Hz) recorded after exposure 12 volunteers (18–30 years; 2 males, 10 females)	Mobile phone antenna emitting GSM-like signal over left ear, 1870 MHz SAR_{10g} 0.61 W/kg 30 min	No effect of exposure.	Double blind, counterbalanced, cross-over. Small sample. Differences in MEG activity during retrieval in one brain region and in one of two latency periods (no direction of change provided). Finding was an interaction between exposure and test condition with no effect of exposure in post hoc tests. No correction for multiple comparisons. For cognitive function see Section 5.2.1.	Hinrichs and Heinze (2004)
EEG (ERPs, visual and auditory) recorded during exposure 120 volunteers (18–69 years; 46 males, 74 females)	GSM phone against right (n=60) or left (n=60) ear, 895 MHz SAR_{10g} 0.11 W/kg 30 min	No effect of exposure.	Double blind, randomized, counterbalanced, cross-over. Bonferroni correction for multiple comparisons for explorative comparisons. For cognitive function see Section 5.2.1.	Hamblin et al. (2006)
EEG (somatosensory evoked potentials) recorded before and after exposure 12 volunteers (22–50 years; 5 males, 7 females)	TDMA mobile phone at right side of head, 800 MHz Brain SAR_{10g} 0.02–0.05 W/kg (3 cm from skull) 30 min	No effects of exposure.	Indication of being at least single blind, cross-over. Small sample. Bonferroni correction for multiple comparisons.	Yuasa et al. (2006)
Motor evoked potentials (MEP) recorded before and after exposure using transcranial magnetic stimulation (TMS) 15 male volunteers (20–36 years)	GSM mobile phone 15 mm from left side of head, 902.4 MHz SAR 0.5 W/kg 45 min	No effects of exposure	Double blind, cross-over. No correction for multiple comparisons.	Ferreri et al. (2006)

EEG (ERP, auditory) recorded before and after exposure 36 volunteers (19–28 years; 16 males, 20 females). Only 29 volunteers included in final ERP analysis	UMTS (3G) handset-like exposure emitted by planar antenna at right side of head (no carrier frequency provided) Brain SAR_{1g} 1.75 W/kg (0.39 W/kg 30 mm from skull) 20 min	No effect of exposure.	Double blind, counterbalanced, cross-over. No correction for multiple comparisons. For cognitive function see Section 5.2.1.	Stefanics et al. (2008)
EEG (ERP, visual and auditory) recorded before, during, and after exposure 15 male volunteers (20–35 years)	GSM signal emitted by a broadband antenna against left ear, 900 MHz SAR_{10g} 1.0 W/kg UMTS handset-like signal against the left ear, 1950 MHz SAR_{10g} 0.1, 1 W/kg 30 min	No effect of exposure.	Double blind, randomized, cross-over. Bonferroni correction for multiple comparisons. For cognitive function see Section 5.2.1; for resting EEG see Kleinlogel et al. (2008a) in Section 5.2.2.2); for subjective endpoints see Section 5.2.4.	Kleinlogel et al. (2008b)
EEG (ERP, auditory) recorded before and after exposure 59[c] volunteers (18–30 years; 61 males, 73 females) [d]	UMTS mobile phone against test ear, 1947 MHz Max SAR 0.069 W/kg in brain 30 mm from the surface 20 min, concurrent speech signal	No effect of exposure.	Double blind, counterbalanced, cross-over. For auditory sensory functions see Section 6.2.	Parazzini et al. (2009)
EEG (ERP, auditory) recorded before and after exposure 52[c] volunteers (18–30 years; recruited: 35 males, 38 females) [d]	Signals from UMTS mobile phone transmitted by a patch antenna against test ear, 1947 MHz SAR_{1g} 1.75 W/kg in brain 20 mm from the surface 20 min, concurrent speech signal	No effect of exposure.	Similar to Parazzini et al. (2009), but with higher exposure level. Double blind, counterbalanced, cross-over. For auditory sensory functions see Section 6.2.	Parazzini et al. (2010)
EEG (ERP component: mismatch negativity (MMN), auditory) recorded during exposure 17 volunteers (23.1 ± 4.5 years; 5 males, 12 females)	GSM handset-like signal from generator emitted by mobile phone antenna close to either side of head, 902 MHz SAR_{10g} 0.82 W/kg 18 min (2 blocks GSM exposure, and 1 block sham, each block 6 min) to each ear	No effect of exposure.	Indication of being at least single blind, partially counterbalanced, cross-over. EMF interference with recorded EEG tested. Decreased peak MMN amplitude during exposure compared to sham. However, pairwise comparisons for peak MMN amplitude gave $p > 0.05$. Bonferroni correction for multiple comparisons for pairwise comparisons.	Kwon et al. (2009)
EEG (peak amplitude of alpha ERD) recorded before and after exposure 11 volunteers (24–63 years; 8 males, 3 females)	GSM phone set by test card at left side of head, 902.4 MHz SAR_{10g} 0.5 W/kg 45 min	High frequency alpha ERD amplitude lower in the post-exposure session when compared with sham. No effect of exposure in the low frequency alpha band.	Double blind, partially counterbalanced, pseudo-randomized, cross-over. Small sample. For cognitive function see Section 5.2.1.	Vecchio et al. (2012a)

Mobile phone related studies including patients				
EEG (ERPs, visual) recorded during exposure 22 patients with narcolepsy (48 ± 11.7 years; 9 males, 13 females)	GSM mobile phone at right side of head, 900 MHz SAR_{10g} 0.06 W/kg 45 min	Increased P3a amplitude and decreased N2 amplitude with one of three target variants. No effects on latency..	Double blind, cross-over. No information about steps to prevent interference with recorded signals. Bonferroni correction for multiple comparisons. For sleep EEG see section 5.2.2.3.	Jech et al. (2001)
EEG (auditory evoked potentials (AEPs), time and frequency domains) recorded during exposure 9 healthy volunteers (21–32 years; 3 males, 6 females) 6 epileptic patients (25–39 years; 4 males, 2 females)	GSM mobile phone at left side of head, 900 MHz SAR_{10g} 1.4 W/kg Duration of exposure not specified	Variable exposure-related modifications to AEPs in both healthy and epileptic participants (changes in correlation coefficients, latencies, and amplitudes).	Single blind, cross-over. Small samples. AEP signal low pass filtered to remove EMF interference. No correction for multiple comparisons.	Maby et al. (2005; 2006)
EMP recorded before and after exposure using TMS 10 healthy volunteers (22–51 years; 5 males, 5 females) 2 multiple sclerosis patients (no demographic details provided)	TDMA mobile phone at left side of head, 800 MHz SAR_{10g} 0.05 ± 0.02 W/kg 30 mm from skull 30 min	No effects of exposure.	Double blind, cross-over. Small samples, in particular few patients. Bonferroni correction for multiple comparisons.	Inomata-Terada et al. (2007)
Mobile phone related studies including children or adolescents				
EEG (ERD and ERS (0–20 Hz), auditory and visual tasks) recorded during exposure 15 children (10–14 years; 6 males, 9 females)	GSM mobile phone at left side, 902 MHz SAR_{1g} 1.4 W/kg 30 min	Increased ERD and ERS responses during encoding (4–8 Hz) and during recognition (4–8, and 15 Hz), each in 2–3 of 5 cortical regions.	Double blind, partially counterbalanced, cross-over. No information about steps to prevent EMF interference with EEG. No correction for multiple comparisons. For discrimination see Section 5.2.4.	Krause et al. (2006)
EEG (ERP components: mismatch negativity (MMN) and 3 others, auditory) recorded during exposure 17 children (11–12 years, 4 males, 13 females)	GSM handset against left and right ear, 902 MHz SAR_{10g} 0.82 W/kg 6 min RF EMF and 2 x 6 min sham at each side	No effect of exposure.	Single blind, partially counterbalanced, cross-over. EMF interference with recorded EEG tested. Bonferroni correction for multiple comparisons ($p < 0.0083$).	Kwon et al. (2010a)

EEG (ERD and ERS in alpha band and three ERP components) recorded during exposure 103 volunteers of 3 different age groups: 41 adolescents (13– 15 years; 21 males, 20 females) 42 young adults (19–40 years; 21 males, 21 females) 20 elderly (55–70 years; 10 males, 10 females)	GSM (2G) handset against left and right ear, 894.6 MHz SAR_{10g} 0.7 W/kg UMTS (3G) standard handset against left and right ear, 1900 MHz SAR_{10g} 1.7 W/kg About 55 min	Increased N1 amplitude during 2G exposure in one task, and delayed alpha ERD and ERS response during 2G and 3G exposures in the other task. All effects independent of age.	Double blind, randomized, partially counterbalanced, cross-over. No information about steps to prevent EMF interference with EEG. No correction for multiple comparisons. For cognitive function see Section 5.2.1; for resting EEG see (Croft et al., 2010) in Sections 5.2.2.2.	Leung et al. (2011)

Abbreviations: 2G: second-generation wireless telephone technology; 3G: third-generation wireless telephone technology; AEP: auditory evoked potentials; CW: continuous wave; EEG: Electroencephalogram; ERD: event related desynchronisation; ERP: event-related potentials; ERS: event related synchronisation; GSM: Global System For Mobile Communication; MEG: magneto-encephalography; MEP: motor evoked potentials; TDMA: Time Division Multiple Access; UMTS: The Universal Mobile Telecommunications System.

[a] If not otherwise stated, only healthy volunteers participated. The maximal number of volunteers participating in the analyses is provided.

[b] SAR with relevant averaging volume (e.g. SAR_{10g}) is specified if included in the paper.

[c] The highest number of participants included in any single analysis was 52; the age range and the number of males and females are based on all study participants.

5.2.2.2 Resting/waking EEG

Studies with adults

In an early study Röschke and Mann (1997) investigated effects of GSM mobile phone emissions on the resting EEG in 34 male volunteers. Exposure was supplied by a digital GSM mobile phone (900 MHz) positioned at a distance of 40 cm from the vertex of the participant, giving a power density 0.05 mW/cm^2 (0.5 W/m^2). In a single-blind cross-over design, participants were exposed for approximately 3.5 minutes to both a sham and active field exposure. The two exposure conditions were separated by a break of approximately 30 minutes and the order was random and counterbalanced. Four EEG frequency bands in the range 1–15 Hz were analysed separately. No effects of exposure were observed. [However, given that no SAR was provided and the large distance of the exposure source to the participant, the exposure was likely negligible and therefore may make these results uninformative].

In a study exploring potential effects of RF EMF on resting EEG, Hietanen et al. (2000) exposed 19 participants to exposure signals from 5 different mobile phone handsets (three analogue with different types of antennas and two GSM at 900 and 1800 MHz, respectively) and a sham condition. Each exposure was applied single blind, lasted for 20 minutes, and was both preceded and followed by 5 minutes of sham exposure. The output power of the mobile phones was controlled and set to emit at maximum output power, which was between 1 and 2 W [but with no specification for each mobile phone]. The phones were placed on a pillow approximately 1 cm from the head of the participant. All exposures were on separate days and applied in a random order. Resting EEG was continuously recorded during exposure. Shielding and other preventions were taken to avoid any potential influence of the RF exposure on the recorded EEG signal, and testing indicated no interference. For each of four cortical regions analyses were performed for the absolute and relative powers in four frequency bands between 1.5 and 25 Hz. (Relative power was the amount of EEG activity in the actual band divided by that in all other bands). An increase in absolute power in the delta band of the EEG recording (p = 0.004) during exposure to one of the analogue phones was observed, however, no difference was seen in the relative power of the same band, and no changes were observed during any of the other exposures. [It is not clear why only one of the three analogue phones was related to a change in resting EEG. The phones all used different antenna types (a helix, fixed whip, or extended whip antenna) which would likely result in different exposure distributions; however, no exposure or dosimetric data were provided for the individual models and therefore the interpretation of this result is difficult. In addition, this study was conducted single blind and even though the significance criterion was set to 0.01, it is not unlikely that at least one of the high number of comparisons (36) would reach significance by chance.]

In a study that also investigated the sleep EEG, Huber et al. (2002) endeavoured to look at the effects of a handset-like signal on the waking EEG. They attempted to explore whether the pulse modulation of the signal was an important factor. The 16 male volunteers underwent three exposure conditions at weekly intervals: a pulse modulated handset-like signal, a continuous wave signal, and a sham condition without exposure, all on separate days before sleep and with order of conditions counterbalanced. Both RF signals were at 900 MHz and were emitted by an antenna placed 11.5 cm from the left side of the head resulting in SAR_{10g} of 1 W/kg. The duration of exposure was 30 minutes following which EEG was recorded continuously prior to the onset of sleep and then subsequently during sleep (sleep results are presented in Section 5.4.2.3). Spectral analysis (1 – 25 Hz frequency range) showed an enhancement of the EEG during waking prior to sleep onset in the alpha frequency range, around 10 Hz for one single frequency bin (0.25 Hz width), ($p < 0.05$) following the pulse modulated exposure condition, but not following the continuous wave exposure.

In an attempt to replicate the findings of Huber et al. (2002), Perentos et al. (2007) investigated the effects of continuous wave versus pulse modulated RF EMF exposure on the resting EEG. Using a model handset that approximated a GSM mobile phone, 12 participants attended a 2-hour recording session in which RF exposure occurred for two 15-minute intervals (15-minute continuous wave and 15-minute pulse modulated, both at 900 MHz, SAR_{10g} = 1.56 W/kg), as well as a 15-minute sham exposure, all while resting EEG was recorded. The handset was placed against the left side of head, but it did not produce thermal and auditory cues during operation. The order of exposures were counterbalanced and randomly assigned. Analyses were done by comparing data recorded before and after exposure for four predefined frequency bands (delta, theta, alpha and beta). No changes to alpha EEG power, as well to theta and beta powers, were found for either modulated or unmodulated radiofrequency fields. In the delta band a main effect was observed for exposure ($p = 0.034$), but post hoc comparisons between the exposure conditions did not reveal any significant differences (comparisons with sham resulted in $p = 0.5$ for the pulse modulated exposure and $p = 0.082$ for the continuous wave exposure; significance criterion in the post hoc analyses was $p < 0.002$ by Bonferroni correction). They also tested whether exposure had any effect on non-linearity features of the EEG signal, but without observing any significant effect. [This study failed to replicate the finding by Huber et al. (2002) of increased power by the pulsed exposure in the alpha band. However, several features differed between the studies. Among these are the exposure system, methods for statistical analyses of EEG power spectra and difference in number of volunteers (somewhat lower in this latter study). The study by Perentos et al. (2007) was designed to be double blind, but since the EMF exposure resulted in visible artefacts during exposure, the study was considered single blind.]

D'Costa et al. (2003) investigated the potential effects of GSM 900 MHz mobile phone exposure on the EEG using a mobile phone positioned horizontally behind the head, with the antenna closest to the head and the tip 2 cm from the head. Ten participants were exposed single blind to two different conditions, one with RF exposure generated by a GSM mobile phone with the speaker disabled and configured to transmit at full-radiated power (mean output power 0.25 W) and one generated by a non-modified GSM mobile phone in active standby mode. In each of these conditions, EEG was recorded during five 5-minute intervals with the mobile phone on and five 5-minute intervals with the phone off (sham). The order of the intervals was random and there was a short break between them. For each of the exposure conditions, sham and real exposures were compared. This was done separately for three brain areas (frontal, central and occipital) and for four EEG power bands (delta, theta, alpha, and beta). No significant difference was observed in recorded EEG between the standby mode and sham exposure. Differences in EEG power were observed for the full-power condition compared to sham, with decreases reported in the alpha and beta bands in the central region ($p = 0.038$ and 0.045) and decreases in the beta band in the occipital region ($p = 0.049$). [No correction for multiple comparisons was applied in this study. Therefore the few reported effects may well be due to chance even though they included the brain area closest to the antenna. Uncertainties in results are also related to the low number of participants. While output power of the phones was at maximum level, the exposure is not well characterised and SAR is not provided. (In standby mode the phone most likely transmitted one burst of signal lasting only for approximately 2 seconds when the phone was switched on (Hansson Mild, Bach Andersen & Pedersen, 2012). The authors did not inform about any measures to prevent or control for influence of the exposures on the recorded EEG signal.]

In four studies Hinrikus and colleagues (2004; 2008a; 2008b; 2011) tested effects of a 450 MHz pulse modulated EMF exposure on EEG in awake resting volunteers. In all studies the same exposure setup was used: the signal was emitted at 1 W output power by the same quarter wave antenna placed 10 cm from the side of head. The pulse frequency varied between studies, while the duty cycle was always 50%. Information about

SAR was only included in the two later studies (Hinrikus et al., 2008a; Hinrikus, Bachmann & Lass, 2011) and was estimated according to standardized methods, resulting in a spatial peak SAR of 0.30 W/kg averaged over 1 g. In all studies, a narrow band filter (0.2 Hz width) was used to remove EEG frequencies around the pulse modulation frequency used in the actual exposure. During the exposure session, 60 seconds with RF exposures alternated with 60 seconds without and in all studies the EEG power in neighbouring segments (one with and one without exposure) was compared. Similar to the real exposure sessions, sham sessions were provided. Sham and real exposure sessions, as well as the different pulse modulations, were applied in a random order. In a single blind study, Hinrikus et al. (2004) first investigated the effects of low frequency modulated EMF by exposing 20 participants to a 450 MHz signal pulse modulated at 7 Hz. Participants underwent an exposure and a sham condition, each at separate days. During each session their EEG was continuously recorded, lasting approximately 22 minutes. The alpha and theta bands as well as total EEG power (0.5–38 Hz) were analysed for eight different brain regions and mean values as well as standard deviations of EEG activity levels were compared between the RF EMF and sham exposure conditions. Changes in the EEG were reported; however these changes were highly variable between individuals and did not reach overall significance. [No correction for multiple comparisons was reported.]

The following studies were conducted double blind. Hinrikus et al. (2008b) explored the effects of different modulation frequencies (7, 14, and 21 Hz) on the EEG. The study included 13 volunteers and each was exposed in two RF EMF sessions and two sham sessions at separate days, approximately at the same time of day. All sessions lasted 40 minutes starting with a 10-minute reference interval with no exposure, and immediately after the participants were exposed for 30 minutes (10 minutes of each modulation frequency in random order, or 30 minutes for the sham condition). EEG power in each of four frequency bands in the range 4–38 Hz was analysed separately for the first 30 seconds and the last 30 seconds of the 60-second exposure segments. Analysis of variance, including the initial reference interval and the three exposure conditions, indicated some effects of exposure mainly in the first 30 seconds of the segments. Similar analyses for the sham sessions did not reveal any statistical differences. Pairwise comparisons with the reference condition and each of the three exposure types showed no significant differences at the modulation frequency of 7 Hz. For the 14 Hz modulation condition, alpha (8–13 Hz) and beta (15–20 Hz) frequencies were both increased in the first half-period of the exposure interval (30 s), and for the 21 Hz modulation, increased powers were observed for these EEG frequencies as well as for the higher range of the beta band (22–38 Hz) (p-values ranged from 0.0058 to 0.042, with Bonferroni correction for multiple comparisons). No significant differences were obtained for the theta (4–6.8 Hz) band. [This study, which was carefully conducted by filtering the modulation frequencies from the recorded EEG signals, failed to include any statistical comparisons between the sham sessions and the exposure sessions. However, graphs showing mean values and standard deviations for the sham exposures as well as for the reference and RF exposures, indicate that in all cases with a significant difference between the RF exposure and the reference condition, also the difference between the respective sham and RF conditions would be significant (the sham signals exhibited smaller mean values than the respective references and not larger standard deviations, thus making the differences compared to the RF conditions larger and a with higher statistical significance). It should be noted that the number of participants in this study was low.] In a similar study, Hinrikus et al. (2008a) followed-up these results and explored the effects of exposure and whether effects differed for individuals. The experiments were carried out on four different groups of participants (with sample sizes ranging from 13 to 19), with each group receiving different combinations of modulation frequencies (1: 7 Hz; 2: 14 and 21 Hz; 3: 40 and 70 Hz; 4: 217 and 1000 Hz). Exposure to each of the pulse modulated signals lasted 20 minutes (10 cycles with exposure on and off), resulting in 40-minute sessions (20 minutes for the 7-Hz group). Similar sham sessions were conducted on separate days, with each even minute representing exposure and each odd minute representing sham. The same four frequency bands were analysed as in the previous study. Descriptive data suggested increases in both alpha and beta EEG frequencies during the first 30 seconds of the exposure intervals compared to the initial period of the previous sham intervals. Individual results varied, but indications of increased EEG power during exposure were reported to be most stable in the beta 1 band (15–20 Hz). In this band the percentage of subjects significantly affected was similar across modulation frequencies used ($p < 0.05$ with Bonferroni correction), except for the 1000 Hz pulse modulation where no effects were seen (7 Hz: 3 participants (16 %); 14 Hz: 4 participants (31%); 21 Hz: 3 participants (23%); 40 Hz: 3 participants (20%); 70 Hz: 2 participants (13%); 217 Hz: 3 participants (16%); and 1000 Hz: 0 participants). Similar analyses were not provided for the other EEG bands. No significant difference was observed for any individual for the sham sessions. [The findings in the study were only based on comparisons between the RF segments and the preceding sham segments in each session separately. Given the very short interval between segments with exposure on and exposure off, the possibility of carry-over effects cannot be excluded. Statistical comparisons between the RF and sham sessions would have added confidence to the results.]

Using a somewhat different approach, Hinrikus et al. (2011) investigated the influence of different modulated RF signals on the EEG, using higher frequency resolution than in the earlier studies by the same group. Resting eyes closed EEG was recorded during exposure in two groups of volunteers while lying in a relaxed position in a dark room. Group one was exposed to a 450 MHz signal modulated at 7, 14, and 21 Hz separately, while group two was exposed to the same signal modulated at 40 or 70 Hz. For group one, 14 participants were randomly exposed to the three different modulation frequencies over a period of 30 minutes, and with a similar sham session on another day. For group two, 14 participants were randomly exposed to the two different modulation frequencies over a period of 20 minutes and during the same session a 20-minute sham exposure was included. Ten or 11 EEG frequency bands (each with 1 Hz width) were analysed for each modulation used. To account for the total number of statistical comparisons, Bonferroni correction was used with a significance criterion of $p < 0.0008$. Results showed no changes in EEG during sham sessions or from 7 Hz modulation. Increased power was observed at 7 and 10.5 Hz with 14 Hz modulation, at 10.5 and 16 Hz with 21 Hz modulation, at 10, 20, and 30 Hz from 40 Hz modulation, and at 17.5 and 35 Hz with 70 Hz modulation ($p < 0.0008$). No increase in EEG power was detected at EEG frequencies higher than the modulation frequency. When expressing EEG frequencies as rations of the modulated frequency applied, all observed significant differences in power occurred at 0.25, 0.5 and 0.75, which was predicted from the theoretical model. [This suggestion of modulation frequency specific enhancements of the EEG is in contrast to recent sleep studies in which changes occurred in similar regions of the EEG regardless of modulation frequency applied (Schmid et al., 2012a) (Section 5.2.2.3). Also in this study the authors only compared the short RF segments with the preceding sham segments and failed to include analyses comparing results from the whole RF session with those from the sham session. Given the very short interval between segments with exposure on and exposure off, the possibility of carry-over effects cannot be excluded.]

Curcio et al. (2005) investigated whether a GSM mobile phone signal affects the EEG and whether this only occurs during exposure or if the effect continues after exposure cessation. Twenty participants were randomly assigned to one of two experimental groups, with group 1 receiving 45-minute EMF exposure prior to resting EEG recording, and group 2 receiving 45-minute EMF exposure, part of which (the last 7 minutes) occurred during the resting EEG recording. To ensure that no sound from the transmitting mobile phone was heard as it was held 1.5 cm from the left side of head, acoustic noise was delivered by a loudspeaker. Both groups underwent three conditions: a baseline (with no exposure and no phones placed at the head), a sham (no exposure but phone present), and a real exposure (phone switched on at left side of head). The conditions were at least 48 hours apart and in random order. The analyses included the EEG frequency range from 1 to 24 Hz with 1 Hz resolution, and were performed for signals from each of five electrodes. Results from analyses of variance with $p < 0.003$ (Bonferroni correction for multiple comparisons) were followed up with post hoc analyses, which also were adjusted for multiple comparisons (Jeffe's test). Results showed an increase in EEG power in one brain location (the central one) in the alpha frequency range (at 9 and 10 Hz) when compared with both the baseline ($p = 0.02$) and sham (p: 0.004 and 0.4 for 9 and 10 Hz, respectively) conditions. In addition, at parietal sites this increase in alpha (11 Hz) was found to be higher in group 2 than group 1, suggesting that the effect may be greater during exposure than following exposure. [No information was provided concerning time of day for the different sessions or about measures to prevent the RF EMF exposure to interfere with the recorded EEG signal. Also the low number of participants should be noted when weighting this study.]

Regel et al. (2007a) also investigated effects on the resting EEG, specifically looking at whether pulse modulation played a role in mediating effects on brain activity. EEG was recorded in 24 participants who underwent three 30-minute exposure conditions: a 900 MHz GSM pulse modulated signal, a 900 MHz continuous wave signal, both of which were applied at 1 W/kg (averaged over 10 g) by a planar patch antenna placed 11,5 cm from the left side of the head, and a sham condition. Each exposure condition was at separate days, but at the same time of day for each participant, and the order of conditions was randomized and counterbalanced. The EEG was recorded at several different time-points: a baseline recording prior to exposure, then at 0, 30, and 60 minutes after exposure cessation and analyses included frequencies in the range 5–15 Hz with 0.5 Hz resolution. Analysis revealed higher EEG power in the alpha frequency range (10.5–11 Hz) 30 minutes after the pulse modulated exposure ($p < 0.01$), and lower alpha power (12 Hz) 60 minutes after pulse modulated exposure ($p < 0.03$). No effects were seen following the continuous wave exposure, suggesting that pulse modulation of the signal is required to induce effects on the EEG. [However, there is no indication that adjustments for multiple comparisons were done for the provided EEG analyses. To reduce variability, the EEG powers were related to the EEG recorded at baseline before comparisons between real and sham exposures.]

Vecchio et al. (2007) tested whether EMF from a GSM mobile phone is able to modulate interhemispheric synchronization of cerebral rhythms, specifically EEG alpha rhythms. Ten participants underwent two exposure conditions (real and sham exposure) separated by a week and each lasting 45 minutes, with resting EEG recorded for 5 minutes before and at the end of the exposure period. The exposure consisted of a 902.4 MHz GSM handset-like signal produced by a standard mobile phone positioned 1.5 cm from the side of the head. Coherence between left and right hemispheres was analysed for four brain areas (frontal, central, parietal and temporal) and for five frequency bands (delta band, theta band and three alpha bands, each 2 Hz wide). EEG coherence was found to be lower in the alpha range (individual alpha frequency (IAF) – 2 Hz to IAF + 2 Hz, about 8–12 Hz) in the exposure condition between frontal areas ($p < 0.003$), whereas coherence in a similar alpha range (IAF – 2 to IAF Hz, about 8–10 Hz) was higher in the exposure condition between temporal areas ($p < 0.04$), which are closest to the site of stimulation. Following this finding, the same authors investigated whether these effects might vary on physiological aging as a sign of changes in the functional organization of cortical neural synchronization (Vecchio et al., 2010). Using the same experimental procedures and same exposure (here informed that SAR_{10g} was 0.5 W/kg), 16 elderly participants and 15 young participants (10 from Vecchio et al. (2007) and 5 added in the current study) underwent real and sham exposure for 45 minutes. The same brain areas and frequency bands were included in the analyses as for the previous study. Compared with the young subjects, the elderly subjects showed an increase of inter-hemispheric coherence in the alpha frequency range (approximately 8–12 Hz) at a frontal region ($p < 0.00026$) and in a somewhat more restricted alpha frequency range (approximately 10–12 Hz) at a temporal region ($p < 0.04$) during the GSM condition. Based on these two studies, the results suggest that GSM exposures influence inter-hemispheric synchronization of alpha rhythms, and that this varies as a function of age. [It was informed in the latter paper that the order of the two exposure conditions was pseudo-randomized to obtain the same number of participants with real exposure first and sham first, while no information about assignment of exposure order was provided in the first paper. Similarly, only the second paper informed that all exposures were approximately at the same time of day. To test for blinding, the participants in the first study were requested to report any possible heating and buzzing produced by the device. None of them reported sensing this. In both studies adjustments for multiple comparisons were done in post hoc tests by applying Duncan's test.]

In one of the largest studies performed, Croft et al. (2008) investigated the effects of GSM mobile phone handset exposure on alpha activity in the resting EEG. Two exposures (real and sham) were used, with 120 participants recruited for the study, half receiving left hemisphere exposure and the other half receiving right hemisphere exposure. For each participant the exposure conditions were one week apart and the order of real and sham was random and designed to be counterbalanced. Exposure consisted of a 894.6 MHZ GSM handset-like signal ($SAR_{10g} = 0.67$ W/kg) that was produced by a mobile phone handset that was modified to prevent the participants from hearing any sound from the phone when operating. Participants performed a battery of tests, followed by an electro-oculographic calibration task. Exposure was then applied for 30 minutes in which resting EEG was recorded and another test battery performed. Following exposure, resting EEG was again recorded. Based on previously published results, the authors hypothesized that a general increase in the alpha band would occur during exposure, which was supported by their results ($p = 0.022$, one-tailed) and that the increase in alpha activity during exposure would be greater at the same side of exposure than at the opposite. For this latter case, only a trend was found ($p = 0.066$, one-tailed). A number of exploratory analyses were also performed with some positive findings (in these cases p-values adjusted for multiple testing). [The study was well designed and conducted and generally methodology is carefully reported. The blinding of exposure conditions was ensured by reducing acoustic cues and omitting heat from the phones to be sensed, with results suggesting that the participants could not distinguish between real and sham exposure. The designed counterbalance may have been distorted by dropouts and data loss reducing the number of volunteers to 94–109 in individual analyses.]

Hountala et al. (2008) reported on two studies that investigated the effects of different EMF signals on spectral power coherence (SPC) of the EEG, which estimates the functional interaction between two brain regions. The first experiment used a 900 MHz EMF (output power 64 mW) and the second a 1800 MHz EMF (output power 128 mW), both emitted by a dipole antenna at a distance of 20 cm from the participants head, and both unmodulated. The duration of exposure was not clear, but was most likely 45 minutes which corresponds to the duration of each series of tests. Exposure was applied single blind and the two exposure conditions were two weeks apart and applied in a random order. The SPC was calculated for the pre-stimulus EEG signal while participants performed an auditory memory task. For the analyses, the results from the sham sessions were combined for both groups. Results showed that the SPC under EMF exposure was different for the genders ($p < 0.001$). For males no significant difference in the overall SPC was observed between the off condition and the 900 MHz condition, but the SPC was significantly reduced compared to the other conditions when applying the 1800 MHz exposure. Females, however, displayed a significant increase in the SPC under the 900 MHz EMF condition and the 1800 MHz condition compared to off. [However, it should be noted that no p-values for the post hoc statistics were provided in this study, although Bonferroni correction was applied at $p < 0.05$. Little information is provided about the exposure system; however in another paper, the same group (Papageorgiou et al., 2006) provided details about the antenna used and informed that the electric field strength at the place of the head of participants was 3 V/m (see Section 5.2.2.1). Apparently the same exposure system was used in this study.]

Kleinlogel et al. (2008a) performed a study to investigate the effects of both GSM and UMTS mobile phone technologies on the EEG and wellbeing. Fifteen participants underwent four different 30-minute exposure conditions at weekly intervals in random order (plus an initial training session): a GSM base station-like signal (900 MHz) with SAR similar to a mobile phone handset exposure (1.0 W/kg averaged over 10 g), a weak UMTS handset-like signal (1950 MHz, SAR_{10g} = 0.1 W/kg), a high UMTS handset-like signal (1950 MHz, SAR_{10g} = 1.0 W/kg), and sham. Both RF EMF signals were emitted by a small antenna mounted at the normal mobile phone position. EEG wires were configured to prevent the EMF signals from interfering with the recorded EEG signals, and testing confirmed no interference. Before, at the beginning and end of and immediately after exposure resting EEG was recorded. Separate analyses were performed for the different time periods of EEG recordings and for each period six frequency bands in the range 1–32 Hz were included. No significant effects of any of the exposures were seen on the EEG. [During exposure and between the resting EEG recordings, ERP stimuli were provided (data published in Kleinlogel et al. (2008b), see the ERP section of the current chapter).]

Studies in adults and with uncertainties related to inclusion criteria

Eibert et al. (1997) investigated whether a GSM mobile phone signal may influence the EEG. Using a between-subjects design, 52 participants were exposed to a GSM mobile phone signal (900 MHz), positioned at a distance of approximately 45 cm from the head with an E-field of approximately 40 V/m. During a 30-minute test period the exposure started after 10 minutes and lasted 10 minutes). No effects of exposure were reported. [The results of the study cannot be further evaluated since no EEG data nor any results from the statistical analysis were provided beyond the statement of no significant differences.]

In a between-subjects study looking at potential effects on the nervous system, De Sèze et al. (2001) investigated the potential effects of mobile phone exposure on healthy and epileptic volunteers. Using a standard GSM mobile phone (900 MHz), 30 volunteers were exposed for an unspecified amount of time using a test SIM card which resulted in a peak output power of 2 W. When comparing data from before and after the RF EMF exposure, a small increase in the alpha and beta frequency ranges was reported in both the healthy and epileptic volunteers. No significant changes were reported for the healthy group from before to after sham exposure. [No statistics were provided and there was no statistical comparison between the RF EMF exposed and sham exposed groups. Therefore the results cannot be evaluated.]

In the same single blind study where Croft et al. (2002) measured effects on phase-locked neural responses to auditory stimuli (see Section 5.2.2.1) they aimed to test whether exposure to a GSM mobile phone affects the EEG as a function of time. The 24 participants were exposed to a mobile phone handset for 20 minutes (either turned on or off) while resting EEG were recorded. Spectral analysis of the EEG showed an exposure-related decrease in delta (1–4 Hz) and increase in alpha (8–12 Hz) activity ($p < 0.05$) as a function of exposure duration. [Despite these findings, the study is not included in the analysis because of lack of verification of exposure level, which was subsequently pointed out by Croft et al. (2008)].

In a study specifically aimed at testing potential gender differences, Papageorgiou et al. (2004) investigated the gender-related influence of mobile phone EMF on brain activity. Ten women and nine men performed a short memory task both with and without exposure to a 900 MHz signal emitted by an antenna while their EEG was recorded. The series of tests lasted for 45 minutes and were performed during exposure [the exposure duration was not explicitly given]. Differential results were obtained based on gender, with decreasing EEG power in males and increasing EEG power in females during RF exposure. [There is no indication that exposure conditions in the study were blinded to the participants. The low number of male and female participants respectively should also be noted.]

Mobile phone related studies including patients

Vecchio et al. (2012b), who had previously reported that mobile phone exposure modulated inter-hemispheric synchronization of temporal and frontal resting EEG rhythms in normal young and elderly subjects (Vecchio et al., 2007; Vecchio et al., 2010), investigated whether exposure to mobile phone RF EMF also modulates the inter-hemispheric coupling of resting EEG rhythms in epilepsy patients. EEG was recorded both before and after GSM handset exposure (902.4 MHz, SAR_{10g} = 0.5 W/kg) in 10 right-handed epileptic volunteers and compared with 15 age- and sex- matched controls. Each participant underwent two 45-minute exposure sessions (real and sham) separated by a week. Randomization was used to determine the sequence of real and sham exposures in such a way that counterbalancing was obtained. The coherence of the EEG data was computed in both the baseline pre-stimulus period and in the post-stimulus period for both exposure conditions and separate analyses were done for four cortical areas for five EEG frequency bands. After Bonferroni correction for multiple comparisons in post hoc analyses, compared to the control group epileptic participants showed a statistically significant higher inter-hemispheric coherence following exposure at frontal ($p < 0.0001$ at alpha 2 (individual alpha frequency -2 Hz)) and temporal ($p < 0.005$ at alpha 3 (individual alpha frequency + 2 Hz)) sites compared to sham exposure.

Studies including children or adolescents

In a large study, Croft et al. (2010) examined the effects of 2G (GSM) and 3G (UMTS) mobile phone exposures on EEG spectral power in three different age groups. EEG was recorded during exposure to a modified GSM mobile phone handset and a standard UMTS handset in 103 participants separated into 41 adolescents, 42 young adults, and 20 elderly. Each participant underwent three 55-minute exposure conditions, a 2G exposure (894.6 MHz, SAR_{10g} = 0.7 W/kg), a 3G exposure (1900 MHz, SAR_{10g} 1.7 W/kg), and a sham condition on separate days at least 4 days apart. The order of exposure conditions and side of exposure were counterbalanced across participants, exposures were randomly assigned, and for each individual, side of exposure and time of day were consistent. None of the phones produced any audible sound during operation. During the exposures two different cognitive tasks (auditory 3-stimulus oddball task and N-back task) were performed. While performance and potentials recorded during the tasks were reported elsewhere ((Leung et al., 2011), see Sections 5.2.1 and 5.2.1.1), Croft et al. (2010) reported analysis of resting EEG. The primary aim was to test for changes between power in the alpha band recorded immediately before exposure and that recorded during exposure (before, between and after cognitive tasks). Results showed increased alpha power in the 2G exposure condition ($p = 0.043$) in the young adults group, with no effects seen for the adolescents or elderly participant groups. No effect of 3G exposure was found for any of the age groups. [The authors did not report about any measures taken to control for interference between the EMF signal and the EEG signal.]

Table 5.2.5. Studies assessing resting EEG

Endpoint and Participants[a]	Exposure[b]	Response	Comment	Reference
Mobile phone handset related studies with healthy adults				
EEG (1–15 Hz, 4 bands) recorded during exposure 34 male volunteers (21–35 years)	GSM handset-like signal 40 cm from subjects head, 900 MHz Peak output power 8 W, average power density 0.05 mW/cm^2 (0.5 W/m^2), 3.5 min	No effect of exposure.	Single blind, randomized, cross-over. No correction for multiple comparisons.	Röschke & Mann (1997)
EEG (1.5–25 Hz, 4 bands) recorded during exposure 19 volunteers (28–57 years; 10 males, 9 females)	Three analogue phones (900 MHz), two GSM phones (900 and 1800 MHz), 1 cm from subjects head Peak output power 1–2 W [Not specified for each phone.] 20 min	Decrease in absolute power in the delta band in one brain region for one of the analogue exposures, however, no difference was seen in the relative power of the same band. No other changes were observed.	Single blind, randomized, cross-over. Measures to prevent RF EMF interference with recorded signals. Significance criterion $p < 0.01$. No other correction for multiple comparisons.	Hietanen et al. (2000)
EEG (1–25 Hz, 0.25 Hz resolution) recorded after exposure and before a night-time sleep episode 16 male volunteers (20-25 years)	GSM handset-like signal 900 MHz, PM 2, 8, 217 and 1736 Hz (12.5 % duty cycle) and CW, 900 MHz; both emitted by planar antenna 11.5 cm from left side of head SAR_{10g} 1 W/kg 30 min	EEG spectral power was increased in the alpha frequency range (one frequency bin at approx. 10 Hz) after PM GSM.	Double blind, counterbalanced, cross-over. No correction for multiple comparisons.	Huber et al. (2002)

EEG (2–32 Hz, 4 bands) recorded before, during and after exposure (only before and after analysed) 12 volunteers (19–32 years; 6 males, 6 females)	Two different signals emitted by a model handset at left side of head: GMS-like PM (2, 8, 217, 1736 Hz) and CW, 900 MHz SAR_{10g} 1.56 W/kg 15 min	No effects of exposure.	Partial replication of Huber et al.(2002), Single blind, randomized, counterbalanced, cross-over. Small sample. In the delta band a main effect was observed for exposure (p = 0.034), but post hoc comparisons between the exposure conditions did not reveal any significant differences. Bonferroni correction for multiple comparisons in post hoc analyses.	Perentos et al. (2007)
EEG (1–18 Hz, 4 bands) recorded during exposure 10 volunteers (10–30 years; 5 males, 5 females)	GSM phone horizontally behind head with antenna 2 cm from head, 900 MHz 1) Mean output power 0.25 W 2) Standby mode 5 x 5-min real and 5 x 5-min sham	No effect in standby mode. 0.25 W mean output power: decreases in alpha and beta bands in the central brain area and in beta band in occipital area; no effect on delta and theta bands and no effects in frontal area.	Single blind, randomized, cross-over. Small sample. No information about steps to prevent EMF interference with recorded EEG. No correction for multiple comparisons.	D'Costa et al. (2003)
EEG (4–38 Hz, primarily theta and alpha) recorded during exposure 20 volunteers (19–23 years; 11 males, 9 females)	Quarter-wave antenna 10 cm from left side of head, 450 MHz, PM at 7 Hz (duty cycle 50%) Output power 1 W; SAR 0.30 W/kg (Hinrikus et al., 2008a) Approx. 22 min (1 min on/1 min off)	No effect of exposure.	Single blind, randomized, cross-over. PM frequency filtered from EEG signals. No correction for multiple comparisons.	Hinrikus et al. (2004)
EEG (4–38 Hz, 4 bands) recorded during exposure 13 volunteers (21–30 years; 4 males, 9 females)	Quarter-wave antenna 10 cm from the left side of the head, 450 MHz, PM at 7, 14, and 21 Hz separately (duty cycle 50%) SAR_{1g} 0.30 W/kg (Hinrikus et al., 2008a) 10 min per modulation (1 min on/1 min off)	No differences in conditions were seen at the modulation frequency of 7 Hz. For the 14 and 21 Hz modulations, alpha (8-13 Hz) and beta (15-20 Hz) frequencies were both increased in the first half-period of the exposure interval (30 s).	Double blind, randomized, cross-over. Exposure conditions were compared to an initial reference condition and not to sham. Small sample. PM frequency filtered from EEG signals. Bonferroni correction for multiple comparisons.	Hinrikus et al. (2008b)

EEG (4–38 Hz, four bands) recorded during exposure in 4 groups: 1) 19 volunteers (19–23 years; 10 males, 9 females) 2) 13 volunteers (21–30 years; 5 males, 9 females) 3) 15 volunteers (21–24 years; 8 males, 7 females) 4) 19 volunteers (21–24 years; 8 males, 11 females)	Quarter-wave antenna 10 cm from left side of head, 450 MHz, PM at 7 Hz (group 1), 14 and 21 Hz (group 2), 40 and 70 Hz (group 3), 217 and 1000 Hz (group 4); (all: duty cycle 50%) SAR_{1g} 0.30 W/kg 20 min per modulation (1 min on/1 min off), except 7 Hz (group 1): 20 min (1 min on/1 min off)	Significant changes in EEG power for some individuals at all modulation frequencies except 1000 Hz. For all other frequencies, the rate of individuals affected was 13–31%.	Double blind, randomized, cross-over within sessions. Partly small samples. PM frequency filtered from EEG signals. Bonferroni correction for multiple comparisons.	Hinrikus et al. (2008a)
EEG (4–42 Hz, 12 frequency bands, each 1 Hz wide) recorded during exposure in two groups during exposure 1) 14 volunteers (20–27 years; 6 males, 8 females) 2) 14 volunteers (21–24 years; 7 males, 7 females)	PM signal emitted by quarter-wave antenna 10 cm from left side of head, 450 MHz (duty cycle 50%) SAR_{1g} 0.303 W/kg 1) PM at 7, 14, and 21 Hz, 30 min 2) PM at 40 and 70 Hz, 20 min 10 min per modulation (1 min on/1 min off)	Increased power at 7 and 10.5 Hz with 14 Hz modulation, at 10.5 and 16 Hz with 21 Hz modulation, at 10, 20, and 30 Hz with 40 Hz modulation, and at 17.5 and 35 Hz with 70 Hz modulation	Double blind, randomized, cross-over within each group). Small samples. PM frequency and its third harmonics filtered from EEG signals. Bonferroni correction for multiple comparisons (significance criterion: 0.0008).	Hinrikus et al. (2011)
EEG (1–24 Hz, 1 Hz resolution) recorded during (n = 10) and after exposure (n = 10) 20 volunteers (22–31 years; 10 males, 10 females)	GSM mobile phone 1.5 cm from left side of head, 902.4 MHz Max SAR 0.5 W/kg 45 min	Increased EEG alpha power (9 and 10 Hz) in central brain region, and alpha power (11 Hz) was greater during than after exposure in parietal region. No effects in three other brain regions.	Double blind, randomized, cross-over. Small sample for each group. No information about steps to prevent EMF interference with recorded EEG. Bonferroni correction for multiple comparisons in main analyses (significance criterion: 0.003) and Scheffe's test in post hoc analyses. For sleepiness see Section 5.2.4.	Curcio et al. (2005)
EEG (5–14 Hz, 0.5 Hz resolution) recorded before and 0, 30, and 60 min after exposure 24 male volunteers (19–25)	GSM PM and CW signal emitted by planar patch antenna 11.5 cm from left side of head, 900 MHz SAR_{10g} 1 W/kg 30 min	Higher alpha power (10.5–11 Hz) 30 min after the PM exposure, and lower alpha power (12 Hz) 60 min after PM exposure. No effects following the CW exposure.	Double blind, randomized, counterbalanced, cross-over. No correction for multiple comparisons. For cognitive function see Section 5.2.1.	Regel et al. (2007a)

EEG (coherence; about 2–12 Hz, 2 Hz resolution) recorded before and after exposure 10 male volunteers (20–36 years)	GSM mobile phone 1.5 cm from left side of head, 902.4 MHz, PM 217 Hz No SAR mentioned, but follow-up study (Vecchio et al., 2010) had SAR_{10g} 0.5 W/kg 45 min	Decreased alpha (about 8–12 Hz) coherence at frontal areas and increased alpha about 8–10 Hz) coherence at temporal areas. No effects in central and parietal areas and in delta and theta bands.	Double blind, cross-over. Small sample. Correction for multiple comparisons in post hoc tests (Duncan).	Vecchio et al. (2007)
EEG (coherence in about 2–12 Hz, 2 Hz resolution) recorded before and after exposure 16 elderly volunteers (47–84 years; 7 males, 9 females) 15 young male volunteers (20–37 years)	GSM mobile phone1.5 cm from left side of head, 902.4 MHz, PM 8.33 and 217 Hz SAR_{10g} 0.5 W/kg 45 min	Compared with the young, the elderly subjects showed an increase of inter-hemispheric coherence in the alpha frequency range (about 8–12 Hz) at both frontal and (about 10–12 Hz) temporal regions during exposure. No differences for central and parietal regions.	Double blind, randomized, cross-over. Correction for multiple comparisons in post hoc tests (Duncan).	Vecchio et al. (2010)
EEG (8–12 Hz in primary analyses) recorded during and after exposure 120 volunteers (18–69 years; 46 males, 74 females). Due to data loss/dropouts, 94–109 participants in each analysis	GSM handset-like signal (half participants received left and half right side exposure), 894.6 MHz, PM 217 Hz SAR_{10g} 0.67 W/kg 30 min	Increased alpha activity during exposure. A larger increase at the same side of exposure than at the opposite side during exposure was not confirmed in hypothesis driven test.	Double blind, randomized, partially counterbalanced, cross-over. No interference by EMF with EEG signal confirmed. For discrimination see Section 5.2.4; for cognitive functions and event related potentials see (Hamblin et al., 2006) in Sections 5.2.1 and 5.2.2.1, respectively.	Croft et al. (2008)
EEG (coherence in theta, alpha, and beta bands) recorded during exposure. 1: 19 volunteers (23.3 ± 2.23 years, 9 males, 10 females)[b] 2: 20 volunteers (22.75 ± 2.71 years, 10 males, 10 females)	Dipole antenna positioned 20 cm from right ear Study 1: 900 MHz (not modulated); mean output power 64 mW Study 2: 1800 MHz (not modulated), mean output power 128 mW Exposure duration appeared to be approximately 45 min	EEG coherence was different for the genders. For males no change with 900 MHz but a reduction with 1800 MHz exposure. For females an increase with 900 MHz and with 1800 MHz compared to off.	Single blind, randomized, cross-over but results from sham combined for both groups. Bonferroni correction for multiple comparisons in post hoc tests. No p-values for the post hoc statistics provided.	Hountala et al. (2008)

EEG (1–32 Hz, 6 bands) recorded during exposure 15 male volunteers (20–35 years)	Signals emitted by broadband antenna against left ear GSM base station-like, 900 MHz: SAR_{10g} 1.0 W/kg UMTS handset-like, 1950 MHz: SAR_{10g} 0.1, 1 W/kg 30 min	No effect of exposure.	Double blind, randomized cross-over. Configuration to prevent interference of EMF with EEG signal. Bonferroni correction for multiple comparisons in post hoc tests. For subjective endpoints see Section 5.2.4; for cognitive function and event related potentials see Kleinlogel et al. (2008b) in Sections 5.2.1 and 5.2.2.1.	Kleinlogel et al. (2008a)
Mobile phone related studies including patients				
EEG (coherence in about 2–12 Hz, 2 Hz resolution) recorded before and after exposure 10 epileptic volunteers (19–43 years; 5 males, 5 females) 15 age- and sex-matched controls (20–37 years).	GSM mobile phone 1.5 cm from left side of the head, 902.4 MHz SAR_{10g} 0.5 W/kg 45 min	Compared to control group, increased inter-hemispheric coherence in epileptic patients in frontal and temporal regions at about 8–12 Hz following exposure. No effects in central and occipital regions.	Double blind, pseudo-randomized, counterbalanced, cross-over. Small sample with epileptic volunteers. Bonferroni correction for multiple comparisons in post hoc analyses.	Vecchio et al. (2012b)
Mobile phone related studies including children or adolescents				
EEG (alpha: 8–12 Hz) recorded before, during and after exposure 103 volunteers of 3 different age groups: 41 adolescents (13–15 years; 21 males, 20 females) 42 young adults (19–40 years; 21 males, 21 females) 20 elderly (55–70 years; 10 males, 10 females)	GSM (2G) handset against left and right ear, 894.6 MHz SAR_{10g} 0.7 W/kg UMTS (3G) standard handset against left and right ear, 1900 MHz SAR_{10g} 1.7 W/kg About 55 min	Increased alpha power during 2G exposure in the young adults. No effect of 2G on adolescents or elderly, and no effect of 3G on any of the age groups.	Double blind, randomized, partially counterbalanced, cross-over. No information about steps to prevent EMF interference with EEG. Bonferroni correction for multiple comparisons in secondary analyses. For cognitive function and event related potentials see (Leung et al., 2011) in Sections 5.2.1 and 5.2.2.1; for discrimination see Section 5.2.4.	Croft et al. (2010)

Abbreviations: 2G: second-generation wireless telephone technology; 3G: third-generation wireless telephone technology; CW: continuous wave; EEG: Electroencephalogram; GSM: Global System For Mobile Communication; PM: pulse modulated; UMTS: The Universal Mobile Telecommunications System.

[a] If not otherwise stated, only healthy volunteers participated. The maximal number of volunteers participating in the analyses is provided.

[b] SAR with relevant averaging volume (e.g. SAR_{10g}) is specified if included in the paper.

1654

5.2.2.3 Sleep EEG

Most of the identified sleep studies tested effects on EEG power in various frequency bands in different sleep stages, as well as sleep architecture describing sleep parameters like sleep latency, time between sleep stages, wakening after sleep onset and sleep efficiency. Sleep architecture is usually derived by visual assessment of the signals and in all included sleep studies this, as well as assessment for potential artefacts due to muscle activity, has been done by investigators blinded to the exposure conditions. For studies where this information was not reported in the paper, additional information was obtained by e-mail correspondence with authors for Mann & Röschke (1996) and Wagner et al. (2000) (J. Röschke. E-mail correspondence with G. Oftedal 2014.05.18); for the studies of the Acherman group (Borbély et al., 1999; Huber et al., 2000; Huber et al., 2002; Regel et al., 2007b; Schmid et al., 2012a; Schmid et al., 2012b) (P. Achermann. E-mail correspondence with G. Oftedal 2014.06.23) and for Danke-Hopfer et al. (2010) (H. Danker-Hopfe. E-mail correspondence with G. Oftedal 2014.05.19).

Mobile phone handset related studies with healthy adults

The earliest study investigating effects of GSM mobile phone emissions on brain activity was performed by Mann and Röschke (1996), in which the focus was on sleep and the sleep EEG. Fourteen male participants spent three consecutive nights in the sleep laboratory, the first being an adaptation night and the following two nights being exposure nights (one field exposure and one sham exposure). The order of the two exposure conditions was randomized and designed to be counterbalanced across the participants. Exposure was supplied by a digital GSM mobile phone (900 MHz) positioned at the head of the bed at a distance of 40 cm from to vertex of the participant, giving a power density 0.5 W/m^2, and lasting for a duration of 8 hours while sleep EEG was continuously recorded. Statistical analyses were based on results from 12 participants since two were excluded due to technical reasons. EEG power in five frequency bands in the 1–20 Hz range was analysed for REM sleep and non-REM sleep periods. Compared with the sham condition, sleep latency was reduced ($p < 0.005$). No effects were observed for sleep efficiency or on other sleep parameters. REM sleep percentage was reduced ($p < 0.05$), and during REM sleep an increase of EEG power density was observed in all frequency bands ($p < 0.05$) on the exposure night. [However, given that no SAR was provided and the large distance of the exposure source to the participant, the exposure was likely negligible and therefore may make these results questionable. The low number of participants in the study should also be noted.] In a subsequent study by the same group Wagner et al. (1998), also briefly reported in Mann et al. (1998), the influence of mobile phone emissions on sleep and the sleep EEG was again investigated. Using the same protocol of three consecutive nights (adaptation followed by an exposure and sham exposure night, order of the experimental nights counterbalanced), 24 male volunteers were exposed all night to a GSM mobile phone signal (900 MHz), however this time the signal was produced by a circular polarized flat antenna positioned 40 cm below the pillow of the bed resulting in a lower power density than in the previous study (0.2 W/m^2) and a SAR of 0.3 W/kg. Analyses included sleep parameters and spectral analyses included four frequency bands (total range 1–15 Hz). Unlike their original study (Mann & Röschke, 1996), no effects of exposure were observed. [After excluding two participants due to poor sleep quality, data from 22 remained for the analyses.] In order to further investigate these effects, as well as the discrepancy between the results of their sleep studies, Wagner et al. (2000) performed another similar study, with 20 male participants undergoing two sessions consisting of three consecutive nights (adaptation plus two exposure nights, real and sham counterbalanced) and performed mainly the same statistical analyses as in the previous study. In addition, a much stronger exposure was employed (a power density of 50 W/m^2, vs 0.5 and 0.2 W/m^2 in the previous studies on sleep). As in the study by Wagner et al. (1998), the EMF was circular polarized and the signal was again emitted by an antenna 40 cm below the pillow. Despite the significantly higher exposure level, no effects of exposure were reported. [The authors suggest that the difference in exposures applied across the studies (i.e. the polarization of the field) may possibly account for the differences in results observed, however, since the exposures applied were not well characterized or described, it is difficult to ascertain how much this may have influenced the results. In the latter two papers the authors informed that a phantom was used to test for potential interference of the RF EMF exposure with the recorded EEG signal, and the results showed no influence. When interpreting the results, it should also be taken into account that they did not correct for multiple analyses.]

A group from Switzerland performed a series of early studies aiming to explore the effects of GSM-like EMF on sleep activity and the EEG during sleep. In a first study, Borbély et al. (1999) exposed 24 young male volunteers during an entire night-time sleep episode to an intermittent radiation schedule consisting of 15 minutes on and 15 minutes off intervals. Exposure was produced with an array of three dipole antennas mounted behind the bed and 30 cm from the head of participants, producing a pseudo GSM base station-like signal (900 MHz) with SAR comparable to that from a handset (SAR_{10g} = 1 W/kg). Interference by the RF signals with the recording equipment was eliminated by shielding and by using filters for all input and output connections. EEG was recorded on two separate occasions one week apart, once with exposure on and once with exposure off in random order. An adaptation night proceeded each experimental night. Compared with sham, the amount of waking after sleep onset was reduced ($p < 0.01$), while no other sleep parameters were changed. Spectral analyses were performed for frequencies in the 1–25 Hz range, for each 0.25 Hz bins as well as for the five conventional frequency bands. Spectral power in the alpha and sleep spindle frequency ranges (8–15 Hz) was increased during NREM sleep ($p < 0.05$). No effects were observed during REM-sleep, and there was no indication that the position of the individual peak in the range 10–15 Hz was affected by exposure. Following this finding, Huber et al. (2000) exposed 16 young male volunteers for 30 minutes to the same base station-like signal (giving rise to the same SAR) prior to a 3-hour daytime sleep episode after a night with sleep time restricted to 4 hours. This time the signal was produced by a planar antenna mounted on both sides of the head, with participants undergoing three different exposure conditions (left, right, and sham) at one week intervals in random order. No effect of EMF was seen on sleep parameters, however, analysing 0.25 Hz frequency bins in the 1–25 Hz range, EEG in the alpha and spindle frequency ranges (9.75–11.25 Hz and 12.25–13.25) was again enhanced in the first 30 minutes of NREM sleep following both the left and right EMF exposure conditions compared to sham ($p < 0.05$). Even though significant differences were seen for more frequency bins at right than left hemisphere, irrespective of side of exposure, no significant differences between left and right side EEG powers were observed. No changes were observed during REM sleep episodes. An extended analysis of these first two papers was reported by Huber et al. (2003), however the results and conclusions from the original two papers were not changed. In this paper the exposures and the dosimetry was described in more details. Given these previous results, Huber et al. (2002) endeavoured to look at the effects of a handset-like signal on the brain more generally, again using sleep and EEG, as well as implementing measures of regional cerebral blood flow (reported in Section 5.2.3). In addition, they also wanted to explore whether the pulse modulation of the signal was an important factor. For the sleep experiment, 16 male volunteers underwent three exposure conditions: a pulse modulated handset-like signal and a continuous wave signal, both at 900 MHz and both with equivalent SARs (1 W/kg averaged over 10 g) , and a sham condition without exposure. The conditions were separated with by least one week, each preceded by an adaption night, and the order was counterbalanced. The RF signals were emitted by a planar antenna placed 11.5 cm from left side of the head. The duration of exposure was 30 minutes prior to an 8-hour night-time sleep episode, during which EEG was recorded. Spectral analyses again included the 1–25 Hz frequency range with 0.25 Hz resolution. As in the previous study with a day time sleep episode, none of the sleep parameters were reported to be influenced by the exposure. Again, after pulse modulated exposure spectral analysis showed enhancement of the EEG during subsequent NREM sleep in the spindle frequency range (12.25–13.5 Hz, $p < 0.05$). Although this enhancement wasn't present following the continuous wave exposure, a decrease in one single frequency bin was observed (at approximately 13.5 Hz). No effects of exposure were observed for other frequencies during NREM sleep and for no frequencies during REM sleep. Effects were generally only seen following the pulse modulated exposure condition. [suggesting that pulse modulation may be an important factor in the influence EMF on brain activity. No corrections were made for multiple comparisons in any of these three studies despite the high numbers of comparisons. However, in the last of these studies Huber et al. (2002) also tested EEG powers in the nights preceding the sham, the pulse modulation and the continuous wave exposures, without finding any significant differences.]

In one of the largest studies investigating potential effects on sleep, Loughran et al. (2005) exposed 50 participants to a GSM mobile phone handset (real and sham conditions) for 30 minutes prior to an overnight sleep episode. The real exposure (894.6 MHz, $SAR_{10g} = 0.674$ W/kg) and sham exposure sessions were one week apart and in random order. Measures were taken to prevent acoustic cues or heat to be sensed from the operating phone that was mounted on the right side of the head. During exposure participants sat quietly and at the end of exposure electrodes were attached and EEG recorded during subsequent sleep. The study attempted to replicate the studies by Borbély et al. (1999), Huber et al. (2000) and Huber et al. (2002) to test whether EEG power in frequency bands between 11.5 and 14 Hz would be enhanced by the exposure. Spectral analysis of the sleep EEG revealed a significant enhancement of EEG power in alpha/spindle frequency range (11.5–12.25 Hz) in the first NREM period following the real exposure condition ($p = 0.022$) while no effects were observed for the two other frequency bands analysed. In addition a decrease in REM sleep latency was observed ($p = 0.02$). Other sleep parameters did not exhibit any significant change following exposure. In a partial replication of this earlier study, Loughran et al. (2012) attempted to investigate whether the exposure-related effects on the sleep EEG were subject to individual variability, that is, whether effects were different for different people. A subset of 20 participants from their original study (Loughran et al., 2005) agreed to participate again and spent three consecutive nights in the sleep laboratory (adaptation followed by the two exposure nights in which participants were randomly exposed to the EMF and sham conditions). Exposure consisted of the same modified mobile phone handset previously used and with the same exposure frequency and exposure level. The exposure lasted for 30 minutes, after which the electrodes were attached before a full night sleep EEG recording. Results were consistent with their previous study, showing an overall increase of sleep EEG power only between 11.5 and 12.25 Hz following EMF exposure at the beginning of NREM sleep after exposure ($p = 0.046$). The increase was more prominent in those that had also shown an increase previously (Loughran et al., 2005) compared to those that had originally shown a decrease ($p = 0.038$). Additionally, the changes also appeared to be related to gender, with females responding more than males overall ($p = 0.035$). No effects on sleep architecture were found, suggesting the initial effects observed on REM latency in Loughran et al. (2005) were likely due to chance. These results were a replication of changes previously seen on the sleep EEG, and for the first time showed that potential effects may be susceptible to individual variability. [There were no adjustments for multiple comparisons in these two studies, but the spectral power analyses were restricted to a few comparisons that were hypothesis driven.]

In a study investigating potential dose-dependent effects of GSM mobile phone-like exposure on the sleep EEG and cognition, Regel et al. (2007b) applied three exposure conditions, separated by 1-week intervals, in random order to 15 participants: a GSM handset-like signal at 5 W/kg, a GSM handset-like signal at 0.2 W/kg (both emitted by a planar antenna positioned 11.5 cm from the left ear), and a sham condition. Exposure lasted for 30 minutes, during which participants performed cognitive tasks (see Section 5.2.1), and then sleep EEG was recorded during the night. The time between exposure and lights off was 10 minutes, and each exposure night was preceded by an adaptation night. Spectral analysis of the sleep EEG was done with a 0.25 Hz resolution for frequencies up to 25 Hz. The results revealed an increase of power during NREM sleep in the fast spindle frequency range (13.5–13.75) across the night following exposure ($p < 0.02$), with post hoc analysis showing that only the 5 W/kg condition differed significantly from the sham exposure condition ($p < 0.04$). No effects on REM sleep or slow wave sleep EEG or sleep architecture were observed. [No adjustments for multiple comparisons were made for these provided results.]

In a single-blind study aimed at assessing potential effects on the EEG with a focus on sleep onset and EEG power in the delta band (1–4 Hz), Hung et al. (2007) applied three different exposures from a GSM 900 MHz mobile phone (talk, listen, and standby modes) and a sham exposure to 10 participants prior to a 90-minute daytime sleep episode. The order of exposures was random and the different conditions were tested at the same time of day at weekly intervals. The different exposure conditions gave rise to different SAR values averaged over 10 g (talk mode: 0. 13 W/kg, listen mode: 0.015 W/kg and standby: <0.001 W/kg) as well as including different modulation frequencies. The phone was placed 2 cm from the right side of head and material was used to insulate the phone to avoid sensation of heat or acoustic cues from the phones. No pre-exposure differences between conditions in relation to sleepiness were observed, however, the authors report that sleep latency was delayed after talk mode exposure ($p = 0.03$), and that delta EEG power increased 10 minutes after the listen and sham exposures, and 20 minutes after the standby exposure, but for no period after exposure in talk mode ($p < 0.006$). No effects were reported for latency of stage 2 sleep. [Few volunteers participated in this study.]

Danker-Hopfe et al. (2011) investigated the effects of both GSM 900 MHz and WCDMA 1966 MHz exposures emitted by a head-worn antenna (SAR_{10g} = 2 W/kg by both exposures) on the macrostructure of sleep in 30 volunteers. Participants underwent one adaptation night and nine experimental nights (3 nights for each of the active exposure conditions and 3 nights of sham in random order) in which continuous exposure was applied throughout the 8 hours of sleep. All nights in the laboratory were at 2-week intervals. The signals were emitted by a head-worn antenna positioned around the ear so that the spatial field distribution was similar to that from a dual band mobile phone. For both exposures SAR_{10g} was 2 W/kg. Steps were taken to prevent the RF signal from interfering with recording equipment and the success was tested by using a phantom. A very large number of statistical comparisons were performed to characterize initiation and maintenance of sleep, which included parameters related to sleep stages, sleep cycles, sleep time and efficiency and wakening. However, after Bonferroni correction no significant effects of either GSM or WCDMA exposure were seen on the macrostructure of sleep. Spectral analysis of the sleep EEG data was not performed (or reported).

In a study by Schmid et al. (2012a), specific aspects of the GSM signal were investigated separately in order to determine whether effects previously observed on the EEG were due to individual pulse modulation frequencies. EEG was recorded in 30 volunteers during 8 hours of night-time sleep following a 30-minute exposure to three different conditions: 1) a 900 MHz RF EMF pulse modulated at 14 Hz; 2) a 900 MHz RF EMF pulse modulated at 217 Hz; and 3) sham exposure. The RF EMF signals were emitted by a planar antenna 115 mm from the left side of head, which resulted in a SAR_{10g} of 2 W/kg under both GSM exposures. Acoustic noise was used to mask any sound that might accompany the RF EMF exposure. All participants underwent all exposure conditions in random and partially counterbalanced order at weekly intervals. During exposure participants also performed a series of cognitive tasks (see Section 2.2.1), and each exposure night was preceded by an adaptation night. No exposure-related effects were seen on sleep architecture. Frequencies between 0.75 and 20 Hz were analysed with 0.25 Hz resolution. Spectral analysis of the sleep EEG revealed an increase of power in the spindle frequency range in the second NREM sleep episode following exposure. This effect was significant for the 14 Hz pulse modulated condition for both NREM sleep ($p < 0.05$: 12.75–13.25 Hz frequency range) and stage 2 sleep ($p < 0.05$: 11.25, 12.75–13 Hz frequency range). In addition, analysis of spectral data during REM sleep showed a few scattered significant p-values for both EMF exposure conditions in the second and third REM sleep episodes, and an increase for the 217 Hz pulse modulated condition in the fourth REM sleep episode ($p < 0.03$: 11.75–12.25 Hz).

In a follow-up study, Schmid et al. (2012b) further investigated the effects of different signal characteristics, specifically looking at whether low frequency pulse modulation without higher harmonics is sufficient to induce effects on the sleep EEG, as well as whether a magnetic field pulsed at the same frequency would also influence the sleep EEG. Using the same study design as the previous study, 25 volunteers were exposed to three different conditions: 1) a 900MHz EMF field pulsed-modulated at 2 Hz emitted by a patch antenna 115 mm from left side of head (SAR_{10g} = 2 W/kg); 2) a magnetic field pulsed at 2 Hz produced by Helmholtz-like coils (spatial peak magnetic flux density = 0.70 mT); and 3) sham exposure. As in the previous study, EEG frequencies between 0.75 and 20 Hz were included and similar analyses were conducted. Although a frequency resolution of 0.25 Hz was used, in the current study it was specified that a power change in a frequency range was considered to be significant only if at least three consecutive frequency bins reached significance. Similar to their previous results and based on data from 23 volunteers (two were excluded due to poor signal quality and low sleep efficiency, respectively), exposure was not found to affect sleep architecture, however less REM sleep contributed to the second sleep cycle following RF exposure compared with sham ($p < 0.03$). Increased spectral power in the sleep spindle frequency range was again found following the RF exposure condition (13.75–15.25 Hz: $p < 0.03$ for NREM sleep and $p < 0.04$ for stage 2 sleep). In addition and in contrast to previous results, other frequency ranges were also affected by the pulsed RF condition as well as the pulsed magnetic field condition, with the delta and theta frequency ranges, between 1.25 and 9 Hz, showing increases following exposure ($p < 0.05$, NREM and stage 2 sleep). Spectral analysis of the EEG during REM sleep also showed that power in the alpha range (7.75–12.25 Hz) was increased following pulsed RF exposure ($p < 0.05$) and power in the lower delta range (0.75–1.5 Hz) was increased following both exposure conditions ($p < 0.04$). [Although a large number of comparisons were made without correction, taken together, the results of these two studies suggest that the specificity of the pulse modulation frequency is not a critical component in inducing effects on the EEG.]

Mobile phone handset related studies including volunteers with IEI-EMF

Following early reports of EMF-related effects on sleep, Jech et al. (2001) investigated whether a GSM mobile phone signal (900 MHz) would have an even larger influence on patients with narcolepsy, who suffer from hypersomnia and fall asleep suddenly or unexpectedly. Twenty-two patients were exposed on two consecutive days to a real and sham exposure for 45 minutes. The mobile phone, placed at the right side of the head, was thermally insulated so that the participants should not sense the heat from the phone and the authors report that “it was impossible to see or hear whether the phone was on or off”. In each session, after 5 minutes of exposure the participants were asked to complete a visual discrimination task during which visual ERPs were recorded (see Sections 5.2.1 and 5.2.2.1). Following exposure, patients were then allowed to sleep while EEG was recorded. Assessments were done for latencies of extinction of alpha waves, onset of theta waves, sleep onset and occurrence of spindle frequencies. No effects on the EEG during sleep were reported. [It should also be noted that the SAR reported for this study (SAR_{10g} = 0.06 W/kg) is extremely low and therefore the detection of potential effects may have been difficult.]

In order to see whether the duration of exposure may be influential, as well as whether effects may be different for people attributing symptoms to GSM mobile phones, Lowden et al. (2011) exposed participants to GSM 884 MHz handset-like signals emitted by a micropatch antenna placed some centimetres from the left side of the head (SAR_{10g} = 1.4 W/kg) for 3 hours prior to a 7 hour night-time sleep. In order to mimic the sensation from a warm phone, a small ceramic plate connected to the left ear lobe was heated to 39 ºC during all exposure sessions. A habituation session was performed at least a week or more before the exposure sessions. The real and sham exposure sessions were separated by at least one week and the order was randomised. During exposure participants were resting, reading, or performing tests. The study group consisted of 71 participants, however, only 48 (23 with IEI-EMF and 25 in a control group) were included in the final analyses, and only 32 participants (14 and 18, respectively) were included in the spectral analysis of the EEG. Several sleep-related effects of exposure were reported, an increase in minutes of stage 2 sleep ($p = 0.044$), decrease in minutes of stage 4 ($p < 0.001$), and a decrease of slow wave sleep ($p = 0.014$), as well as an increase in latency to stage 3 sleep ($p = 0.002$). No differences between the sensitive and non-sensitive group were seen. EEG power of each frequency bin (width 0.25 Hz) in the range 0.5–16 Hz was compared between real and sham exposure. Spectral analysis showed power increases following exposure in the frequency ranges 0.5–1.5 Hz and 5.75–10.5 Hz (first 30 minutes of stage 2 sleep; $p < 0.05$ for majority of frequency bins), 7.5–11.75 Hz (first hour of stage 2 sleep; $p < 0.05$), and 4.75–8.25 Hz (second hour of stage 2 sleep; $p < 0.05$). No effects remained during the third hour of stage 2 sleep and no effect was observed at any frequency during the first hour of slow wave sleep. [Although some results of this study are similar to other previous research, overall there are several limitations that make this study difficult to interpret. In particular, the large amount of participants excluded from the analysis was extreme and therefore might introduce bias to the results. A large number of statistical comparisons were performed without correction, while the habituation night being performed a week or more in advance of the actual study nights is also not ideal. Therefore interpretation remains difficult.]

Base station related studies with healthy adults

Using a slightly different approach, Danker-Hopfe et al. (2010) performed an experimental field study to investigate the effects of EMF (GSM 900 and 1800 MHz) emitted by a base station on sleep in a rural sample in their home environment. An experimental base station was used in 10 villages where no mobile phone service was available and other RF EMF field exposures were negligible. Furthermore, DECT telephones were replaced by corded phones during the study period. To assure blinding the base station was operated in test mode so that the functioning could not be detected by mobile phones. In total 397 residents were exposed to sham and GSM base station signals during sleep during two periods of six nights, each starting with an adaptation night. The 10 experimental nights consisted of 5 nights sham and 5 nights exposure in random order. After drop outs (21), exclusions because living more than 500 meters from the base station (11) or because of problems with recorded EEG (30), 335 participants remained for the final analyses. A sample size of 294 subjects was calculated for the primary endpoint objective of sleep efficiency and derived from the data obtained in a previous feasibility study taking into consideration a two-sided $p < 0.05$, a power of 90% and a drop-out rate of 10%. Objective (EEG) and subjective sleep quality were both measured. In addition to the primary endpoint, also other sleep parameters such as total sleep time, delay of sleep stages, and waking after sleep onset were assessed. No difference between exposure and sham was seen for either objective or subjective sleep quality, without corrections for multiple tests. [While exposure information is sparse in the paper, the authors referred to a paper by Bornkessel et al. (2007) describing methods for measuring exposure levels in the bedrooms, and the results were presented in a report (Danker-Hopfe et al., 2008) showing that more than 90% of the participants were exposed to electric field strengths between 10 and approximately 1000 mV/m. In the sham condition the field strength was lower than 0.1 mV/m for about 85% of the participants. The large sample size, lengthy exposures and realistic set-up of this experiment provide good evidence that exposures from new base stations are unlikely to cause substantial effects on the quality of sleep of a host community].

Base station related studies with IEI-EMF volunteers

Leitgeb et al. (2008) assessed the impact of radiofrequency fields on the sleep of 43 people attributing their sleep problems to RF EMF from mobile telecommunication base stations. The study was conducted in the participants' own home and they slept in their own bed. After an adaptation night EEG was recorded during nine consecutive nights. Two types of netting were applied for three nights each and three nights were without netting. The order of the conditions was randomly determined. The netting was either genuinely protective against external electromagnetic fields, acting as a Faraday cage, or it was composed of ineffective material that was "optically and tactually indistinguishable" from the protective material. The environmental RF fields in the bedroom of the participants were recorded for frequencies in the range 80–2500 MHz with and without the shielding. Detailed exposure information is provided in a report (Leitgeb, 2007). With no shielding the exposure was between 1 and 10% of ICNIRP reference levels for 77.5% of the participants, above 10% for 15%, with the highest recorded value 3.5% of the reference level, and just below 1% of the reference level for the remaining 7.5% of the participants. The shielding reduced the exposure levels significantly; the median reduction was about 19 dB and the quartiles were about 15 and 24 dB, respectively. Experts blind to the exposure conditions analysed the recorded EEG signals to determine parameters describing the sleep architecture. Detailed results from individual analyses were provided. Of the 43 participants, 10 exhibited "effects of exposure" for between one and three of the 11 objective sleep parameters. Partly these effects indicated "improved sleep" and partly "impaired sleep" and the affected parameters exhibiting "an effect" differed between the participants. No numerical results were provided for the pooled analysis. However, the authors stated that pooled analysis "did not exhibit statistically significant EMF sleep parameters". [An unorthodox method was applied to decide about statistical significance for the individual analyses, by considering differences between each of the three exposure conditions. This resulted in a significance criterion that was slightly more stringent than by applying Bonferroni adjustment. However, no adjustment was made to account for the high number of individual analyses. Therefore, it is likely that some individual “significant effects” appeared by chance, which also was supported by no indication of effect of exposure in the pooled analyses. In this study, the use of the intervention by reducing the exposure that the participants assumed was the reason for their sleeping problems was a good approach to test whether these environmental RF exposures were reasons for the experienced poor sleep quality.]

Table 5.2.6. Studies assessing effects on sleep EEG

Endpoint and Participants[a]	Exposure[b]	Response	Comment[c]	Reference
Mobile phone handset related studies with healthy adults				
EEG (1–20 Hz, sleep architecture) recorded during 8h night-time sleep during exposure 12 male volunteers (21–34 years)	GSM handset- 40 cm from head, 900 MHz Average power density 0.05 mW/cm^2 (0.5 W/m^2) 8 h	Decreased sleep latency, decreased REM sleep percentage, and increased EEG power density during REM sleep in all frequency bands.	Double blind, randomized, counterbalanced, cross-over. Small sample. No information about control of EMF interference with recording equipment. No correction for multiple comparisons. For subjective endpoints see Section 5.2.4; for autonomic system see Mann et al (Mann et al., 1998) in Section 9.2.1.	Mann and Röschke (1996)
EEG (1–15 Hz, sleep architecture) recorded during 8h night-time sleep during exposure 22 male volunteers (18–37 years)	GSM handset-like signal emitted by a circular polarized antenna 40 cm from head, 900 MHz SAR 0.3 W/kg, average power density 0.2 W/m^2 8 h	No effect of exposure.	Single blind, counterbalanced, cross-over. RF exposure Interference on recorded signals tested with phantom. No correction for multiple comparisons. For endocrine system see Mann et al. (1998) in Section 7.1.	Wagner et al. (1998)
EEG (1–15 Hz, sleep architecture) recorded during 8h night-time sleep during exposure 20 male volunteers (19–36 years)	GSM handset-like signal emitted by a circular polarized antenna 40 cm from head, 900 MHz Average power density 50 W/m^2 (SAR_{10g} < 2 W/kg) 8 h	No effect of exposure.	Single blind, counterbalanced, cross-over. RF exposure Interference on recorded signals tested with phantom. No correction for multiple comparisons.	Wagner et al. (2000)
EEG (1–25 Hz, sleep architecture) recorded during 8h night-time sleep during exposure 24 male volunteers (20–25 years)	GSM base station-like signal emitted by array of 3 half-wave antennas 30 cm from head behind bed, 900 MHz, PM 2, 8, 217, 1736 Hz and 50 kHz (87.5 % duty cycle)SAR_{10g} 1 W/kg All night intermittent exposure (15 min on, 15 min off, for 8 h)	Waking after sleep onset reduced; no effect on sleep architecture. EEG spectral power increased during NREM sleep (8–15 Hz). No change during REM sleep, and no shift in position of individual spectral peak frequency.	Double blind, randomized cross-over. Shielding to prevent EMF interference. No correction for multiple comparisons. For subjective endpoints see Section 5.2.4; for cardiovascular system see Section 9.2.1.	Borbély et al. (1999)

EEG (1 – 25 Hz, sleep architecture) recorded during 3h daytime sleep episode after exposure 16 male volunteers (20–25 years)	GSM base station-like signal emitted by planar antenna 11.5 cm from head, left and right exposures in separate sessions, 900 MHz PM 2, 8, 217, 1736 Hz and 50 kHz (87.5 % duty cycle) SAR_{10g} 1 W/kg 30 min	No effect on sleep architecture. EEG spectral power increased during NREM sleep (9.75–11.25 and 12.25–13.25 Hz).No effects on other frequencies. or on REM sleep.	Double blind, randomized, cross-over. No correction for multiple comparisons. For subjective endpoints see Section 5.2.4; for cardiovascular system see Section 9.2.1.	Huber et al. (2000)
EEG (1–25 Hz, sleep architecture) recorded during 8h night-time sleep episode after exposure 16 male volunteers (20-25 years)	GSM handset-like signal, 900 MHz, PM 2, 8, 217 and 1736 Hz (12.5 % duty cycle) and CW, 900 MHz; both emitted by planar antenna 11.5 cm from left side of head SAR_{10g} 1 W/kg 30 min	No effect on sleep architecture. EEG spectral power increased during NREM sleep (12.25–13.5 Hz) for PM condition. No effects on other frequencies, on shift in position of individual spectral peak frequency or on REM sleep.	Double blind, counterbalanced, cross-over. No correction for multiple comparisons. For regional brain blood flow see Section 5.2.3.	Huber et al. (2002)
EEG (11.5–14 Hz, sleep architecture) recorded during sleep after exposure 50 volunteers (18–60 years; 27 males, 23 females)	GSM handset-like signal emitted by a standard handset at right side of head, 894.6 MHz, PM 217 Hz SAR_{10g} 0.674 W/kg (as per Loughran et al. (2012)) 30 min	Increased EEG power during NREM sleep (11.5–12.25 Hz) and decreased REM sleep latency. No other effects on sleep architecture.	Partial replication of Borbély et al. (1999), Huber et al. (2000; 2002). Double-blind, randomized, partially counterbalanced, cross-over. No correction for multiple comparisons. For discrimination see Section 5.2.4.	Loughran et al. (2005)
EEG (11.5–14 Hz, sleep architecture) recorded during sleep after exposure 20 volunteers (20–51 years; 7 males, 13 females)	GSM handset-like signal emitted by a standard handset at right side of head, 894.6 MHz, PM 217 Hz SAR_{10g} 0.674 W/kg 30 min	Following exposure, an overall increase of sleep EEG power (11.5–12.25 Hz) at the beginning of NREM sleep. This increase was more prominent in those that had shown an increase previously compared to those that had originally decreased. The effect was greater in females. No effect on sleep architecture.	Partial replication of and with participants from Loughran et al. (2005). Double-blind, randomized, counterbalanced, cross-over. No correction for multiple comparisons. For sleepiness see Section 5.2.4.	Loughran et al. (2012)
EEG (1–25 Hz, sleep architecture) recorded during 8 h sleep episode after exposure 15 male volunteers (20–26 years)	GSM signal emitted by planar antenna11.5 cm from left ear, 900 MHz SAR_{10g} 0.2, 5 W/kg 30 min	No effect on sleep architecture. Increased spectral power in fast spindle frequency range during NREM (13.5–13.75 Hz) following the 5 W/kg exposure; no effects during REM or slow wave sleep.	Double blind, randomized cross-over. Exposure setup described in Huber et al. (2003) No correction for multiple comparisons for EEG analysis. For cognitive function see Section 5.2.1.	Regel et al. (2007b)

EEG (1–4 Hz, latency of sleep onset and stage 2 sleep) recorded during a 90 min daytime nap after exposure 10 volunteers (18–28 years; gender not specified)	GSM mobile phone (controlled by GSM900 base-station simulator located in another room) 2 cm from right ear, 900 MHz SAR_{10g} talk mode: 0.13 W/kg, listen mode: 0.015 W/kg, standby: <0.001 W/kg	Sleep latency delayed after talk mode exposure; delta EEG power (1–4 Hz) increased 10 min after listen mode and sham exposures, 20 min after standby exposure and at no period after talk mode.	Single blind, randomized, cross-over. Small sample. Bonferroni correction for multiple comparisons.	Hung et al. (2007)
EEG (sleep architecture) recorded during 8 h sleep episode during exposure 30 male volunteers (18–30 years)	GSM handset-like signal, 900 MHz; WCDMA handset-like signal, 1966 MHz; both emitted by head-worn antenna at side of head SAR_{10g} 2 W/kg 8 h	No effect of exposure on sleep architecture. (No spectral analyses reported.)	Double blind, randomized, cross-over. Shielding of recording equipment. Bonferroni correction for multiple comparisons.	Danker-Hopfe et al. (2011)
EEG (0.75–20 Hz, sleep architecture) recorded during 8 h sleep episode after exposure 30 male volunteers (20–26 years)	PM signal emitted by planar antenna 115 mm from left side of head, 900 MHz, PM 14 Hz with pulse width 2.3 ms and 217 Hz with pulse width 0.577 ms, respectively SAR_{10g} 2 W/kg 30 min	No effect on sleep architecture. Increased spectral power in spindle frequency range during NREM (12.75–13.25 Hz) and stage 2 (11.25, 12.75–13 Hz) sleep following the 14 Hz exposure. Increased spectral power in REM sleep (11.75–12.25 Hz) following the 217 Hz exposure.	Double blind, randomized, partially counterbalanced, cross-over. No correction for multiple comparisons for EEG analysis. For cognitive function see Section 5.2.1; for heart rate see Section 9.2.1; for subjective endpoints see Section 5.2.4.	Schmid et al. (2012a)
EEG (0.75–20 Hz, sleep architecture) recorded during 8 h sleep episode after exposure 23 male volunteers (20–26 years)	PM signal emitted by patch antenna 115 mm from left side of head, 900 MHz, PM 2 Hz SAR_{10g} 2 W/kg Pulsed magnetic field from Helmholtz coils over both sides, pulse frequency 2 Hz Peak magnetic flux density 0.70 mT 30 min	No effect on sleep architecture. NREM and stage 2 sleep: increased spectral power in spindle frequency range following pulsed RF (13.75–15.25 Hz), and increased delta and theta power following both exposure conditions (1.5–9 Hz) REM sleep: increased spectral power in alpha range (7.75–12.25 Hz) following pulsed RF, and increased power in lower delta (0.75–1.5 Hz) in REM sleep following pulsed magnetic field.	Double blind, randomized, cross-over. No correction for multiple comparisons for EEG analysis. For cognitive function see Section 5.2.1; for heart rate see Section 9.2.1; for subjective endpoints see Section 5.2.4.	Schmid et al. (2012b)
Mobile phone handset related studies including patients and volunteers with IEI-EMF				

EEG (latencies in alpha extinction, theta onset, sleep and spindle appearance) recorded after exposure during sleep 22 patients with narcolepsy (48 ± 11.7 years; 9 males, 13 females)	Signals from GSM mobile phone close to right side of the head, 900 MHz SAR_{10g} 0.06 W/kg 45 min	No effects of exposure..	Double blind, cross-over. Bonferroni correction for multiple comparisons. For visual event related potentials see Section 5.2.2.1; for cognitive function see Section 5.2.1.	Jech et al. (2001)
EEG (0.5–16 Hz, sleep architecture) recorded during 7 h sleep episode after exposure Analysis of sleep stages: 23 IEI-EMF volunteers (27 ± 1.3 years; 8 males, 15 females) and 25 controls (29 ± 1.3 years; 13 males, 12 females) EEG spectral analysis: 14 IEI-EMF volunteers and 18 controls	GSM handset-like signal emitted by a micropatch antenna on headset at left side of head, 884 MHz, PM 2, 8, 217, 1736 Hz SAR_{10g} 1.4 W/kg 3 h	Duration of stage 2 sleep increased, stage 4 and slow wave sleep decreased. EEG power increased during first 30 min (0.5–1.5, 5.75–10.5 Hz), first hour (7.5–11.75 Hz) and first 2 hours (4.75–8.25 Hz) of stage 2 sleep: no effect on power in slow wave sleep.	Double blind, randomized, cross-over. No correction for multiple comparisons. More than half of the 71 participants were excluded in the spectral analysis which may introduce bias. For cognitive function see Wiholm et al. (2009) in Section 5.2.1; for symptoms see Hillert et al. (2008) in Section 5.2.4.	Lowden et al. (2011)
Base station related studies with healthy adults				
EEG (sleep architecture) recorded during night time sleep 335 volunteers recruited from 10 villages with no pre-existing mobile phone coverage (18–81 years; 179 male, 186 female)	An experimental base station within 500 m of volunteer's bedroom, generic GSM signals in test mode with two 900 MHz and two 1800 MHz channels at maximum power Five nights of GSM exposure and five nights of sham exposure	No effect of exposure.	Double blind, randomized, cross-over field study. No correction for multiple comparisons. For subjective sleep quality see Section 5.2.4.	Danker-Hopfe et al. (2010)
Base station related studies with IEI-EMF volunteers				
EEG (sleep architecture) recorded during night time sleep 43 IEI-EMF volunteers (17 males, 55.0 ± 10.5 years; 26 females, 56.0 ± 0.6 years)	Shielding of EMF by Faraday cage of electric conductive material mounted around the participant's own bed at home, reduced RF exposure 9 nights of sleep: 3 under genuine protective material (median reduced exposure ~19 dB), 3 under sham material and 3 under no material	No effect of exposure.	Intervention study, single-blind, randomized, cross-over. Correction for multiple tests. (See text for details.) No numerical data provided for pooled analysis. For subjective sleep quality see Section 5.2.4.	Leitgeb et al. (2008)

Abbreviations: CW: continuous wave; EEG: Electroencephalogram; GSM: Global System For Mobile Communication; IEI-EMF: Idiopathic environmental intolerance attributed to EMF; PM: Pulse modulation; WCDMA: Wideband Code Division Multiple Access.

[a] If not otherwise stated, only healthy volunteers participated. The maximal number of volunteers participating in the analyses is provided.

[b] SAR with relevant averaging volume (e.g. SAR_{10g}) is specified if included in the paper.

[c] Assessment of recorded EEG was done blinded in all included studies.

Excluded studies

(Fritzer et al., 2007)

5.2.3 Cerebral blood flow and metabolism

WHO (1993) reports no human volunteers studies on effects of RF exposure on cerebral blood flow and metabolism. The literature search for such volunteer studies published later resulted in 14 relevant papers, representing 13 studies (one study was reported in two papers). Of these, 12 studies are included in the overall review section, and one was deemed to be have uncertainties related to the inclusion criteria (see Appendix X) and is therefore reported on briefly at the end of the section and not included in the summary table. All included studies explored effects of RF exposures similar to those from mobile phone handsets, on cerebral blood flow or brain glucose metabolism. Twelve of these studies were performed in healthy adults and one investigation was on children.

At the end of the section a table summarizes results and provides information about study details including study design. Similar and further details are included in the following text, with exceptions that the use of double-blind design, meaning that neither participant or researcher was aware of the exposure conditions, is not reported in the text. In all studies included in the analysis as a basis for the health risk assessment, the exposure was controlled. The number of participants in studies was generally low which is usually the case with studies employing such imaging techniques to measure cerebral blood flow and metabolism.

Regional cerebral blood flow (rCBF) is defined as the amount of blood flow in a specific area of the brain at a particular time and generally reflects neural activity in local brain regions. Cerebral blood flow is influenced by the metabolic demand of the brain for oxygen and glucose, therefore measurements of these two parameters are highly related. The brain imaging methods that have been used to explore potential effects of mobile phone RF EMF on brain function have been positron emission tomography (PET) imaging, functional magnetic resonance imaging (fMRI), near-infrared spectroscopy (NIRS), and transcranial Doppler sonography. Most studies have been performed using PET imaging, with the use of the other techniques being a more recent addition. All PET studies explored whole brain images, while most often signals from selected brain areas were investigated in other studies.

Studies with healthy adults

Huber et al. (2002) investigated the effect of RF EMF on regional cerebral blood flow (rCBF) in 16 young male participants. Positron emission tomography (PET) scans were taken after head exposure to 30 minutes of a GSM pulse modulated handset-like signal (900 MHz, SAR_{10g} = 1 W/kg) emitted by a planar antenna placed 11.5 cm from the left side of the head. The participants underwent the RF exposure and an equivalent sham exposure with at least one week interval between the conditions. The time between the end of exposure and the first PET scan was 10 minutes, followed by two more scans at intervals of 10 minutes. The results from the three scans were pooled for statistical analysis. For technical and logistical reasons not all participants were able to complete the study, and therefore only 13 were included in the analysis, resulting in the order of conditions not being completely balanced as intended. Results showed that relative rCBF was increased in the dorsolateral prefrontal cortex of the left hemisphere ($p < 0.01$) in the exposure condition compared to sham. In the same experiment, the participants were also exposed to a base station-like RF signal for 30 minutes and results comparing effects of mobile phone-like exposure and a base station-like exposure were published in (Huber et al., 2005). This second study by Huber et al. (2005) aimed to investigate the effects of the two different modulation schemes. The base station-like exposure was obtained using the same exposure setup and resulted in the same $SAR_{10g.}$ The two types of signals included the same pulse modulation frequencies but the low frequency components were stronger for the mobile-phone like exposure. Because of technical problems and logistical reasons, only 12 of the 16 subjects completed all three conditions and order of conditions was again not completely balanced; however, order was included as a factor in the analyses and no significant effect found. Results presented in the latter paper were analysed slightly differently from that in the first one, but gave similar results for the mobile-phone-like exposure. Base-station-like exposure did not result in any significant changes in rCBF when compared with the sham exposure condition. Huber et al. (2005) also compared areas with changes in rCBF with the distribution of SAR. The changes coincided with brain areas with high exposure levels but the exposed region was much larger than the areas exhibiting a change in rCBF.

In contrast to the study performed by Huber et al. (2002; 2005), where effects were measured after exposure, Haarala et al. (2003a) investigated the effects of RF EMF on rCBF during exposure. PET data was acquired in 14 male participants during 45-minute exposure to either a modified GSM mobile phone handset (902 MHz, SAR_{10g} = 0.99 W/kg with an approximate 22% further increase due to the PET scanner) or sham while performing a working memory task (see Section 5.2.1 for cognitive results). All participants were exposed to both conditions on the same day [no information about the interval between the exposure was provided] and the order was counterbalanced across participants. During exposure the mobile phone was placed against the left ear. A relative bilateral decrease of rCBF in the auditory cortices was observed during exposure ($p = 0.004$ for left side; $p = 0.009$ for right side, both p-values corrected for multiple comparisons). However, as the effect was bilateral and not found in the area of maximum EMF exposure, the authors attributed this finding as likely being caused by an auditory signal emitted by the battery of the mobile phone. The loudspeaker from the mobile phone had been removed but still there was an acoustic signal from the battery of the operating phone. However, in pilot studies with independent participants there was no indication that the participants could discriminate between the real and the sham condition. They were also not able to confirm the finding of relatively increased rCBF in the dorsolateral prefrontal cortex of the left hemisphere reported by Huber et al. (2002). In a follow-up study, Aalto et al. (2006) employed a more sensitive experimental design in which the noise from the mobile phone was removed by removing the battery in addition to the loudspeaker, by employing a silent external power source and furthermore by inserting an earplug in the participants' left ear where the phone was positioned. PET data was acquired in 12 male participants during 51-minute exposure to the modified GSM mobile handset (902 MHz, SAR_{10g} = 0.74 W/kg with an approximate 22% further increase due to the PET scanner) or sham while performing a working memory task (see Section 5.2.1 for cognitive results). For this study the authors detailed that the participants underwent the sham and the real exposures with an interval of 15 minutes, in a counterbalanced order. Decreased rCBF during EMF exposure was found in the left fusiform gyrus in the posterior inferior temporal lobe beneath the antenna ($p = 0.003$) while increased rCBF was reported on both sides in a cluster of areas in the frontal lobe more distal from the antenna (p between 0.001 and 0.007). All p-values were corrected for multiple comparisons.

In order to look at potential effects of third generation technology, Mizuno et al. (2009) investigated the influence of 30 minutes W-CDMA mobile phone exposure on rCBF in nine male participants. PET data was acquired before, during and after real and sham exposures. For each individual the real and sham exposures were at least a week apart and the order was randomized. The 1950 MHz CDMA signal was emitted by a microstrip patch antenna mounted on the right side of the participants head (SAR_{10g} = 2.02 W/kg). No significant effects of W-CDMA exposure were found on rCBF. This was also the case when analysing specifically for cortical areas where earlier studies had shown significant differences between real and sham conditions (Aalto et al., 2006; Huber et al., 2005). In all analyses correction for multiple comparisons was applied. Although the study conditions were randomized, they were not counterbalanced and the study was conducted single-blind.

Using a slightly different approach to these earlier studies, Kwon et al. (2011) investigated the effects of RF EMF on cerebral glucose metabolism. PET data was acquired in 13 male participants after a 30-minute exposure to a GSM handset-like signal (902.4 MHz, SAR_{10g} = 0.7 W/kg) emitted by a mobile phone placed on the right side of the head. The battery and the loudspeaker of the phone was removed and the antenna was fed with signals from another identical mobile phone via a coaxial cable in order to keep the temperature of the phone constant during exposure. Sham and real exposures were at least a week apart and the order of conditions was only partially counterbalanced due to the odd number of participants. During real and sham exposures the participants performed a simple visual vigilance task (see Section 5.2.1 for cognitive results). In addition, subjects fasted for at least 8 hours prior to the experiment in order to stabilize blood glucose concentration. ^{18}F-deoxyglucose PET images were taken after exposure. Results showed reductions in relative cerebral metabolic glucose rate in brain areas closest to the mobile phone (the temporoparietal junction and anterior temporal lobe of the right hemisphere) following real exposure compared to sham. [Even though glucose concentration was stabilised by applying an 8-hour fasting period before exposure, no pre-exposure measurements were taken to control for initial baseline values for the real and the sham conditions, and the number of participants was low.]

In a second study, Kwon et al. (2012b) investigated the potential influence of 902 MHz GSM handset-like exposure location on cerebral blood flow in 15 male participants. The study consisted of four different exposure conditions (left: SAR_{10g} = 1.0 W/kg, right: 0.7 W/kg, front: 0.7 W/kg, and sham exposure). The phones and the exposure system were the same as in the previous study. Each exposure lasted for 5 minutes, with the PET bolus injected 3 minutes after each exposure onset and PET images recorded during the last 2 minutes of exposure. The sequence of the four exposure conditions was repeated three times for each participant, with a 10-minute exposure free interval between the exposures. Across all participants the order of conditions was partially counterbalanced. During each exposure, participants performed a simple visual match-to-sample task (see Section 5.2.1 for cognitive results). Exposure was not found to have any influence on cerebral blood flow. [The repeated exposures in the latter study would make it more likely that a potentially small effect would be detected. However, the short intervals between exposures increased the risk for carry-over effects. In both of these studies the order of conditions was balanced across participants, but due to the number of participants, and for the last study also due to the number of repeated sequences of exposure, a complete counterbalance was not possible.]

Using a different technique, a recent study by Curcio et al. (2012) investigated the effects of GSM mobile phone emissions on brain activity as measured by fMRI (applying blood-oxygen-level dependent (BOLD) contrast to image changes in blood flow), as well as on reaction times and cognitive performance (see Section 5.2.1 for cognitive results). The mobile phone was placed 1.5 cm from the right ear in order to avoid any potential thermal sensations from the phone. Whole brain fMRI data was acquired in 12 healthy volunteers, and BOLD response was assessed (while participants performed a somatosensory task) both before and after a 45-minute exposure to a GSM handset (902.4 MHz, SAR_{10g} = 0.5 W/kg at 2 cm depth) and to a sham condition. Each participant underwent the real and sham exposures a week apart and the order was counterbalanced across participants. No exposure-related effects on brain activity (BOLD response) were reported.

More recently the use of NIRS has been used as a method for investigating a potential influence of RF EMF on the brain. Wolf et al. (2006) investigated the effects of GSM 900 MHz signals on cerebral blood circulation. The different types of responses investigated were changes in the concentrations of haemoglobin with and without oxygen (oxyhaemoglobin and deoxyhaemoglobin) during exposure and between exposures (short term responses) as well as differences in trends between exposure and sham sessions over the entire experiment (long term responses). Eighteen volunteers participated, however only 16 were used for final analysis due to movement artefacts in the data. Each participant underwent three exposure conditions (SAR_{10g} 0.15 W/kg, 1.5 W/kg, sham exposure) on three separate days in randomized order. The exposure was emitted by a planar patch antenna (11 cm from left side of head) and consisted of 15 repeated cycles, which included 20-s exposure (alternating 2 s on / 2 s off periods) followed by 60 s rest, and lasted for a duration of 20 min (preceded by a 4 min baseline period). NIRS signals were recorded continuously bilaterally from prefrontal cortical areas. Since a preliminary test demonstrated that simultaneous EMF exposure interfered with the NIRS signals, only signals from the 2-second exposure free periods were used for analyses. Analyses were done separately for NIRS signals from three depths under the scull, where the shortest distance mostly detects superficial changes (at the level of the skin and the skull) while the longest distance also includes information about the brain. Furthermore, the three exposure conditions were compared for each of three different "short-term" periods. For the left hemisphere (exposed side), four of 182 comparisons resulted in significant differences (defined as $p < 0.016$). For the right hemisphere, there were two significant differences. The significant findings occurred at different depths and included differences for both oxyhaemoglobin and deoxyhaemoglobin. These changes, which correspond to a decrease in cerebral blood flow and volume, were reported to be smaller than regular physiological changes, and also given the number of comparisons, leaves open the possibility of the results being due to chance, as also suggested by the authors. No long term haemoglobin concentration changes were reported. In a similar study from the same group, Spichtig et al. (2012) used NIRS to investigate the effects of UMTS base-station-like signals on cerebral blood circulation in the auditory cortex at the exposed side of head. Sixteen volunteers underwent three different exposures (sham, SAR_{10g} 0.18 W/kg and 1.8 W/kg) emitted via a planar patch antenna placed 4 cm from the left side of head. Measures were taken to minimize potential EMF interference by the UMTS signals, and a test was performed without indicating any effect of exposure on the recorded signals. The exposure conditions were performed at the same time of day, each on separate days, and the order was determined randomly. Exposure sessions consisted of 16 cycles (exposure segments of 20 s or sham were alternated with 60 s recoveries), lasting for a total of 31 min including NIRS recordings before and after the cycles. In addition to the three exposure sessions, participants also completed a fourth session in which a motor activation measurement was performed without EMF exposure. For the EMF exposure sessions the NIRS-signals were recorded in the temporal area. Analyses were done separately for the first 80-second segment (short term) and for the remaining recording period (80 seconds to 31 minutes.), with Tukey correction for multiple comparisons applied. Results showed a significant short-term increase of oxyhaemoglobin and total haemoglobin concentrations during exposure to 0.18 W/kg ($p < 0.01$), but not during the 1.8 W/kg exposure, and a decrease in the medium-term deoxyhaemoglobin concentration at 0.18 and 1.8 W/kg exposures ($p < 0.01$), both of which are in the range of physiological fluctuations and smaller than the motor activated responses. No other parameters were affected.

Also using NIRS, Curcio et al. (2009) investigated the effects induced by exposure to a GSM mobile phone handset (902.4 MHz, SAR_{10g} = 0.5 W/kg) positioned at the left side of the head about 1.5 cm from the ear on the oxygenation of the frontal cortex. Eleven female participants underwent two sessions (real and sham exposure), consisting of 10 min baseline, 40 min exposure, and 10 min recovery. The sessions were separated by two days, were at the same time of day, and the order of conditions was determined randomly. A potential confounding effect of the cyclical ovarian hormonal impact on the cerebral hemodynamics was controlled for, with subjects only tested during the first few days of the follicular phase. By using optical fibres and placing the light detector unit and the display at some distance from the emitting mobile phone, there was no EMF interference as confirmed by a separate test. During the experiment, subjects laid on a bed with their eyes open. NIRS signals were recorded from left and right frontal areas. The results of the functional NIRS analysis showed a linear increase in deoxyhaemoglobin as a function of time in the real RF exposure condition ($p < 0.04$) compared to sham. However, further analyses did not reveal any significant difference at any point of time between the real and the sham conditions. Furthermore, no difference in effect of exposure was observed between the different recording sites. The concentrations of oxyhaemoglobin and of total haemoglobin did not show any exposure-related changes.

In the only study to use transcranial Doppler sonography, Ghosn et al. (2012) investigated the effects of GSM mobile phone exposure on middle cerebral artery blood flow. Twenty-nine participants attended two 20-min experimental sessions (a sham exposure and a real exposure session) in which a mobile phone was positioned on the left side of the head (900 MHz, SAR_{10g} = 0.49 W/kg). The sham exposure was obtained by connecting an external load to the external antenna connector of the phone resulting in no measurable SAR; a dummy load was used for the real exposure. The order of the sessions was randomized. Hemodynamic variables, blood flow velocity and indexes for the systolic-diastolic variation in the blood flow, were recorded at both sides and analysed before, during and until 20 minutes after exposure. A voluntary breath holding physiological test was also carried out and served as a positive control. No changes in middle cerebral artery blood flow were observed in either exposure conditions, and no significant differences were found in results from left and right sides. The positive control resulted in significant changes in all parameters measured ($p < 0.001$).

Studies with children

Only one study to date has been performed in children, with Lindholm et al. (2011) aiming to examine thermal and local blood flow responses in the head area of 26 preadolescent (14-15 years old) boys during exposure to a GSM mobile phone (902.4 MHz). The mobile phone was placed 4 mm from the right ear, which resulted in head and brain SAR_{10g} of 2.0 and 0.66 W/kg, respectively. The phone was operated and modified in the same was as in the study by Kwon et al. (2011). Thereby, the temperature of the phone was constant during exposure, as confirmed by recorded surface temperature of the phone. The participants were randomly exposed to 15-min RF and 15-min sham separated by a 5-min period of no exposure. NIRS signals were recorded bilaterally in frontal and parietal areas with a penetration depth of about 2.2 cm. Due to technical problems with NIRS recordings for three participants, only data from 23 boys was included in the analyses. No change of the total haemoglobin content, as measured by NIRS and reflecting regional blood flow, was found between the RF and sham exposure conditions.

Papers with uncertainties related to inclusion criteria

One study that failed to fully meet the defined inclusion criteria was a study by Volkow et al. (2011) which aimed to investigate if mobile phone exposure affects brain glucose metabolism. Exposure was applied to 47 healthy adult participants via a mobile phone handset (837.8 MHz) at the right side of the head for a period of 50 minutes. Following this, PET scans were performed. Increased brain metabolism in relation to exposure was reported. [The study was conducted single-blind and was not counterbalanced. Insufficient exposure information was provided, and the exposure level was also not controlled in the "on condition" in which the phone was receiving a call.]

Table 5.2.7. Mobile phone handset related studies assessing cerebral blood flow and brain metabolism

Endpoint and Participants	Exposure	Response	Comment	Reference
Studies with healthy adults				
rCBF recorded by PET 10 min after exposure 13 male volunteers out of 16 recruited (20–25 years)	GSM handset-like and base-station-like signals emitted by a planar antenna 11.5 cm from left side of head, 900 MHz (2, 8, 217, 1736 Hz and corresponding harmonics), crest factor 4.8 or 1.2, respectively SAR_{10g} 1 W/kg 30 min	Increased relative rCBF in several different regions of dorsolateral prefrontal cortex of exposed hemisphere following handset-like exposure only. No effects in other regions.	Double blind, partially counterbalanced, crossover. Correction for multiple comparisons.	Huber et al. (2002 ; 2005)
rCBF recorded by PET during exposure 13 male volunteers (21–35 years)	Modified GSM mobile phone against left ear, 902 MHz SAR_{10g} 0.99 W/kg (SAR increased by approximately 22% by the PET scanner) 45 min	Relative bilateral decrease of rCBF in auditory cortices during exposure. No effects in other regions.	Double blind, partially counterbalanced, crossover. P- values corrected for multiple comparisons provided. Effect attributed to auditory signal from mobile phone battery rather than EMF. For cognitive function see Section 5.2.1.	Haarala et al. (2003a)
rCBF recorded by PET during exposure 12 male volunteers (mean 25 years, no range provided)	Modified GSM mobile phone against left ear, 902 MHz SAR_{10g} 0.74 W/kg (SAR increased by approximately 22% by the PET scanner) 51 min	Decreased rCBF during EMF exposure in left fusiform gyrus in posterior inferior temporal lobe and increased rCBF in left and right frontal lobe.	Double blind, counterbalanced, crossover. Correction for multiple comparisons. For cognitive function see Section 5.2.1.	Aalto et al. (2006)
rCBF recorded PET before, during and after exposure 9 male volunteers (no ages provided)	W-CDMA handset-like signal emitted by microstrip patch antenna (right side of head), 1950 MHz SAR_{10g} 2.02 W/kg 30 min	No effect of exposure.	Single blind, randomized, crossover. Correction for multiple comparisons.	Mizuno et al. (2009)
Cerebral glucose metabolism recorded by PET after exposure 13 male volunteers (21–29 years)	GSM mobile phone) against right ear, 902.4 MHz SAR_{10g} 0.7 W/kg 30 min	Reductions in relative cerebral metabolic glucose rate in temporoparietal junction and anterior temporal lobe of right hemisphere.	Double blind, partially counterbalanced, cross-over Correction for multiple comparisons. For cognitive function see Section 5.2.1.	Kwon et al. (2011)
CBF recorded by PET during exposure 15 male volunteers (20–28 years)	GSM mobile phone against left ear, right ear and forehead, respectively , 902.4 MHz SAR_{10g} 0.7 W/kg (right exposure), 1.0 W/kg (left exposure), 0.7 W/kg (front exposure) 5 min, 3 times for each condition	No effect of exposure.	Double blind, partially counterbalanced, cross-over. Bonferroni correction for multiple comparisons. For cognitive function see Section 5.2.1.	Kwon et al. (2012b)
BOLD whole brain data recorded by fMRI[d] before and after exposure 12 male volunteers (19–25 years)	GSM mobile phone 1.5 cm from right ear, 902.4 MHz (8.33 and 217 Hz modulation components) SAR_{10g} at 2 cm depth: 0.5 W/kg 45 min	No effect of exposure.	Double blind, counterbalanced, crossover. Correction for multiple comparisons. For cognitive function see Section 5.2.1.	Curcio et al. (2012)

CBF in left and right prefrontal areas recorded by NIRS during and between exposures [Only values from 2-s "off periods used for analyses.] 16 male volunteers (31.2±6.3 years)	GSM handset-like signal emitted by planar antenna 11 cm from left side of head, 902.4 MHz, SAR_{10g} 0.15, 1.5 W/kg 20 min (15 times 80-second cycles: alternating 2 s on/ 2 s off signal for 20 s, then 60 s exposure free)	Short term effects in four of 182 comparisons for the left hemisphere (exposed side), and in two of 182 comparisons for the right hemisphere. No long term effects.	Double blind, randomized, cross-over. Correction for multiple tests by applying p<0.016 as significance level; a moderate correction since there was a very high number of tests. Significant findings partly for oxyhaemoglobin, partly for deoxyhaemoglobin and at different depths.	Wolf et al. (2006)
Blood circulation in the left auditory region recorded by NIRS during exposure 16 male volunteers (26.8±3.9 years)	UMTS base-station-like signal emitted by planar patch antenna 4 cm from left side of head. 1900 MHz SAR_{10g} 1.8, 0.18 W/kg 22 min (alternating on/off signal)	Short-term increase in oxyhaemoglobin and total haemoglobin concentrations during exposure to 0.18 W/kg; decrease in medium-term response of deoxyhaemoglobin concentration at 0.18 and 1.8 W/kg.	Double blind, randomized, cross-over. No EMF interference. Tukey correction for multiple comparisons. For subjective endpoints see Section 5.2.4; for heart rate see Section 9.2.1.	Spichtig et al. (2012)
Blood oxygenation in left and right frontal areas recorded by NIRS during exposure 11 female volunteers (20–23 years)	GSM mobile phone ~1.5 cm from left ear, 902.4 MHz (8.33 and 217 Hz modulation components) SAR_{10g} 0.5 W/kg 40 min	Linear increase in deoxyhaemoglobin concentration as a function of time during real exposure. No effect for oxyhaemoglobin and total haemoglobin.	Double blind, randomised, cross-over. No EMF interference. No correction for multiple comparisons. For subjective endpoints see Section 5.2.4; for heart rate see Section 9.2.1.	Curcio et al. (2009)
Middle left and right cerebral artery blood flow recorded by transcranial Doppler sonography before, during and after exposure 29 volunteers (21–35 years; 10 males,19 females)	GSM mobile phone at left side of head, 900 MHz SAR_{10g} 0.49 W/kg 20 min	No effect of exposure.	Double blind, randomized, cross-over. No correction for multiple comparisons. For autonomic nervous system responses see Section 9.2.1.	Ghosn et al. (2012)
Studies with children				
Blood flow in left and right frontal and parietal areas recorded by NIRS during exposure 23 male children (14–15 years)	GSM mobile phone 4 mm from right ear, 902.4 MHz, SAR_{10g} 2.0 W/kg (head), 0.66 W/kg (brain) 15 min	No effect of exposure.	Double blind, randomized, cross-over. No correction for multiple comparisons. For autonomic nervous system responses see Section 9.2.1.	Lindholm et al. (2011)

Abbreviations: BOLD: blood-oxygen-level dependent; fMRI: functional MRI; GSM: Global System For Mobile Communication; NIRS: near-infrared spectroscopy; PET: positron emission tomography; rCBF: regional cerebral blood flow; SAR_{10g}: SAR averaged over 10 g tissue; UMTS: The Universal Mobile Telecommunications System; W-CDMA: Wideband Code Division Multiple Access.

5.2.4 Symptoms and well-being

This section covers subjective endpoints including perception of RF, symptoms and parameters related to well-being. As reflected in the WHO 1993 Monograph, earlier experimental volunteer studies of relevance for this section focussed on sensations related to heating. Studies with two different exposure scenarios were included in the Monograph. One used exposures to MRI with SAR up to 4 W/kg for 20–30 minutes and with the primary aim to assess effects on thermoregulation responses. At the highest SARs the participants reported that they felt warm. In the other group of studies, small skin areas were exposed to assess perception of warmth or pain. Mainly frequencies in the 3–10 kHz range were used. Perception thresholds were lower for the highest frequencies, the longer exposure durations (tested in the range of few seconds) and for the largest exposed areas. As an example, exposure to 2450 MHz for 10 seconds over an area of 10 cm^2 resulted in a mean sensation threshold of 270 W/m^2, but with a large individual range (Justesen et al., 1982).

Over the past 20 years, the main focus of research has been on potential symptoms resulting from exposures far below thresholds for warmth sensation. A minority of people have reported that exposure to RF causes them to experience acute symptoms (Blettner et al., 2009; Levallois et al., 2002; Oftedal et al., 2000). The symptoms described do not seem to form any particular syndrome (Hillert et al., 2002; Röösli et al., 2004a; Schüz et al., 2006). For most of those affected, the symptoms typically develop minutes to hours after exposure, but for some people the latency period can be longer (Röösli et al., 2004a). In the absence of any generally recognised physiological mechanism through which exposure to low levels of RF could trigger symptoms a debate has arisen as to whether exposure to RF is responsible for causing these symptoms or whether other mechanisms explain the symptoms. In particular, psychological mechanisms including a 'nocebo effect' have been proposed by some (Rubin, Das Munshi & Wessely, 2006; Rubin et al., 2006; Stovner et al., 2008), whereby the belief that exposure is occurring is sufficient to trigger symptoms. The ongoing debate in this area has implications for the appropriate name for this condition. While proponents of an RF connection often use terms such as 'electromagnetic hypersensitivity' or 'electrosensitivity,' the more aetiologically neutral phrase 'idiopathic environmental intolerance attributed to electromagnetic fields' or IEI-EMF has been suggested as preferable (Hillert, Leitgeb & Meara, 2005). Resolving the debate over aetiology is important, not least because of the implications it has for developing an appropriate treatment for people with IEI-EMF (Rubin, Cleare & Wessely, 2008). Although disagreement exists as to the causes of the condition, it is unarguable that some of those affected suffer from severe social and functional impairment (Carlsson et al., 2005; Röösli et al., 2004a; Rubin, Cleare & Wessely, 2008) and that some form of intervention is required.

Subsequent to the completion of the 1993 WHO Monograph, a few studies have tested exposure resulting in thermal effects, while many single or double-blind experimental studies have tested whether RF exposures at much lower exposure levels can cause symptoms. These can broadly be categorised as studies which have tested effects of RF exposures that are analogous to those that can be received from a mobile phone handset and studies which have focused on exposures that are analogous to those which can be received from a mobile phone base station. While many studies have used only healthy volunteers as their participants, others have included a sample of people with IEI-EMF. Outcomes in this literature typically include acute symptoms or measures of subjective sleep quality or wellbeing, and the participant's ability to detect whether they are being exposed to an RF signal or not. This section reviews the results of this body of work.

Our search retrieved 59 relevant citations. Another nine citations were subsequently identified by reviewing the volunteer studies included in other sections of this monograph. Some of these papers reported the results of two or more studies (Cinel et al., 2008; Koivisto et al., 2001), while others reported different analyses relating to a single study (Hillert et al., 2008; Huber et al., 2000; Huber et al., 2003; Lowden et al., 2011). Taking these overlaps into account, details relating to 69 studies were considered. Two studies were excluded and are listed at the end of the section. They did not meet the inclusion criteria (listed in Appendix X); one of which reported the results of a non-blind provocation and another because it reported the effects of a bandage that can shield against electromagnetic fields on muscle soreness, but without providing any description of the shielding effectiveness of the bandage. Fifty-one studies remained to be included in the Monograph. For 13 of these there were uncertainties related to the inclusion criteria. These are discussed briefly in separate sections and are not included in the summary tables. Further three papers contained the results of a formal meta-analysis. Of the studies that met the inclusion criteria in full, 41 related to handset exposure, eight related to base stations and two assessed the perception thresholds of participants for signals of varying frequencies.

Tables are provided at the end of each section below which summarize the results of these studies and provide information about their methods. Similar details as well as more details about results are included in the text. Unless otherwise noted in the text or tables, the studies that were identified were double-blind, with neither the participant nor the relevant research personnel being aware of which experimental condition was which. When information about measures to ensure blinding was given in the paper, this has been included in the text. Information about estimates of statistical power for each study is provided in both the text and tables, where this was available. When no power estimation has been provided, comments about particularly small samples sizes are made since the smallest samples are attached with highest uncertainties provided other study details are similar. When there was no such information, studies with particularly small samples sizes have been highlighted. Exposure was controlled in all studies that are included in the analysis as basis for the health risk assessment. Where SAR was provided for a study, this is specified in both the tables and text. Otherwise power density or electric field strength is given, or, if none of these quantities were provided, output power along with other details of exposure setup. In general, aspects of study design and methodology have been discussed in greater detail if they were assessed to be of importance for the interpretation of the study results.

In the majority of the studies, outcomes other than subjective endpoints were also measured. These outcomes are not discussed in this section, but are covered in Sections 5.2.1–5.2.3 and 6.2, 7.2 and 9.2.

5.2.4.1 Mobile phone handset related exposures

The basic design and results of the 41 studies which related to handset exposures are summarised in Table 5.2.8. Most of these used signals and localised exposures typical of those that occur when using mobile phones. A few studies with base station like exposures applied local exposures and exposure levels that are comparable to those caused by exposure when talking on a mobile phone. These have also been included in this section. Thirty of the studies assessed healthy participants only. Eleven included a sample of participants with IEI-EMF.

Studies with healthy adult volunteers

In the earliest study identified, Mann et al. (1996) asked 14 healthy male volunteers to spend three nights in their sleep laboratory. The first night was used as a habituation session, while in the second and third nights volunteers were randomly allocated to be exposed to a GSM 900 MHz signal (average power density: 0.5 W/m^2) for 8 hours while they slept or to a sham signal. Although volunteers were not informed which condition was which, and neither was the technician responsible for scoring EEG measures, it was not clear from the paper whether other staff in contact with the volunteers were also blinded. Rating scales for sleep quality and well-being were completed on the morning following each exposure, while other ‘side-effects’ were assessed in brief non-standardised interviews. Data for two participants had to be excluded due to technical problems. No effect was observed for sleep quality or for three of the four symptoms that were assessed. A small increase in self-rated calmness was noted following exposure (mean exposed calmness 71.09, mean sham calmness 62.73, $p < 0.05$). No other side effects were reported. [No statistical adjustments were made to account for the number of endpoints that were measured in this study, however, leaving open the possibility that the significant result was a chance finding. Equally, the small sample size in this study suggests that even relatively large effects on subjective endpoints might not have been detected as significant.]

In a similar experiment, Borbély et al. (1999) asked 24 healthy men to spend two 2-night periods in their sleep laboratory. The first night of each period was used as a habituation session, while in the second night volunteers were exposed to either intermittent 900 MHz exposure (a cycle of 15 minutes exposed followed by 15 minutes unexposed, lasting over an 8 hour sleep) or sham exposure. The two exposure conditions were given a week apart and in random order. A GSM base station-like signal was emitted by three antennas placed behind the bed and 30 cm from the head of the participants resulting in a SAR comparable to that from a handset (SAR_{10g} = 1 W/kg). Sleep quality and mood were assessed on the morning after each exposure. The authors reported that among participants who received the sham exposure first, there was a non-significant trend (p = 0.07) for self-reported waking to be reduced following exposure (mean sham 20.0 min, mean RF 10.5 min). This was not apparent for participants who received the RF exposure first. Although the authors reported measuring “subjective sleep variables and mood” after waking, only the results of self-reported waking were given. [The relatively small sample size was a limitation of this study and may have prevented small yet important effects from being observed.]

Following a night spent sleeping in their laboratory for screening purposes, Huber et al. (2000) exposed 16 men to three conditions: a 30-minute exposure to a 900 MHz GSM base station-like signal on the left side of their head, an identical exposure to the right side of the head and a sham condition. The exposure was emitted by antennas placed 11 cm from the head resulted in maximum SAR averaged over 10 g of 1 W/kg. Exposures took place prior to a three-hour sleep during the late morning. To ensure volunteers were able to sleep during the morning, their sleep the night before was restricted to only four hours. One week separated each condition from the next. Subjective sleep variables (waking after sleep onset, sleep latency, sleep quality) and mood were assessed 15 minutes after waking in each condition. No significant effects were observed for these sleep variables, while no result was reported for mood. In a subsequent paper (Huber et al., 2003), the team also noted that the participants were no better than chance at detecting which condition was active and which was sham. [Again, however, the small sample size may have limited the ability of this study to detect small effects.]

A paper by Koivisto et al. (2001) described the results of two experiments testing whether exposure to a 902 MHz GSM signal (generated by a phone with a mean power of 0.25 W positioned next to the head) caused greater symptom reporting than exposure to a sham condition. The phone was placed in a leather bag to prevent phone heating during operation to be sensed, and skin temperature measurements suggested that thermal cues were unlikely. In both of these experiments, 48 volunteers (different participants for each experiment) were exposed to the two conditions and then asked to complete ratings for six symptoms. The duration of exposure was about 60 minutes for the first experiment and about 30 minutes for the second experiment. The order of sham and real exposures was counterbalanced in both experiments. In the first one the two conditions were given in separate sessions 24 hours apart, while in the second one both conditions were in the same session. The second experiment also differed from the first in that it used a 9-point scale to measure symptom severity, rather than a 4-point scale, in the hope that this might prove more sensitive to small changes. Despite this, no effects of exposure were observed in either experiment. [These experiments were single-blind. Nonetheless, the reasonable sample size and the replication of the results in two experiments are positive features of this work.]

Haarala et al. (2003a) investigated the effects of RF EMF on regional cerebral blood flow during exposure. A modified GSM mobile phone handset (902 MHz, SAR_{10g} = 0.99 W/kg) was used to generate the exposure. In a pilot study prior to the main experiment, 10 participants were exposed ten times each of active or sham conditions, with order of conditions counterbalanced, in order to check whether they could discriminate between them. Response accuracy of 51% was reported. [Very few details about the pilot study were provided in the paper, including details concerning blinding, length of exposure and intervals between exposure].

In a pilot study run prior to a main experiment testing the effects of mobile phone exposure on performance during an auditory task, Hamblin et al. (2004), tested whether two volunteers could detect the difference between the sham and RF exposure conditions. The volunteers were each exposed to five one-minute long exposures to a GSM 895 MHz signal and an equivalent number of sham signals in randomized order. [It was unclear from the reporting whether these exposures were single or double-blind.] In the real exposure condition the GSM phone was set to transmit at maximum output power, with a mean value of 0.25 W, while placed next to the right side of the head. When forced to give their best guess as to whether each condition was active or not, the participants were correct in 11 out of 20 trials. [Relatively few details for this pilot study were provided including the nature of the blinding and the interval between conditions.]

As part of a study that was primarily intended to test autonomic function, Tahvanainen et al. (2004) exposed 32 healthy participants to a 900 MHz GSM signal (maximum SAR = 1.57 W/kg), a 1800 MHz GSM signal (maximum SAR = 0.7 W/kg) and a sham condition, each lasting for 35 minutes. Exposures were generated using a dual band mobile phone held next to the dominant-hand side of the head. Each volunteer participated in two sessions at least one week apart, one session included the 900 MHz exposure and sham exposure and the other the 1800 MHz exposure and sham. Volunteers were randomly allocated to receive the 900 MHz or 1800 MHz condition in the first session, and were also randomly allocated to receive either the GSM signal first or the sham condition first in each of the sessions. The order the two RF signals as well as the order of RF and real exposures were counterbalanced across the participants. Following each exposure, and after completing a range of tests designed to assess autonomic function, participants were asked whether they could tell whether the phone was emitting or not and to describe how they felt. Relatively few volunteers reported any subjective sensations and these were equally distributed between the GSM and sham conditions. [A formal power calculation and an associated stopping rule were reported for the study. However, these were based on the study's ability to detect a change in blood pressure, rather than any subjective endpoint.]

Curcio et al. (2005) exposed 20 healthy participants to a GSM 902.4 MHz signal (maximum SAR = 0.5 W/kg) generated by a handset held against the left side of the head or a sham exposure. To ensure that no potential sound from the transmitting mobile phone should be heard, acoustic noise was delivered by a loudspeaker. Each exposure lasted 45 minutes and was separated by a minimum of 48 hours. The order of conditions was randomized. In addition to having various EEG measurements taken, participants completed a widely used measure of sleepiness immediately following each exposure. While the numerical results of the analysis of this secondary outcome variable were not explicitly reported, the authors did say that “no significant main effects or interactions were noted.” [Given the sample size, however, it is unlikely that this study had sufficient statistical power to detect small effects of exposure on sleepiness.]

As part of a sleep experiment exploring EEG parameters, Loughran et al. (2005) asked 50 healthy participants to spend two, 2-night periods sleeping in their laboratory. The first night of each occasion was a habituation session. For the second night, participants were exposed to either a 30-minute GSM 894.6 MHz signal immediately prior to sleep or a 30-minute sham condition. The order of exposures was determined randomly. Exposures were generated with a mobile phone handset held against the right side of the head, which resulted in maximum SAR of 0.674 W/kg averaged over 10 g (Loughran et al., 2012). Measures were taken to prevent acoustic cues or heat to be sensed from the operating phone. As a secondary outcome, participants were asked at the end of the experiment if they had been able to tell which condition was which. No evidence was found that participants could make this distinction.

In a subsequent sleep experiment, Loughran et al. (2012) asked 20 healthy volunteers who had previously taken part in an earlier experiment by this team (Loughran et al., 2005) to spend three consecutive nights in their laboratory. The first night served as a habituation session. The second and third nights were randomized to involve sham exposure or exposure to a 894.6 MHz GSM signal and to obtain counterbalance in the order of exposures. The same modified mobile phone was used in this study as in the previous one; also this time SAR_{10g} was 0.674 W/kg. Each exposure lasted for 30 minutes and was followed by a full night’s sleep. The next morning, participants completed a sleep questionnaire. There was no evidence of any effect of exposure on sleepiness the following morning. This result also held true in a second analysis with participants grouped according to the type of changes apparent in their EEG results during non-REM sleep in this group’s earlier experiment. [The small sample size for this study is a weakness].

In a paper providing limited methodological details, Aalto et al. (2006) described a study with counterbalanced design that was at least single blind. Ten healthy volunteers were exposed 10 times each to active and sham conditions using a 902 MHz GSM mobile phone resulting in a SAR_{10g} of 0.74 W/kg. [There was no information about exposure times.] By applying an external power supply, the battery as well as the loudspeaker was removed to prevent noise to be generated when operating, and in addition, an earplug was inserted in the ear of the mobile phone side. This experiment was performed as part of the piloting for a second study described in the paper in more detail. The authors reported that “the subjects could not detect the EMF exposure condition any better than by guessing (response accuracy 51%).” [Although the level of detail for this study was sparse and the number of participants was limited, the use of multiple trials for each participant represents an important positive feature, increasing the likelihood that the study would have identified an effect had one existed.]

Keetley et al. (2006) aimed at investigating the effect of exposure to a GSM 900 MHz signal on neuropsychological performance. In a preliminary pilot study to test the double-blinding of their exposures, 19 volunteers were exposed to a GSM signal (phone set to transmit at the mean output power 0.23 W; [no SAR provided]) and to a sham one (phone set on stand-by). During exposures the phones was placed next to the left ear. Since the phone emitted “just-perceptible buzzing sound” when transmitting at full power (even though the loudspeaker was removed), the phone was covered with soundproofing material, and heat insulation between the phone and the head was applied to prevent the participants from sensing the difference in temperature in the two conditions. Only five of the volunteers believed they could detect a difference between the conditions. Of these five, two determined the condition correctly and three were incorrect. [Very limited methodological details were available for this small study, including the length of exposure, the number of exposures per participant and the interval between exposures.]

Wolf et al. (2006) investigated the effects of GSM 900 MHz signals on cerebral blood circulation (see Section 5.2.3). Eighteen volunteers participated, however only 16 were used for final analysis due to movement artefacts in the data. Each participant underwent three exposure conditions (SAR_{10g} 0.15 W/kg, 1.5 W/kg, sham exposure) on three separate days in randomized order. The exposure was emitted by a planar patch antenna (11 cm from left side of head) and consisted of 15 repeated cycles, which included 20-s exposure (alternating 2 s on / 2 s off periods) followed by 60-s rest, and lasted for a duration of 20 min. After each exposure, participants stated whether they believed they had been exposed or not. No significant correlation was reported between the guesses of the participants and the true exposure status. [No numerical data were reported for this outcome, however, and the small sample size of the study is notable].

In a sleep study conducted by Fritzer et al. (2007), 20 healthy male volunteers spent eight consecutive nights in a sleep laboratory which used foam absorbers to assure a well-defined electromagnetic field within the testing chamber. In all cases, participants were not exposed to any RF EMF during the first two nights, which served as habituation and baseline nights. For the next six nights, participants were randomly assigned to be exposed to either a 900 MHz GSM signal ($n = 10$) or a sham condition ($n = 10$). The groups were matched with respect to age and education background. The GSM signal was emitted by three antennas 30 cm behind the head of the participants, which resulted in a maximum SAR of 0.875 W/kg averaged over 1 g. Self-report questionnaires were used to measure quality of sleep and well-being immediately before and after sleeping, and data from the third and eighth night were analysed. No effects of exposure condition were observed. [Although a power calculation was performed for this study, this was based on detecting an effect size larger than 1.32 for sleep and neuropsychological variables. The ability of this study to detect subtle changes in subjective sleep quality is doubtful.]

As part of a study to assess heart rate variability in response to exposure, Parazzini et al. (2007) exposed 26 volunteers to a 900 MHz GSM signal for 26 minutes and to an equivalent sham signal. Sessions were separated by at least 24 hours and their order was determined randomly. The mobile phone was operated at maximum output power (2 W during the pulse) while positioned against the side of head. SAR was measured for the area of interest for the autonomic regulations, 10.5–13.5 cm of deepness in the brain, and in this area SAR was less than 0.02 W/kg. Following several tests of heart rate variability, volunteers were asked to complete a questionnaire concerning their comfort and to test whether they could discriminate between the real and sham conditions. Twenty of the participants reported that the two sessions appeared identical, four reported warming sensations during the real exposure and two during the sham exposure. As with other studies, therefore, no evidence was found that participants could detect the exposure at better than chance levels.

A paper by Cinel et al. (2008) described the results of three separate double-blind experiments performed by their team. In each experiment, healthy volunteers were exposed to two 40-minute conditions: a sham condition and a condition involving exposure to either an 888 MHz GSM signal or a continuous wave signal (both signals: $SAR_{10g} = 1.4$ W/kg (Cinel et al., 2007)) emitted by a mobile phone next to the head. The two experimental conditions occurred about a week apart in each case, with the order counterbalanced between participants. In addition to completing a range of cognitive tests, participants were asked to rate five symptoms before and after each exposure. Between 159 and 167 participants took part in each experiment. To adjust for the number of statistical tests conducted in these studies, the authors adjusted their criterion for statistical significance to $p < 0.01$. One symptom (dizziness) in one of the experiments was significantly increased during real exposure. When the data from the three studies were pooled, dizziness increased significantly during the real exposure ($p < 0.01$). However, this effect was only due to the results from the one experiment, since no difference between sham and real exposures were found for the other two experiments. Therefore the observed increase for dizziness was not a consistent finding. No other symptoms showed any effect. [The sample size for this study was impressive (pooled n=486) while its general methodological quality was good.]

In one of the largest studies performed, Croft et al. (2008) investigated the effects of GSM mobile phone handset exposure on alpha activity in the resting EEG. Two exposures (real and sham) were used, with 120 participants recruited for the study, half receiving left hemisphere exposure and the other half receiving right hemisphere exposure. For each participant the exposure conditions were a week apart and the order of real and sham was random and designed to be counterbalanced. Exposure consisted of a 894.6 MHZ GSM handset-like signal ($SAR_{10g} = 0.67$ W/kg) that was produced by a mobile phone handset that was modified to prevent the participants from hearing any sound from the phone when operating. Participants performed a battery of tests, followed by an electro-oculographic calibration task. Exposure was then applied for 30 minutes in which resting EEG was recorded and another test battery performed. Participants were asked to report whether they believed each session was 'on' or off.' During the active exposure, 78% of participants believed the phone was off. During the sham exposure 84% believed it was off. [The study was well designed and conducted and generally methodology is carefully reported. The blinding of exposure conditions was ensured by reducing acoustic cues and omitting heat from the phones to be sensed.]

Kleinlogel et al. (2008a) explored the effects of both GSM and UMTS signals on well-being by exposing 15 healthy men to four experimental conditions: a GSM 900 MHz signal ($SAR_{10g} = 1$ W/kg), two forms of UMTS 1950 MHz signal (SAR_{10g}: 0.1 W/kg and 1 W/kg respectively) and a sham condition emitted by antenna against the left ear. Each exposure lasted for 30 minutes and was separated from the others by an interval of one week. The order of exposures for each participant was determined randomly. Testing took place within a basement room that was equipped with electromagnetic field absorbers to minimise any extraneous exposure. Questionnaires were administered before and after each exposure to assess subjective discomfort and impairment. No effect of exposure was found for change in these outcomes from pre to post-exposure. [However, as the authors acknowledged, the small sample size means that only relatively strong effects would have been detected.]

Eleven healthy volunteers were exposed by Curcio et al. (2009) to 40 minutes of a GSM 902.4 MHz signal and 40 minutes of a sham signal, primarily to study the effects of exposure on frontal cortex hemodynamics. A mobile phone placed about 1.5 cm from the left ear was used for exposure with SAR_{10g} estimated to be 0.5 W/kg. The exposures took place in an “electromagnetically quiet” basement room. Testing sessions for each participant were separated by two days, were at the same time of day and the order was determined randomly. At the end of each exposure, participants completed measures of 10 symptoms. Only one symptom showed any association with the exposure condition, with participants being more likely to experience a headache following the sham exposure ($p = 0.04$). [Given that no adjustment was made for the number of statistical tests performed in this study and that the single significant finding was of borderline significance, it seems likely the finding was a type one error. The small sample size of the study limits the ability to conclude that small effects of exposure do not exist, however.]

In a single blind study, Kwon et al. (2010b) tested the ability of 17 volunteers to detect exposure to GSM 902.4 MHz mobile phone signals (SAR_{10g} = 0.82 W/kg). The signals were emitted by the antenna of a mobile phone connected to an external signal generator. The loadspeaker and the buzzer of the mobile phone was removed. Each participant was exposed to 100 trials involving five seconds exposure each, using a procedure and set-up described as similar to that reported for Kwon et al. (2008), which was a randomised and counterbalanced experiment. Participants performed no better than expected by chance at detecting the signal.

To test the impact of TETRA signals on the well-being of emergency service personnel who regularly use a TETRA handset, Riddervold et al. (2010) tested 53 emergency service workers on two occasions. On one occasion, they were exposed for 45 minutes to a TETRA 420 MHz signal generated by a handset but emitted by a separate antenna placed in the “cheek position” resulting in a SAR_{10g} of 2 W/kg. On the other occasion, an equivalent sham exposure was used. The order of exposures was randomized and designed to be counterbalanced and exposures were separated by at least 24 hours. Testing took place within a room lined with radio-wave absorbers to prevent outside fields from affecting the testing. As well as completing a range of cognitive tasks during the exposures, participants were also asked to report the severity of 11 symptoms before and after each exposure. A power calculation was performed based on one of the cognitive endpoints. Despite the relative large size and methodological strengths of the study, no effect of exposure on symptoms was observed, nor were participants able to discriminate between the two conditions.

Schmid et al. (2012a) exposed 30 men to three experimental conditions in their sleep laboratory with the primary aim to test effects of different pulse modulation frequencies on sleep EEG. These conditions consisted of a sham condition, a 900 MHz GSM condition pulse-modulated at 14 Hz, and a 900 MHz GSM condition pulse-modulated at 217 Hz. The RF EMF signals were emitted by an antenna 115 mm from the left side of head, which resulted in a SAR_{10g} of 2 W/kg under both GSM exposures. Acoustic noise was used to mask any sound that might accompany the RF EMF exposure. Each exposure occurred immediately before bedtime and lasted for 30 minutes. Each exposure night was preceded by an adaptation night and was separated from the next exposure night by one week. The order of exposure conditions was determined randomly. Participants were asked to record subjective mood, sleep quality, well-being and whether they could discriminate between the conditions. Although numerical data for subjective endpoints were only reported for the discrimination results in the paper, the authors reported finding no significant differences in any of these variables.

To further test effects of features of pulse modulations primarily on sleep EEG, the same team, Schmid et al. (2012b) asked 25 men to attend their sleep laboratory for three 2-night periods at weekly intervals. The first night of each period served as a habituation session. On the second night participants received 30 minutes of exposure to either a 900 MHz RF signal emitted by a patch antenna 115 mm from left side of head (SAR_{10g} = 2 W/kg), a pulsed magnetic field produced by Helmholtz-like coils (spatial peak magnetic flux density = 0.70 mT) or a sham condition prior to sleep, with the order of exposures determined randomly. Participants were asked to complete questionnaires on waking concerning their ability to detect the field, their mood and their well-being. Various other measurements, including EEG, were taken during the night. Although limited details were supplied in the paper concerning subjective endpoints measured in the study, the authors did report that “no significant differences between the exposure conditions were found for measures of mood, well-being or subjective sleep quality. Additionally, subjects were not able to perceive the applied fields.”

Aiming to test potential effects of exposure from UMTS on various endpoints, Spichtig et al. (2012) exposed 16 men to three relevant experimental conditions on three separate days, with a signal generator being used to produce low (SAR_{10g}: 0.18 W/kg) or high UMTS signals (SAR_{10g}: 1.8 W/kg) and a sham condition. Intermittent (20 second on/60 second off) UMTS base station-like signals were emitted by a planar patch antenna 4 cm from the side of the head. The exposure conditions were given at separate days, always at the same time of day. Each exposure lasted for 22 minutes and the order of conditions was determined randomly. The experiment was conducted in a basement with low level of background electromagnetic fields and with RF absorbers used to provide additional shielding. Subjective tiredness and well-being were assessed immediately before and after each exposure. The authors reported that no effect of exposure was observed for either endpoint, although the numerical data for this analysis were not reported. [As with other studies, however, the low sample size of this experiment means that small effects of exposure might have been missed.]

Studies including children and adolescents

In order to test whether effects on cognitive performance of RF exposure might differ according to age, Haarala et al. (2005) tested 32 children aged 10 to 14 years, who were exposed to a 902 MHz GSM signal (SAR_{10g} = 0.99 W/kg) or a sham exposure for 50 minutes on consecutive days at the same time of day. The order of exposures was counterbalanced across the group. A mobile phone handset placed next to the left side of the head was used for exposure. The loudspeaker was removed to reduce the sound generations, the phone was placed in a case and measurements of temperatures indicated that no difference could be sensed between the real and the sham exposure. As well as performing a variety of cognitive tasks during exposure, the children were asked at the end of each session to say whether they felt the exposure equipment was or was not emitting. As a group, the children were unable to discriminate between these two exposures. In a second study by this team, Krause et al. (2006) exposed 15 children aged 10 to 14 years to two 30-minute conditions; a 902 MHz signal (SAR_{1g} = 1.4 W/kg) and a sham condition. The participants underwent the two exposure conditions in counterbalanced order and with a short break between them. To prevent sound cues from the operation phone placed next to the left side of the head, the loudspeaker was removed and the battery was changed to a model that did not produce any noise. In this study the main aim was to assess effects on ERPs, and in addition the participants were again asked at the end of each condition whether they believed the exposure had been 'on' or 'off.' Again, there was no evidence that they were able to discriminate between the two conditions.

Croft et al. (2010) recruited 41 adolescents (aged 13 to 15), 42 young adults (19 to 40) and 20 'elderly' (55 to 70) participants. All were exposed for 55 minutes to sham, 2G (894.6 MHz, SAR_{10g} 0.7 W/kg) and 3G (1900 MHz, SAR_{10g} 1.7 W/kg) conditions, by placing a phone at the side of the head. The exposure conditions were on separate days at least 4 days apart. The order of conditions and side of exposure were counterbalanced across participants and exposures were randomly assigned, and for each individual side of exposure and time of day were consistent. The phones produced no audible sound during operation. Testing took place within a shielded room. A measure of psychological arousal or 'activation' was completed by participants before exposure, after 50 minutes of exposure and 7 minutes later. Participants were also asked if they could tell which condition involved RF exposure. No evidence was found that participants were able to discriminate between conditions and no evidence was found of any effect of 2G exposure on activation, or of 3G on activation in the adolescent or elderly groups. Activation was higher in young adults during 3G exposure than during sham exposure ($p = 0.046$), however this effect did not remain after a Bonferroni correction for multiple tests was applied which reduced the critical p-value to 0.036.

Studies including volunteers with IEI-EMF

Radon and Masche (1998) tested 11 participants with IEI-EMF using a GSM 900 MHz signal to see whether they were able to discriminate between real and sham exposures. The GSM signal was emitted by an antenna placed 1.9 meters in front of the participants resulting in a power density of 0.24 W/m^2. Participants were tested over 12 trials each, with each trial consisting of three 2-minute exposures to GSM (once) or a sham condition (twice) with a 10-second break between each exposure. Between each trial there was a 30- minute break. The authors estimated that a choice of 12 trials per participant would result in a 1.4% chance of each of them getting more than 67% of trials correct, provided no hypersensitivity to the exposure. The results for each volunteer were assessed to see if any individual was able to discriminate between the conditions. No evidence of this ability was found. Similarly, there was no evidence that the whole group of participants were able to discriminate between the exposures. [All trials were conducted over the course of a single day for each participant, raising the possibility that carry-over effects from the early trials prevented participants from differentiating between the later trials. However, the authors noted that no differences could be observed between the results for the first 6 trials conducted for each participant and the last six trials, providing some evidence that this was not the case. The authors also reported that most of the participants were not able to tell which EMF frequency range they assumed was the reason for their symptoms; therefore it is uncertain whether the chosen exposure was relevant for testing their assumed hypersensitivity. Although it was stated that the 50-Hz background fields were similar to those in everyday life with an electric fields of 5.1 V/m and a magnetic flux density of 57.9 nT. No information was provided about the background level of RF EMF in the testing room. Therefore, it is uncertain whether the testing environment was optimal for the participants to detect the applied exposure.]

In a single blind experiment, Hietanen et al. (2002) tested 20 people who reported usually developing symptoms within 30 minutes of mobile phone use. These participants were exposed to three or four experimental sessions lasting up to 30 minutes each. Experimental sessions involved exposure to a sham condition, analogue NMT with a 900 MHz frequency, GSM 900 MHz and GSM 1800 MHz signals. For each participant, the sham condition occurred either first or second in the order of exposures. SAR values were not reported, although the average output power for the GSM 900 MHz condition was given as 0.25 W, that for the GSM 1800 MHz condition as 0.125 W and that for the NMT condition as 1 W. Testing took place in wooden houses where no electricity was in use in rural locations. Participants were unable to discriminate between the various conditions, while symptom reports were more common in the sham condition than in the genuine exposure conditions. [Fewer symptoms during mobile phone than sham exposure were unexpected since the participants regarded themselves as hypersensitive to RF exposure from mobile phones. It is possible that this may have reflected the decision to place sham conditions relatively early in the order of exposures for each volunteer. Only limited statistical analysis of subjective endpoints was reported in this paper.]

Rubin et al. (2006) exposed 60 participants with IEI-EMF and 60 participants without IEI-EMF to three conditions. These consisted of a GSM 900 MHz signal, a continuous wave (CW) condition and a sham condition. The RF EMF signals were emitted by a standard handset positioned a few millimetres from the left side of the participants head, both signals resulted in a SAR_{10g} of 1.4 W/kg. To ensure that the phone was heated similarly in all conditions, a CW was generated in the sham condition, but the signal was led to an internal load instead of being emitted by the antenna. Each exposure lasted for 50 minutes, was separated from the next by at least 24 hours and the order of exposures was counterbalanced and randomized. All exposures were preceded by a 30 minute adaptation period to test whether the laboratory environment itself triggered symptoms: two participants were excluded based on the findings of these adaptation periods and were replaced. Participants were asked to complete symptom measures before, during and after each exposure and to give their best guess as to which condition was which. The primary outcome for the experiment was headache severity and a power calculation was used to ensure the study was able to detect an effect size of 0.5 for this endpoint. No effect of exposure was observed for any of the eight symptoms that were assessed, nor could participants reliably tell whether a given condition involved a genuine exposure or not. Although 26 ‘severe’ reactions occurred (including withdrawals from the study and requests for exposures to be terminated early), these were just as likely to occur following the sham condition as following the GSM or CW conditions. [Given that IEI-EMF participants were only included if they reported normally experiencing headaches within 20 minutes of using a GSM mobile phone, the study represented a fair test of the volunteer’s sensitivity. The fact that IEI-EMF participants reported a high level of confidence in their ability to discriminate the conditions in this study (although this confidence was misplaced) provides additional evidence that they themselves felt it to be a fair test. Although the testing room used in the study was not screened against outside EMF, the use of the adaptation period provides some reassurance that the results were not adversely affected by external fields. The study therefore represents good evidence against the existence of a sensitivity to GSM signals.]

In a single-blind experiment with a primary focus on physiological and cognitive response, Wilén et al. (2006) tested 20 people with IEI-EMF who reported symptoms in connection with mobile phones only and 20 without IEI-EMF. These participants were exposed to a GSM 900 MHz handset-like signal emitted by a base station antenna 8.5 cm from right side giving a SAR_{10g} of 0.8 W/kg, and a sham condition. Each condition lasted for 30 minutes. The order of conditions was randomized and they were at separate days at the same time of day. Exposure occurred in a room that had been specially designed to ensure a low background level of power frequency and radiofrequency fields. Following each exposure, participants were asked to complete an open-ended questionnaire that allowed them to describe any symptoms that they had experienced during the exposures. Although 18 out of the 20 IEI-EMF participants experienced symptoms during the experiment, these were just as likely to occur during the sham condition as during the genuine condition. No control participants reported any symptoms. [Given that the IEI-EMF participants were specifically recruited based on their apparent sensitivity to mobile phones and that they were given the freedom to record any symptoms that occurred during the exposures, this experiment was a fair test of their sensitivity. Although the results suggest that such a sensitivity does not exist, the relatively small sample size and use of single rather than double-blinding means that the results are not wholly conclusive.]

Oftedal et al. (2007) tested people with IEI-EMF who reported pain or discomfort in the head during or shortly after mobile phone calls which lasted between 15 and 30 minutes. Participants meeting these criteria were first screened using a non-blind provocation test using the study exposure equipment. Only those who experienced symptoms during the non-blind experiment were allowed to continue to the double-bind test. Seventeen participants took part in the double-blind stage in which they were exposed to between one and four pairs of exposure (sham and GSM 902.4 MHz). The same exposure system was applied as by Wilén et al (2006) and SAR_{10g} was 0.8 W/kg. The order of the exposure conditions was randomized and counterbalanced. Each individual exposure lasted for 30 minutes and took place within a shielded testing room. At least two days separated each testing session. Following each exposure, participants were asked to record the severity of their headaches and of any other symptom they might have experienced. A power calculation for this study was performed, based on the ability to detect an increase in headache of half a standard deviation (providing a power of 96%). No effect of exposure was found for symptoms, nor were participants able to tell which condition was which.

With the primary aim to test effects on auditory and vestibular functions, Bamiou et al. (2008) recruited nine people with IEI-EMF who reported symptoms which they attributed to mobile phone usage and which usually occurred within 20 minutes of using a mobile phone, and 21 healthy volunteers. All were exposed to six 30-minute exposures, consisting of two 882 MHz GSM signals, continuous wave and GSM pulse modulated signals, and one sham condition at left and right sides separately. The RF signals were emitted by a generic mobile phone placed next to the side of the head and resulting in a SAR_{10g} of 1.3 W/kg. In the sham condition, the phone was operating to be heated similarly as in the RF exposure conditions by diverting the generated RF power to an internal load instead of emitting the RF signals by the antenna. Exposures all occurred during 4 hours on the same day with the order of the conditions randomized. No shielding was used within the testing rooms. Participants were asked to report which sessions were ‘on’ and which were ‘off,’ but the results of the two groups were consistent with guessing at random. [Although the exposure used in this experiment was consistent with the exposure reported as problematic by the IEI-EMF participants, the fact that all exposures occurred on the same day is problematic. It is notable that some of the IEI-EMF participants reported that the symptoms they normally experienced in everyday life could last for hours or days. A possibility therefore exists that carry-over effects from the earlier exposures may have prevented participants from discriminating between the later exposures. The low sample size also limits the ability to generalise from this study.]

Hillert et al. (2008) and Lowden et al. (2011) reported data from the same experimental study in which 37 people with IEI-EMF and 31 healthy participants were exposed to an 884 MHz GSM signal and a sham condition. The GSM signal was emitted by a micropatch antenna placed some centimetres from the left side of head resulting in SAR_{10g} of 1.4 W/kg. In order to mimic the sensation from a warm phone, a small ceramic plate connected to the left ear lobe was heated to 39 ºC during all exposure sessions. All IEI-EMF participants reported headaches, vertigo or other discomfort in the head following normal use of a GSM mobile phone. Exposures lasted for 3 hours prior to a full night’s sleep in a sleep laboratory and were separated by at least one week, the order was determined randomly. Testing occurred in unshielded rooms, although assessment of low frequency and radiofrequency fields revealed low background levels (< 0.05 V/m). Before and after 90 minutes and 2 hours 45 minutes of exposure participants were asked to report on a range of subjective symptoms and whether they could discriminate between the exposures. The last assessment during exposure was used for the primary analyses. No effects of exposure were found for most outcomes, although an increase in self-reported heat sensations in the ear was noted in one of the three techniques used to measure this (effect size not given; $p < 0.05$) and an increase in headache was also noted (odds ratio 2.49, 95% confidence interval 1.16–5.38; $p < 0.01$). For headache, the effect was due to healthy participants, rather than people with IEI-EMF, reporting more headaches after the GSM condition. [No adjustment for multiple analyses was made.] Only a subset of participants took part in the subsequent sleep component of this study (23 IEI-EMF, 25 healthy participants). Following sleep, no effects of exposure were observed on self-reported sleepiness, fatigue or arousal. [The experiment used lengthy exposures to a signal that the IEI-EMF participants reported being sensitive to and measured outcomes that these participants reported normally experiencing following exposure. As such it was a good test of their reported sensitivities and it is therefore notable that no such effects were found for this group.]

In order to test whether any individual could be found who was particularly adept at detecting RF, Kwon et al. (2008) exposed 78 healthy participants and 6 people who believed themselves to be able to detect mobile phone signals to 600 exposure sessions each. Two of the six people who reported being able to detect mobile phone signals as reported experiencing symptoms in their day to day life which they attributed to mobile phone exposure. The tests consisted of two sets of tasks (300 trials in each): a set where the participant was asked to report whether a field was present or not for 5 seconds and a set where the participant was asked to report whether the field changed during the exposure from on to off or vice versa. In the latter case the field was on for 2.5 seconds and off for 2.5 seconds. Order of exposure conditions was randomized and counterbalanced for each participant. Exposures were generated by an external signal generator and fed to the antenna of a 902 MHz GSM mobile phone (SAR_{10g} = 0.82 W/kg). To prevent sound cues, the loudspeaker and the buzzer of the phone was removed and earplugs with masking noise were used. A monetary prize was offered for participants who performed well in the task. Testing took place in soundproof room, although no mention was made of shielding for EMF. For the majority of participants, no evidence was found that they could discriminate between conditions. However, two participants (neither of whom had IEI-EMF) performed remarkably well in determining whether a signal was present or not, getting the answers correct 97% and 94% of the time. Both participants were retested six months later using another 600 trials each of the on / off task. Neither of them could replicate their initial performances. [This study, with its very large number of trials per participant, represents an impressively strong test of the sensitivity of the participants. How two participants managed to perform so well in the initial test remains unexplained, but their inability to repeat this suggests that it does not relate to some bioelectromagnetic phenomenon. It also highlights the importance of attempting to replicate seemingly impressive results in this field. An issue in this study is the very short durations of on and off conditions; therefore generalization to longer exposure durations cannot be done. For individuals that potentially develop symptoms during the exposures, delayed responses as well as carry-over effects are limiting factor.]

In a single blind study, Nam et al. (2009) exposed 19 healthy volunteers and 18 people with IEI-EMF (all of whom reported sensitivity to CDMA mobile phones) to a CDMA signal generated using a real mobile phone in test mode transmitting at maximal power or a sham condition for 31 minutes. The two exposure conditions were on separate days and in randomized order. The lower part of the mobile phone was wrapped with a 5-mm thick insulating material to prevent the participants from sensing heat from the phone when operating. Exposures occurred in a random order and on separate days. Background ELF electric and magnetic fields were measured at 2.3 plus or minus 0.1 V/m and 0.04 plus or minus 0.02 mT, respectively. Background RF field was measured at 0.7 V/m with a frequency range from 824 to 849 MHz. Participants were asked to judge whether they were genuinely being exposed or not, and to rate the severity of nine symptoms. No effect of exposure on symptoms was detected in either group, nor was there any evidence that either group was adept at detecting the exposure. [Although the study adds to the weight of evidence suggesting that IEI-EMF symptoms are not triggered by radiofrequency fields, the relatively small sample size is a limitation. Manufacturer data for maximum SAR over 1 g was provided to be 1.22 W/kg. Since the mobile phone operated in test mode and with a small distance to the skin due to insulation material, the accuracy of the provided value is uncertain.]

Nieto-Hernandez et al. (2011) tested the effects of exposure to a TETRA signal with a pulsing frequency of approximately 16 Hz, a continuous wave condition and a sham condition on 60 participants recruited from the emergency services and with IEI-EMF and on 60 emergency service personnel without IEI-EMF. All participants with IEI-EMF reported usually experiencing symptoms within an hour of using a TETRA handset. The TETRA and continuous wave conditions had carrier frequencies of 385.25 MHz and both resulted in SAR_{10g} of 1.3 W/kg. Participants were exposed to each condition for 50 minutes. The exposure conditions were at least 24 hours apart, but longer if a participant reported that the recovery after exposure to TETRA usually took more than 24 h. The order of conditions was determined randomly and was counterbalanced. Testing took place in a room that was not shielded against EMF, although participants were asked to report symptoms after 30 minutes at rest in the testing room and excluded if the environment proved problematic for them. In the sham condition, the phone was operating to be heated similarly as in the RF exposure conditions by diverting the generated RF power to an internal load instead of emitting the RF signals by the antenna. Outcomes consisted of measures of mood, eight symptoms and ability to detect the exposure conditions. Initial results showed that the likelihood of headache (p for overall model including all exposure terms = 0.0048) among all participants and of fatigue among participants without IEI-EMF (p for overall model = 0.02) increased during continuous wave exposure, that the likelihood of concentration problems among participants with IEI-EMF increased during both continuous wave and TETRA exposure (p for overall model = 0.04) and that the likelihood of itching among participants with IEI-EMF deceased during continuous exposure (p = 0.003). The likelihood of experiencing any symptom also increased 24 hours after continuous wave exposure (p for overall model = 0.03). After applying a Bonferroni-type (Simes) correction to adjust for the number of endpoints that were measured, only one symptom showed any effect from exposure, with a reduction in itching in the IEI-EMF group as a result of the continuous wave condition. No evidence was found that participants could discriminate between conditions. [The single significant finding, from this methodologically strong study, is paradoxical, given that it related to a decrease in symptoms as a result of exposure to a signal that the IEI-

EMF participants did not report being sensitive to.] The authors calculated that statistical power was 90% to detect an absolute increase of 25% or more of participants reporting headache in the continuous wave condition compared with the sham condition when applying the 5% significance level.

In a second experiment by Kwon et al. (2012a), 17 participants with IEI-EMF and 20 healthy volunteers were exposed to WCDMA-like signal (1950 MHz) or a sham condition for 32 minutes. WCDMA modules transmitted signals continuously at constant mean output power resulting in SAR_{1g} of 1.57 W/kg. The modules were placed in a dummy handset 3 mm from the ear to prevent sensing the phone heating. Participants with IEI-EMF were recruited on the basis that they reported symptoms that were associated with their use of 3G mobile phones. Exposure sessions were separated by one to 10 days, and their order was randomized. For each participant both sessions were at approximately the same time of day. The average background ELF electric and magnetic fields were 1.8 V/m and 0.02 µT respectively. The background RF field was 0.05 V/m (1920 to 1980 MHz). The participants were asked to rate eight symptoms and whether they believed they were being exposed or not. Although detailed numerical data were not provided, the authors noted that with the criterion for statistical significance reduced to $p = 0.0125$ to account for multiple testing, neither group's level of symptom reporting was affected by the exposure. Similarly, no evidence was found that either group were better than chance at detecting the exposure.

Papers with uncertainties related to inclusion criteria

Eight additional studies were identified with uncertainties related to inclusion criteria.

In a brief research letter containing limited methodological detail, Braune et al. (1998) reported a single-blind experiment in which 10 healthy volunteers were exposed to a 900 MHz mobile phone. [Few details on exposure were provided.] For all participants, 35 minutes sham exposure came first, followed by 35 minutes of RF exposure. Each participant was tested in this way on five occasions. Well-being was assessed at the beginning and end of each exposure period. Although the statistical analysis of this scale was not described in detail, the authors reported that no effect of exposure was identified on subjective parameters.

Barth et al. (2000) reported using a double-blind provocation study to test a single individual with IEI-EMF. The patient was repeatedly exposed to a mobile phone which was switched on or off, but showed no consistent reactions to it. No detailed description of the exposure was provided.

In a single-blind study, Bortkiewicz et al. (2002) exposed nine healthy men to 60 minutes of exposure from a 900 MHz mobile phone and 60 minutes of sham exposure immediately prior to full night's sleep. Exposures were generated using a real mobile phone and detailed SAR levels were not provided. On the morning following each night's sleep, participants were interviewed regarding eight symptoms, including three relating to sleep quality. The number of symptoms reported following RF exposure was equivalent to the number reported following sham exposure. [The exposure level was not controlled.]

In a study by Uloziene et al. (2005) half of their 30 volunteers (18–30 years; 18 males, 12 females) were exposed to a GSM 900 MHz signal and the other half to a GSM 1800 MHz signal. During exposures the mobile phone was positioned against the ear that was tested for hearing functions. The same model of a commercial mobile phone was used in all studies and was set to transmit at maximum output power. SAR_{1g} recorded in a position corresponding approximately to that of cochlea (30 mm from the surface) was 0.41 W/kg for the 900 MHz exposure and 0.19 W/kg for the 1800-MHz exposure [SAR values provided by e.g. Parazzini et al. (2005) from the same project]. Sham exposures were obtained by connecting a load to the phone so that the RF signals were dissipated to the load instead of transmitted to the antenna. As well as recording hearing thresholds by pure tone audiometry and transient evoked otoacoustic emissions in 30 volunteers (see Section 6.2), the team asked about subjective symptoms following exposure. [The procedure for enquiring about symptoms was unclear from the publication and no statistical data were reported for these outcomes]. The authors reported that there were no subjective complaints after exposure.

Eliyahu et al. (2006) attempted to establish a link between the exposure of a particular brain region and cognitive functions associated with the specific area. Cognitive tasks were administered to 36 participants under the exposure on the left-side and right-side to a GSM 890.2 MHz signal and under a sham condition. The mean output power was set to 0.25 W. Each exposure condition was performed in two 60-minute sessions separated with a 5-minute break. At the end of the testing sessions, participants were asked to report whether and when the phones had been operating. [No information about statistical analysis and no numerical data were provided in the paper for this outcome.] However the authors noted that they were unable to discriminate between the conditions.

Luria et al. (2009) aimed at replicating and extending the study by Eliyahu et al. (2006). They assigned 48 participants to three different groups: left-side and right-side exposure to GSM 890.2 MHz signals (SAR = 0.54–1.09 W/kg) and sham exposure. Each of them was exposed to the signal in 12 consecutive blocks separated with a few seconds, for about 60 min in total. During this period they completed the only task that in the previous study appeared to be sensitive to RF exposure, i.e. the spatial working memory test. The authors also tested discrimination in this single-blind study, noting simply that “subjects also failed to judge which phone was operating during the experiment.” [No statistical analysis of discrimination was reported, however.]

Hung et al. (2007) assessed sleepiness, before, during and after four 30-minute conditions, consisting of a sham condition and exposure to a GSM 900 MHz signal from a mobile phone in talk (0.133 W/kg), listen (0.015 W/kg) and stand-by mode (< 0.001 W/kg). No statistical analysis was reported for the subjective endpoints recorded in this single-blind study, however the authors did report that mean sleepiness was “similar” in all conditions before exposure and “rose… in a similar manner for all conditions.”

Mortazavi et al. (2011) reported a double-blind experiment in which they tested 20 participants with IEI-EMF using two 10-minute exposures to a sham condition and to “real mobile microwave radiations.” [No details were provided as to the nature of this exposure or about any control of exposure level.] However the authors reported that their participants were no better than chance at discriminating between the two exposures.

Table 5.2.8. Mobile phone handset related studies assessing symptoms, wellbeing or ability to perceive exposure

Endpoint and Volunteers	Exposure[a]	Response	Comment[b]	Reference
Studies with healthy adults				
Alertness in the morning, sleep quality, frequency of bad dreams, calmness, energy level, concentration and anxiety after exposure after sleeping 12 male volunteers (21–34 years)	Handset 40 cm from head, GSM, 900 MHz Average power density 0.05 mW/cm^2 (0.50 W/m^2) 8 h during sleep	Greater calmness on mornings post exposure, but no significant effects otherwise	Single-blind, randomized, counterbalanced, cross-over. Small sample. No correction for multiple endpoints. For sleep EEG see Section 5.2.2.3.	(Mann & Röschke, 1996)
Subjective sleep and mood after exposure after sleeping 24 male volunteers (20–25 years)	Base station like signals from array of 3 half-wave antennas 30 cm behind the head when lying, GSM, 900 MHz; modulation frequencies 2, 8, 217, 1736 Hz and 50 kHz, 87.5% duty cycle SAR_{10g} 1 W/kg 15 min on, 15 min off intervals during the night	No effect of exposure.	Double-blind, randomized, cross-over. Results for only one subjective outcome were reported. For sleep EEG see Section 5.2.2.3; for cardiovascular system see Section 9.2.1.	(Borbély et al., 1999)
Discrimination, subjective assessment of waking after sleep onset, sleep latency, sleep quality, mood assessed after sleep after exposure 16 male volunteers (20–25 years)	Base station like signals from planar antenna mounted 11 cm from head, left and right exposures in separate sessions, 900 MHz; modulation frequencies 2, 8, 217, 1736 Hz and 50 kHz, 87.5% duty cycle SAR_{10g} 1 W/kg 30 min prior to 3 h daytime sleep	No effect of exposure.	Double-blind, randomized, cross-over. No result provided for mood. For sleep EEG see Section 5.2.2.3; for cardiovascular system see Section 9.2.1.	(Huber et al., 2000; Huber et al., 2003)

Headache, dizziness, fatigue, itching or tingling on skin, skin redness, skin warmth before, during and after exposure Experiment 1: 48 volunteers (18–49 years; 24 males, 24 females) Experiment 2: 48 volunteers (18–34 years; 24 males, 24 females)	Handset with antenna 4 cm from left hemisphere, GSM, 902 MHz Mean power of 0.25 W Experiment 1: 60 min Experiment 2: 30 min	No effect of exposure.	Single-blind, counterbalanced, cross-over.	(Koivisto et al., 2001)
Discrimination 10 volunteers (age and gender not reported).	Modified GSM mobile phone against left ear, 902 MHz SAR_{10g} 0.99 W/kg	No effect of exposure	At least single-blind, crossover. Very few details on methodology provided. For cognition see Section 5.2.1; for cerebral metabolism see Section 5.2.3.	(Haarala et al., 2003a)
Discrimination 2 volunteers (age and gender not reported)	GSM phone over the right temporal region, 894.6 MHz Mean output power 0.25 W Ten 1-minute exposures (five sham, five GSM)	No effect of exposure	At least single-blind, randomized, cross-over. Very few details on methodology provided. For cognition see Section 5.2.1; for brain activity see Section 5.2.2.	(Hamblin et al., 2004)
Discrimination and open-ended "how did you feel" question after exposure 32 volunteers (23–55 years; 16 males, 16 females)	Handset held against dominant side of head GSM, 900 MHz: SAR 1.58 W/kg GSM, 1800 MHz: SAR 0.70 W/kg Four 35-min exposures (two sham, GSM 900 and GSM 1800)	No effect of exposure.	Double-blind, randomized, cross-over. Discrimination results not reported. For cardiovascular system see Section 9.2.1.	(Tahvanainen et al., 2004)
Self-rated sleepiness immediately after exposure 20 volunteers (22–31 years; 10 males, 10 females)	Handset 1.5 cm from left side of head, GSM, 902.4 MHz Max SAR 0.5 W/kg 45 min	No effect of exposure.	Double blind, randomized, cross-over. Statistical results from subjective effects not explicitly reported. For sleep EEG see Section 5.2.2.3.	(Curcio et al., 2005)
Discrimination 50 volunteers (18–60 years; 27 males, 23 females)	Handset on right side of head, GSM, 894.6 MHz SAR_{10g} 0.674 W/kg (as per (Loughran et al., 2012)) 30 min immediately prior to sleep	No effect of exposure.	Double-blind, randomized, cross-over. For sleep EEG see Section 5.2.2.3.	(Loughran et al., 2005)
Self-reported sleepiness on waking after exposure and detection 20 volunteers (20–51 years; 7 males, 13 females)	Handset on right side of head, GSM, 894.6 MHz SAR_{10g} 0.67 W/kg 30 min immediately prior to sleep	No effect of exposure.	Double-blind, randomized, counterbalanced, cross-over. For sleep EEG see Section 5.2.2.3.	(Loughran et al., 2012)
Discrimination 10 volunteers (age and sex unclear)	GSM phone positioned next to head, 902 MHz SAR_{10g} 0.74 W/kg 10 trials (duration unclear)	No effect of exposure.	Limited methodological detail available. Blinding unclear but at least single blind. Counterbalanced, cross-over.	(Aalto et al., 2006)

Discrimination 19 volunteers (age and sex unclear)	GSM phone against left ear with antenna 1.5 ± 0.5 cm from head, 900 MHz Mean output power 0.23 W Number of trials and duration unclear	No effect of exposure	At least single-blind, cross-over. Limited methodological detail available. For cognition see Section 5.2.1.	(Keetley et al., 2006)
Discrimination 16 male volunteers (31.2±6.3 years)	GSM handset-like signal emitted by planar antenna 11 cm from left side of head, 902.4 MHz, SAR_{10g} 0.15, 1.5 W/kg 20 min (15 times 80-second cycles: alternating 2 s on/ 2 s off signal for 20 s, then 60 s exposure free)	No effect of exposure	Double blind, randomized, cross-over. No numerical data reported for the outcome. For cerebral metabolism see Section 5.2.3	(Wolf et al., 2006)
Subjective quality of sleep and sense of well-being, assessed before exposure and after exposure after sleeping RF: 10 male volunteers (22–26 years) Sham: 10 male volunteers (23–37 years)	3 antennas oriented vertically 30 cm from vertex of head, GSM, 900 MHz SAR_{1g} 0.875 W/kg Exposure during 6 consecutive nights sleep	No effect of exposure.	Single-blind, randomized, between-participants. Small samples and power calculation based on literature review of effects on sleep and neuropsychological variables. Analyses were based on data from first and final night of exposure. For cognition see Section 5.2.1.	(Fritzer et al., 2007)
Discrimination 26 volunteers (21–28 years; 14 males, 12 females)	Handset next to dominant-hand side of head, GSM, 900 MHz “At full power (2 W)” 26 min	No effect of exposure.	Double-blind, randomized, cross-over.	(Parazzini et al., 2007)
Headache, dizziness, fatigue, itching or tingling of skin, sensation of warmth on skin before and after exposure 496 volunteers (18–42 years; 166 males, 330 females). Three separate experiments with 159 – 167 volunteers in each	Mobile phone next to head (half left side, half right side). GSM PM signal or CW, 888 MHz SAR_{10g} 1.4 W/kg 40 min Half received GSM and sham, half received carrier wave and sham	Increase in dizziness due to increase in experiment 3. No other effects of exposure.	Double-blind, counterbalanced, cross-over. Power calculation based on cognitive effects. Alpha set to p=0.01 to adjust for multiple comparisons. For cognition see (Cinel et al., 2007) and (Russo et al., 2006) in Section 5.2.1.	(Cinel et al., 2008)
Discrimination 120 volunteers (18–69 years; 46 males, 74 females).	GSM handset-like signal (half participants received left and half right side exposure), 894.6 MHz, PM 217 Hz SAR_{10g} 0.67 W/kg 30 min	No effect of exposure.	Double blind, randomized, partially counterbalanced, cross-over. For awake EEG see Section 5.2.2.2; for cognition and event related potentials see (Hamblin et al., 2006) in Sections 5.2.1 and 5.2.2.1, respectively.	(Croft et al., 2008)

Discomfort and impairment before and after exposure in 15 healthy 15 male volunteers (20–35 years)	Small broadband antenna against left ear GSM base station like signal, 900 MHz: SAR_{10g} 1 W/kg UMTS handset-like signal, 1.95 GHz: SAR_{10g} 0.1 W/kg, 1 W/kg 30 min	No effect of exposure.	Double-blind, randomized, cross-over. For awake EEG see Section 5.2.2.2; for cognition and event related potentials see (Kleinlogel et al., 2008b) in Sections 5.2.1 and 5.2.2.1.	(Kleinlogel et al., 2008a)
Self-reported energy, fatigue, tension, difficulty concentrating, skin tingling, dizziness, redness of ears, warmth on skin, pain and headache before and after exposure 11 female volunteers (20–23 years)	Mobile phone ~1.5 cm from left ear, GSM, 902.4 MHz Max SAR_{10g} 0.5 W/kg 40 min	Headache increased in the sham condition. No other effects of exposure.	Double-blind, randomized, cross-over. Testing occurred in an “electromagnetically quiet” basement room. Small sample. No correction for multiple endpoints. For brain oxygenation see Section 5.2.3, for heart rate see Section 9.2.1.	(Curcio et al., 2009)
Discrimination 17 volunteers (25.9 ± 4.3 years, 6 males, 11 females)	GSM mobile phone against one ear at the time, 902.4 MHz 100 five-second trials per participant SAR_{10g} 0.82 W/kg	No effects of exposure	Single-blind, randomized, cross-over. For auditory brainstem response see Section 6.2	(Kwon et al., 2010b)
Sensations of sweat, chilling, breathlessness, tingling, pain, sleepiness, nausea, dizziness, headache and concentration problems measured before and after exposure 53 male emergency service personnel (25–49 years)	Antenna in cheek position on left side of head, TETRA, 420 MHz SAR_{10g} 2.0 W/kg 45 min	No effect of exposure.	Double-blind, randomized, cross-over. Power calculation performed based on a cognitive endpoint. Testing took place in room shielded against outside exposure. For cognition see Section 5.2.1.	(Riddervold et al., 2010)
Discrimination, well-being, sleep quality and mood prior to bedtime and on awakening after exposure 30 male volunteers (20–26 years)	Planar antenna 115 mm from left side of head, GSM, 900 MHz, PM at 14 Hz with pulse width 2.3 ms or at 217 Hz with pulse width 0.577 ms SAR_{10g} 2 W/kg 30 min immediately prior to sleep	No effect of exposure.	Double-blind, randomized, cross-over. Limited methodological detail for the subjective endpoints. Numerical data not reported, but authors describe “no differences between exposure conditions.” For cognition see Section 5.2.1; for sleep EEG see Section 5.2.2.3; for heart rate see Section 9.2.1.	(Schmid et al., 2012a)

Discrimination, well-being, sleep quality and mood on awakening after exposure 25 male volunteers (20–26 years)	Patch antennas 115 mm from left side of head, GSM, 900 MHz SAR_{10g} 2 W/kg Pulsed magnetic field (using Helmholtz coils) 30 min immediately prior to sleep	No effect of exposure.	Double-blind, randomized, cross-over. Limited methodological detail for the subjective endpoints. Numerical data not reported, but authors describe “no significant differences” for mood, well-being or sleep quality and that “subjects were not able to perceive the applied fields. For cognition see Section 5.2.1; for sleep EEG see Section 5.2.2.3; for heart rate see Section 9.2.1.	(Schmid et al., 2012b)
Tiredness and wellbeing pre and post exposure, discrimination after exposure 16 male volunteers (26.8 ± 3.9 years)	Planar patch antenna 4 cm from head, UMTS base-station like signals, 1900 MHz SAR_{10g} 0.18, 1.8 W/kg 22 min, 20 s on and 60 s off	No effect of exposure.	Double-blind, randomized, cross-over. Study carried out in basement with low electromagnetic background and with RF absorbers shielding the participant. Numerical data not reported. For brain metabolism see Section 5.2.3; for heart rate see Section 9.2.1.	(Spichtig et al., 2012)
Studies including child or adolescent volunteers				
Discrimination 32 children (10–14 years; 16 males, 16 females)	A factory model handset next to left side of head, GSM, 902 MHz SAR_{10g} 0.99 W/kg 50 min	No effect of exposure.	Double-blind, counterbalanced, cross-over. For cognition see Section 5.2.1.	(Haarala et al., 2005)
Discrimination 15 children (10–14 years; 6 males, 9 females)	A handset next to left hemisphere, GSM, 902 MHz SAR_{1g} 1.4 W/kg 30 min	No effect of exposure.	Double-blind, counterbalanced, cross-over. For event related potentials see Section 5.2.2.1.	(Krause et al., 2006)
Discrimination and mood (‘activation’) before and after exposure 41 adolescents (13–15 y; 21 males, 20 females) 42 young adults (19–40 years; 21 males, 21 females) 20 elderly (55–70 years; 10 males, 10 females)	Handsets next to head (side of head counterbalanced) GSM (2G), 894.6 MHz: SAR_{10g} 0.7 W/kg UMTS 1900 MHz (3G): SAR_{10g} 1.7 W/kg 55 min	No effect of exposure.	Double-blind, counterbalanced, cross-over. Bonferroni correction for multiple tests. Testing within a shielded room. For cognition and event related potentials see (Leung et al., 2011) in Sections 5.2.1 and 5.2.2.1; for resting EEG see Section 5.2.2.2.	(Croft et al., 2010)
Studies with volunteers with IEI-EMF				
Discrimination 11 IEI-EMF volunteers (28–66 years; 7 males, 4 females)	GSM signals emitted by antenna 1.9 m in front of the participant, 900 MHz Power density 0.24 W/m^2 12 trials per participant, each consisting of three 2-min exposures (one GSM and two sham)	No effect of exposure.	Double-blind, cross-over. All trials occurred on the same day for each participant. Choice of 12 trials per participant justified on the basis of a 1.4% chance of them getting more than 67% of trials correct.	(Radon & Maschke, 1998)

Discrimination Any symptoms during and immediately after exposure 20 IEI-EMF volunteers (37–67 years; 7 males, 13 females)	Mobile phone 1–5 cm from right ear Analogue NMT phone, 900 MHz: output power 1 W GSM phone, 900 MHz: average output power 0.25 W GSM phone, 1800 MHz: average output power 0.125 W 30 min	More symptoms reported during sham exposure than RF exposures. No ability to discriminate.	Single blind, partly randomized order of exposures with sham first or second which may have influenced the results. Results in opposite direction of expected. For cardiovascular endpoints see Section 9.2.1.	(Hietanen, Hämäläinen & Husman, 2002)
Headache, nausea, fatigue, dizziness, skin itching, warmth and eye pain before, during and after exposure and discrimination after exposure 60 IEI-EMF volunteers (37.2 ± 13.2 years; 20 males, 40 females) 60 healthy volunteers (33.5 ± 10.2 years; 27 males, 33 females)	Handset equipment on left side of head, GSM or CW, 900 MHz SAR_{10g} 1.4 W/kg 50 min	No effect of exposure.	Double-blind, randomized, counterbalanced, cross-over. Power calculation based on headache. Protocol registered with Current Controlled Trials.	(Rubin et al., 2006)
Experience of any symptoms assessed after exposure 20 IEI-EMF volunteers (45.4 ± 9.6 years; 16 males, 4 females) 20 healthy volunteers (44.9 ± 10.5 years; 16 males, 4 females)	Signals from GSM test mobile phone emitted by a base station antenna 8.5 cm from right side of the head, GSM, 900 MHz SAR_{10g} 0.8 W/kg 30 min	No effect of exposure.	Single-blind, randomized, cross-over. Testing took place in a room specially designed to have low background EMF levels. For cognition see Section 5.2.1; for autonomic nervous system see Section 9.2.1	(Wilén et al., 2006)
Headache and 'other symptoms' assessed before and after exposure, and discrimination 17 IEI-EMF volunteers (20–58 years; 12 males, 5 females)	Signals from GSM test mobile phone emitted by a base station antenna 8.5 cm from the side of the head, GSM, 902.4 MHz SAR_{10g} 0.8 W/kg Up to eight 30-min exposures per participant (four GSM and four sham)	No effect of exposure.	Double-blind, randomized, counterbalanced, cross-over. Initial non-bind test used as a screening tool. Headache used as primary outcome. Power calculation based on headache. Testing took place in a shielded room. For cardiovascular function see Section 9.2.1.	(Oftedal et al., 2007)
Discrimination 9 IEI-EMF volunteers (20–55 years; 6 male, 3 females) 21 healthy volunteers (20–55 years; 12 males, 9 female)	Generic mobile phone next to side of the head, CW and GSM, 882 MHz SAR_{10g} 1.3 W/kg Six 30-min exposures: two GSM, two CW and two sham	No effect of exposure.	Double-blind, randomized, cross-over. All exposure took place during a single day. For auditory and vestibular functions see Section 6.2.	(Bamiou et al., 2008)

Headache, fatigue, nausea, vertigo, difficulties concentrating, feeling low-spirited, vision problems, swelling in face, itching, reddening in skin, heat sensations, stinging pain, tingling, stress measured before and during exposure. Discrimination after exposure. Sleepiness, arousal, mental fatigue and sleep quality assessed before, during and after exposure (after sleep) 37 IEI-EMF volunteers (18–45 years; 16 males, 24 females) 33 healthy volunteers (18––45 years; 19 males, 14 females). [Sleep data based on a subset of 23 IEI-EMF volunteers and 25 healthy volunteers]	Patch antenna on a headset at side of head, GSM, 884 MHz SAR_{10g} 1.4 W/kg 3 h	Ear heat in one of the three ways of assessing it and headache. For headache the effect was due to control volunteers reporting more headaches in the RF condition. No other effects of exposure.	Double-blind, randomized cross-over. Primary outcomes were headaches and vertigo. Testing occurred in unshielded rooms, although assessment of low frequency and radiofrequency fields revealed low background levels (<0.05 V/m). For cognition see (Wiholm et al., 2009) in Section 5.2.1; for sleep EEG see (Lowden et al., 2011) in Section 5.2.2.3.	(Hillert et al., 2008; Lowden et al., 2011)
Discrimination 6 volunteers who reported being able to detect mobile phone signals, including two with IEI-EMF symptoms (32.8 ± 10.7 years; n=3 males, 3 females) 78 healthy volunteers (mean age 23.8 years; 24 males, 54 females)	Handset in left-cheek position, GSM, 902 MHz SAR_{10g} 0.82 W/kg At least 600 trials of real and sham conditions, each lasting up to 5 seconds	At a group level (excluding two outlier participants [see below]) no effect of exposure. Two volunteers showed correct response rates of 97% and 94%. Neither were able to replicate their performance when re-tested.	Double-blind, randomized, counterbalanced, cross-over. Multiple exposures occurred over a single day.	(Kwon et al., 2008)
Redness, itching, warmth, fatigue, headaches, dizziness, nausea, palpitation, indigestion, discrimination assessed before, during and after exposure 18 IEI-EMF volunteers (26.1 ± 3.4 years; 8 males, 10 females) 19 healthy volunteers (25.0 ± 2.3 years; 10 males, 9 females)	Handset next to left side of head, CDMA, continuous clipped sine waves at 835 MHz (824.64–848.37 MHz) SAR_{1g} 1.22 W/kg 31 min	No effect of exposure.	Single-blind, randomized, crossover.	(Nam et al., 2009)
Headache, fatigue, dizziness, nausea, sensations of warmth, skin itching, negative mood, difficulty concentrating or thinking, and discrimination assessed before, during and after exposure 60 IEI-EMF volunteers (35.6 ± 7.4 years; 53 males, 7 female) 60 healthy volunteers (38.2 ± 8.0 years; 50 males, 10 females)	Exposure system next to left side of head, TETRA and CW, 385.25 MHz SAR_{10g} 1.3 W/kg 50 min	Reduced sensations of itching in IEI-EMF volunteers in response to the continuous wave exposure. No other effects of exposure.	Double-blind, randomized, counterbalanced, cross-over. Protocol registered with Controlled Clinical Trials. Power calculation based on symptoms. Bonferroni type adjustment. For autonomic nervous system see Section 9.2.1.	(Nieto-Hernandez et al., 2011)

Throbbing, itching, warmth, fatigue, headache, dizziness, nausea, palpation, discrimination, recorded before, during and after exposure 17 IEI-EMF volunteers (30.1 ± 7.6 years; 8 males, 9 females) 20 healthy volunteers (29.4 ± 5.2 years; 11 males, 9 females)	WCDMA module in a dummy handset 3 mm from ear, WCDMA, 1950 MHz SAR_{1g} 1.57 W/kg 32 min	No effect of exposure.	Double-blind, randomized, counter-balanced, cross-over. Testing rooms were unshielded, though low background EMF was measured. Criterion for significance reduced to p = 0.0125 to account for multiple testing. For autonomic nervous system see Section 9.2.1.	(Kwon et al., 2012a)

Abbreviations: CDMA: Code Division Multiple Access; CW: continuous wave; EEG: Electroencephalogram; GSM: Global System For Mobile Communication; IEI-EMF: Idiopathic environmental intolerance attributed to EMF; PM: Pulse modulated; TETRA: Terrestrial Trunked Radio; UMTS: The Universal Mobile Telecommunications System; WCDMA: Wideband Code Division Multiple Access.

[a] All participants were exposed to one of each active exposure and one sham condition, unless otherwise noted. SAR with relevant averaging volume (e.g. SAR_{10g}) is specified if included in the paper.

[b] Unless explicitly noted, studies did not report a priori power calculations, pre-registered protocols, or use testing rooms shielded against external EMF.

5.2.4.4 Mobile phone base station related exposures

Table 5.2.9 details the design and results of the eight blind or double-blind studies that assessed the impact of base station related exposures on subjective outcomes.

Studies with healthy adult volunteers

Augner et al. (2009) assessed the effects of exposure to mobile phone base station signals (900 MHz) generated by a real GSM 900 MHz base station on a group of 57 healthy volunteers. By applying different types of shielding, three different exposure levels were obtained. The power density was measured during all exposure sessions and the average values were calculated for each condition: high (2126.8 μW/m²), medium (153.6 μW/m²) and low (5.2 μW/m²). The participants were randomly assigned to receive one of three exposure scenarios, each consisting of five 50-minute exposure sessions separated from each other by 5-minute intervals. The scenarios were “HM” (low exposure, high exposure, low, medium, low) with 22 volunteers, “MH” (low, medium, low, high, low) with 26 volunteers and “LL” (low, low, low, low, high), the control scenario with 9 volunteers. The final, low, session was excluded from all analyses. Analyses were performed by including age, gender, and degree of self-rated electromagnetic hypersensitivity as covariates. Outcomes, assessed at the end of each exposure, included good mood, alertness and calmness. No effects of exposure were found for good mood or alertness. However, the overall results from the three scenarios showed that calmness was higher under the MH and MH scenarios compared to the LL control condition (p = 0.042), and furthermore, calmness showed a greater decrease over time in the LL condition compared to the HM (0.002) and MH conditions (p = 0.009), suggesting that exposure might prevent a natural decline in calmness from occurring. [A limitation of this study is the low number of participants in the LL group, which was due to early termination of the study.]

Danker-Hopfe et al. (2010) took a portable mobile phone base station to 10 villages in Germany which did not previously have mobile phone coverage. This base station was used over the course of 10 nights to broadcast a combined GSM 900 and 1800 MHz signal for five nights (using a test signal that would not register on residents’ mobile phones) or to transmit nothing. In each village, all adult residents were invited to take part in the study. In total 397 healthy villagers agreed to record their subjective sleep quality throughout the experiment while sleeping in their own homes. After drop outs (21) and exclusions because living more than 500 meters from the base station (11) 365 participants remained. This sample size exceeded the sample size calculation which the authors performed based on their ability to detect changes in EEG measures (see Section 5.2.2.3 for details). The subjective data showed no effects of exposure. [While exposure information is sparse in the paper, the authors referred to a paper by Bornkessel et al. (2007) describing methods for measuring exposure levels in the bedrooms. The results were presented in a report (Danker-Hopfe et al., 2008) showing that more than 90% of the participants were exposed to electric field strengths between 10 and approximately 1000 mV/m. In the sham condition the field strength was lower than 0.1 mV/m for about 85% of the participants. On the other hand, the large sample size, lengthy exposures and realistic set-up of this experiment provide good evidence that exposures from new base stations are unlikely to cause substantial effects on the quality of sleep of a host community.]

Studies including children and adolescents

Riddervold et al. (2008) exposed 40 adolescents (15 to 16 years) and 40 adults (25 to 40 years) to a sham condition, a continuous wave (2140 MHz) condition, a signal at 2140 MHz modulated as UMTS and a UMTS 2140 MHz signal including all control features. Each exposure lasted for 45 minutes and took place in a testing chamber that was partly screened by RF absorbers. The signals were emitted by a base station antenna placed 2.8 m from the participants, resulting in field strength for the active conditions between 0.9 and 2.2 V/m, which should simulate exposure of those living 20 meters or more from a base station. The background RF-field between 10 MHz and 6 GHz was less than 0.001 V/m. The 50 Hz magnetic flux density was measured to be 70 nT. Blinding was ensured by having the same acoustic as well as electric noise level during all conditions. The sessions were separated by at least 24 hours, was always at the same time of day and the order of conditions was randomized. Participants recorded the strength of 11 symptoms during each exposure and their perception as to whether a field was present or not. Although no power calculation was reported in the paper, the authors did note that they had lodged their analytic plan with an independent organisation prior to initiating their investigation. For symptom outcomes, only the difference between the UMTS signal with all control features and sham was assessed. No evidence was found that participants could consciously discriminate between the exposures and no evidence was found within either the adult or adolescent groups that exposure resulted in increases for most symptoms. The only exception was a difference in change in self-reported concentration difficulties in adults with more increase from baseline to end of the UMTS condition compared to sham ($p = 0.048$). When data from both groups were pooled together, a significant difference in change in headache was also observed, with most increase in headaches during UMTS exposure ($p = 0.027$). However, the baseline scores for these symptoms in the sham condition were higher than those for the UMTS condition, potentially explaining this effect.

Studies including IEI-EMF volunteers

Regel et al. (2006) assessed the impact of 45-minute exposures to three forms of UMTS base station signals (sham, 1 or 10 V/m) in 33 people with IEI-EMF and 84 healthy volunteers. The signals were emitted by an antenna placed 2 meters behind and targeting the left side. Whole-body average SAR was about 0.0062 and 0.62 mW/kg for the 1 V/m and the 10 V/m exposures, respectively. Maximum SAR for brain tissue averaged over 10 g was about 0.045 and 4.5 mW/kg, respectively. Each testing session was separated by a period of one week at approximately the same time of day and the order of exposures was determined randomly. The testing took place within a chamber shielded from outside exposures. A range of self-reported scales assessing symptoms, well-being and mood were completed during the experiment. There was no evidence of any effect of exposure on any subjective outcome, nor were participants able to judge when they were or were not being exposed. [Although the relatively large sample size of this study was a positive feature, only limited information was provided on the IEI-EMF group who were simply described as reporting sensitivity to RF EMF as emitted by mobile or cordless phones and antennas. Without knowing whether they reported sensitivity specifically to UMTS, whether they typically reacted within the timeframe covered by the experiment or whether their usual experiences would have been captured by the questionnaires used, it is difficult to say whether the study represented a fair test of their reported sensitivities. However, it is notable that the IEI-EMF participants did report perceiving significantly higher field strengths than the control participants during the experiment. As such, they themselves presumably felt that they were able to detect the fields.]

Eltiti et al. (2007a) tested the effects of exposure to a GSM base station signal, including 900 and 1800 MHz components, and a UMTS signal (2020 MHz). All testing took place within a shielded chamber. The signals were emitted by a base station antenna placed 5 meters from the participant, each resulting in a power density of 10 mW/m^2. These signals were tested on 44 participants with IEI-EMF and 115 participants without IEI-EMF. Participants were initially exposed under non-blind conditions to the UMTS, GSM and sham signals for 15 minutes each. Participants reacted as expected to these non-blind conditions, with the IEI-EMF group in particular reporting more symptoms in the UMTS and GSM conditions than in the sham condition. Participants were then exposed under double-blind conditions to three ‘quick’ exposures (GSM, UMTS and sham) lasting 15 minutes each and three ‘long’ exposures lasting 50 minutes each. While the non-blinded and the quick exposures were on the same day with 2 minutes between the different conditions, the long exposures were on separate days, always at the same time of day. The order of exposures was randomized. During the quick exposures the participants’ ability to discriminate between exposure conditions was tested; both discrimination and well-being (‘anxious’, ‘tense’, ‘agitated’, ‘relaxed’, ’discomfort’, and ‘tired’ in addition to 57 symptoms) was tested during the long exposures. The results showed significantly higher levels of arousal following UMTS exposure compared to sham exposure in the IEI-EMF group ($p < 0.0025$) which persisted even after applying a Bonferroni adjustment. No other effect of the double-blind exposures on symptoms was found and no evidence was found that participants in either group were able to differentiate between the conditions. A power calculation for the study, with 90% power, suggested that 66 participants per group would allow the researchers to detect a small effect of exposure. [Unfortunately, because the team were unable to recruit this many people, the study was underpowered for the IEI-EMF group and the authors' attempt to counterbalance the order of exposures failed, with a high proportion of IEI-EMF participants receiving UMTS exposure as their first experimental condition.] When exposure order was controlled for in the analysis, no effects of exposure were noted for any outcome. In a subsequent letter (Eltiti et al., 2008), the authors noted that applying a less conservative adjustment for multiple outcomes would have left them with small (< 1 point on a 10-point scale) yet significant differences in self-reported anxiety ($t (43) = 2.89$; $p = 0.006$) and tension ($t (43) = 2.94$; $p = 0.005$) between the UMTS and sham exposures for participants with IEI-EMF. [Beyond mentioning that the participants with IEI-EMF attributed their symptoms in particular to exposure from mobile phones and/or mobile phone base stations, no information was provided about the IEI-EMF group. Therefore, as in the study by Regel et al. (2006), the applied exposure may not have been fair in testing all IEI-EMF participants.]

The same team subsequently used a similar design to assess the impact of exposure to a TETRA base station 450 MHz signal emitted by an antenna almost 5 meters in front of the participants (Wallace et al., 2010). The resulting power density was 10 W/m^2. Again, although a sample size calculation suggested that they should recruit 66 people in each group to detect a small effect of exposure, in practice 51 people with IEI-EMF and 132 healthy volunteers were exposed to a signal replicating that produced by a TETRA base station and a sham condition. Four short (5 min) exposures (two TETRA and two sham) were applied, followed by two long (50 min) exposures to TETRA and sham. Although TETRA exposure triggered increased symptom reporting compared to sham in an initial non-blind provocation session, the double-blind testing found no evidence of any specific effects of TETRA on well-being or symptoms, or any evidence that participants were able to detect the signal. [Also in this study no other information about the IEI-EMF group was provided than the self-reporting about "being sensitive to EMFs particularly those produced by mobile communication handsets and/or base stations", with no mentioning of experiences with signals from TETRA base station exposures. Only a crude estimate of whole body average SAR was given (~ 0.3 mW/kg).]

Leitgeb et al. (2008) assessed the impact of radiofrequency fields on the sleep of 43 people attributing their sleep problems to RF-EMF from mobile telecommunication base stations. The participants slept at their own home under two different types of netting and without any netting, for three nights each with order of the conditions randomly determined. The netting was either genuinely protective against external electromagnetic fields, acting as a Faraday cage, or it was composed of ineffective material that was "optically and tactually indistinguishable" from the protective material. The environmental RF fields in the bedroom of the participants were recorded for frequencies in the range 80–2500 MHz with and without the shielding. Detailed exposure information is provided in a report (Leitgeb, 2007). With no shielding the exposure was between 1 and 10% of ICNIRP reference levels for 77.5% of the participants, above 10% for 15%, with the highest recorded value 3.5% of the reference level, and just below 1% of the reference level for the remaining 7.5% of the participants. The shielding reduced the exposure levels significantly; the median reduction was about 19 dB and the quartiles were about 15 and 24 dB, respectively. Sleep quality, awaking quality and somatic complaints as well as a total sleep score were estimated for each night based on responses to 20 more specific questions. Although three participants did report an improvement in sleep quality that appeared to relate to the use of the real netting, subsequent analysis of monitoring equipment placed inside the netting suggested that all three participants had unblinded the study by checking whether their netting was real or sham. The authors therefore cautioned that results for these "faking" participants should be discounted. [For this study, although baseline levels of exposure will have been different for each participant, the use of the intervention has good ecological validity. In other words, the authors were protecting participants from exactly the exposure that was apparently disrupting their sleep. In the context of testing the aetiology of symptoms, this is a strong design. An unorthodox method was applied to decide about statistical significance for the individual analyses, by considering differences between each of the three exposure conditions. This resulted in a significance criterion that was slightly more stringent than by applying Bonferroni adjustment. However, no adjustment was made to account for the high number of individual analyses.]

Furubayashi et al. (2009) tested the effects of a 2140 MHz W-CDMA base station signal in 11 people with IEI-EMF that was specific to mobile phone handsets and / or mobile phone base stations and 43 healthy volunteers. The W-CDMA signals were emitted by a horn antenna placed 3 meters behind the participants, resulting in whole body averaged SAR of 0.0015 W/kg and maximum brain tissue SAR averaged over 10 g of 0.0078 W/kg. Participants were exposed to four 30-minute conditions: continuous exposure to the signal, intermittent exposure with the source turned on and off at random over 5-minute intervals, a sham condition involving noise recorded near to the EMF amplifier (65 dBA) and a sham condition without noise. The order of the different conditions was determined randomly. Participants underwent two exposures per day, separated by at least 2 hours, in a shielded testing chamber. No effects of the exposure were found on measures of mood or discomfort and no evidence was found that participants could discriminate the active exposures from the sham. [However, as limited details were given about the nature of the symptoms experienced by the IEI-EMF participants and only 11 such participants took part, it is unclear if the experiment would necessarily be expected to detect a small change in their symptoms.]

Table 5.2.9. Mobile phone base station related studies assessing symptoms, wellbeing or ability to perceive exposure

Endpoint and Volunteers	Exposure[a]	Response	Comment[b]	Reference
Studies with healthy adult volunteers				
Well-being (good mood, alertness, calmness) assessed immediately before and after exposure 57 healthy volunteers (18–67 years; 22 males, 35 females)	GSM 900 MHz base station on the building, shielding to reduce exposure L = 5.2 μW/m^2 M = 153.6 μW/m^2 H = 2126.8 μW/m^2 5 sessions of 50 min each between 09:00 and 13:30 HM scenrio:L+H+L+M+L (n=22) MH scenario:L+M+L+H+L (n=26) LL scenario:L+L+L+L+H (n=9)	Higher exposed volunteers (HM and MH) had higher calmness than LL. Otherwise, no effect of exposure.	Double-blind, randomized between participants. Few volunteers in the LL group due to early termination of study. For neuroendocrine and immune systems see (Augner et al., 2010) in Sections 7.2.2 and 10.2.	(Augner et al., 2009)
Restfulness in bed, subjective sleep latency, subjective wake after sleep onset, subjective total sleep time and subjective time in bed after exposure 365 volunteers recruited from 10 villages with no pre-existing mobile phone coverage (18–81 years; 179 males, 186 females)	Experimental base station within 500 m of volunteer's bedroom, generic GSM signals in test mode with two 900 MHz and two 1800 MHz channels at maximum power Five nights of GSM exposure and five nights of sham exposure	No effect of exposure.	Double-blind, randomized, cross-over. Testing took place within participants own homes. No data on exposure of individual participants. Realistic set-up. For objective sleep parameters see Section 5.2.2.3.	(Danker-Hopfe et al., 2010)
Studies with child and adolescent volunteers				
Sensations of sweating, freezing, breathlessness, tingling, pain, sleepiness, nausea, dizziness, headache and concentration difficulties measured before and after exposure, and discrimination 40 adolescents (15–16 years; 17 males, 23 females) 40 adults (25–40 years; 24 males, 16 females)	Base station type antenna 2.8 m from participant, CW, UMTS, and UMTS with all control features, all: 2140 MHz Field strength 0.9–2.2 V/m 45 min Only difference between sham and UMTS with all features was analysed	A significant overall effect of exposure was observed for headache and concentration, but appeared to be due to baseline differences between conditions.	Double-blind, randomized, crossover. Analytic design registered with Danish Council for Strategic Research prior to start of study. Testing rooms were partly covered in RF absorbers. Headache and concentration difficulties selected a priori as the main subjective endpoints. For cognition see Section 5.2.1.	(Riddervold et al., 2008)
Studies including volunteers with IEI-EMF				

Mood, quality of life, five symptom subscales (anxiety, somatic symptoms, inadequacy, depression, hostility), assessed before and after exposure; discrimination assessed after exposure 33 IEI-EMF volunteers (20–60 years; 19 males, 14 females) 84 healthy volunteers (20–60 years; 45 males, 43 females)	Antenna 2 m behind and to the left, UMTS, 2140 MHz Electric field strength 1, 10 V/m; brain SAR_{10g} 0.045 mW/kg at 1 V/m, 4.5 mW/kg at 10 V/m 45 min	No effect of exposure.	Double-blind, randomized, cross-over. Testing rooms were shielded. For cognition see Section 5.2.1.	(Regel et al., 2006)
Anxiety, tension, arousal, relaxation, discomfort, fatigue and a list of 57 symptoms assessed every 5 min during exposure.; discrimination assessed during exposure 44 IEI-EMF volunteers (46.1 ± 13.5 years; gender of final sample unclear but 57.2% of initial sample was male) 115 healthy volunteers (54.5 ± 15.2 years; gender of final sample unclear but 57.5% of initial sample was male)	Base station antenna 5 m from volunteer GSM, 900 and 1800 MHz: combined power density 10 mW/m^2 UMTS, 2020 MHz: power density 10 mW/m^2 15 and 50 min	No effect of exposure.	Double-blind, randomized, cross-over. 14 IEI-EMF volunteers and 8 healthy controls excluded or dropped out. Bonferroni adjustment applied. Actual sample size less than planned, resulting in difficulties with counterbalancing. Testing rooms shielded. For cognition see (Eltiti et al., 2009) in Section 5.2.1; for autonomic nervous system see Section 9.2.1.	(Eltiti et al., 2007a)
Anxiety, tension, arousal, relaxation, discomfort, fatigue and 57 other symptoms assessed every 5 min during exposure. Discrimination assessed after exposure 51 IEI-EMF volunteers (18–73 years; 30 males, 31 females [estimated from pre-dropout proportions]) 132 healthy volunteers (18–80 years; 65 males, 67 females [estimated]).	Antenna 4.95 m in front of volunteer, TETRA, 420 MHz, 25 kHz bandwidth, with timeslot occupancy 50% Power density 10 mW/m^2; assumed whole body SAR 0.27 mW/kg 4 x 5 min (2 TETRA, 2 sham) separated by 2 min; 2 x 50 min (TETRA, sham)	No effect of exposure.	Double-blind, randomized, cross-over, counterbalanced. Bonferroni correction. Actual sample size less than planned. Testing rooms shielded. For cognition see (Wallace et al., 2012) in Section 5.2.1; for autonomic nervous system see Section 9.2.1.	(Wallace et al., 2010)
Sleep quality, awakening quality, somatic complaints, overall sleep score after exposure 43 IEI-EMF volunteers (17 males, 55.0 ± 10.5 years; 26 females, 56.0 ± 0.6 years)	Shielding of EMF by Faraday cage of electric conductive material mounted around the participant's own bed at home. 9 nights of sleep: 3 under genuine protective material (median reduced exposure ~19 dB), 3 under sham material and 3 under no material	No effect of exposure.	Intervention study, single-blind, randomized, cross-over. Three volunteers showed results indicating significant ($p<0.05$) improvements in outcomes during genuine protective condition, but all three were suspected of having broken the study blinding. For objective sleep parameters see Section 5.2.2.3.	Leitgeb et al. (2008)

Tension-anxiety, depression, anger-hostility, vigour, fatigue, confusion, discomfort before and after exposure, discrimination 11 female IEI-EMF volunteers (27–57 years) 43 female healthy volunteers (21–51 years)	Horn antenna 3 m behind volunteer, 2.14 GHz W-CDMA down-link signal Electrical field strength 10 V/m, SAR_{10g} 0.0013 W/kg Four 30-min exposures: continuous exposure, intermittent exposure (randomly on and off at 5-min intervals), sham without noise, sham with noise	No effect of exposure.	Double-blind, randomized, cross-over. Participants underwent two sessions per day. Testing rooms were shielded. For cognition see Section 5.2.1; for autonomic nervous system see Section 9.2.1.	(Furubayashi et al., 2009)

Abbreviations: CW: continuous wave; GSM: Global System For Mobile Communication; IEI-EMF: Idiopathic environmental intolerance attributed to EMF; TETRA: Terrestrial Trunked Radio; UMTS: The Universal Mobile Telecommunications System; W-CDMA: Wideband Code Division Multiple Access.

[a] All participants were exposed to one of each active exposure and one sham condition, unless otherwise noted. SAR with relevant averaging volume (e.g. SAR_{10g}) is specified if included in the paper.

[b] Unless explicitly noted, studies did not report a priori power calculations, pre-registered protocols, or use testing rooms shielded against external EMF.

5.2.4.5 Other forms of exposure

Two studies assessed the effects of exposure to other types of radiofrequency field in order to determine the threshold at which pain or sensations of warming develop. In the first, Blick et al. (1997) exposed 15 healthy volunteers to increasing and decreasing intensities of far field microwaves at 2.45, 7.5, 10.0, 35 and 94 GHz emitted by antenna positioned 20 to 70 cm from the back of participants. For all frequencies the electric field was parallel to the volunteer's longitudinal axis. Stimuli varied from 0 to 300 W/m^2 and the size of stimulated area was 0.0327 m^2. Exposures lasted for 10 seconds or until the participant detected warming from the exposure, and were presented at 1-minute intervals. A randomisation procedure was to determine exposure levels, so that the participant was blinded to the exposure levels. Power density thresholds at which participants were able to detect warming were, by frequency, 63.1 (2.45 GHz), 19.5 (7.5 GHz), 19.6 (10 GHz), 8.8 (35 GHz), 4.5 (94 GHz). The thresholds corresponded to a 70.7% probability of detection in a standard psychometric procedure. In the second study by the same team, Walters et al. (2000) used a similar procedure to identify the pain threshold for pulse modulated 94 GHz far field microwaves directed at a participant's back. The diameter of the beam was 4 cm. Each exposure lasted for 3 seconds and occurred at 1–2 minutes intervals. The threshold, corresponding to 29.9% probability of sensing pain in a standard psychometric procedure, in this instance was determined as 12.5 ± 0.5 kW/m^2. In average the skin surface temperature was 43 °C at the pain threshold, and the applied exposure had then resulted in an increase in temperature of 9.9 °C from before exposure.

Papers with uncertainties related to inclusion criteria

Five additional studies by this team were also considered had uncertainties related to inclusion critiera on the basis that they assessed the effect of exposure to RF fields on subjective warming, but did not appear to use any statistical analysis for these subjective outcomes (Adair et al., 1998; Adair, Mylacraine & Cobb, 2001a; b; Adair, Mylacraine & Allen, 2003; Adair et al., 2005). They were performed as a series of experiments with similar features with respect to design and thermal environmental conditions. The aim was to obtain knowledge of human thermoregulatory efficiency in RF environments. All RF exposure conditions, including sham, were repeated with ambient temperatures at 24, 28 and 31 °C. Air humidity was relatively low and there was a constant air flow. Dorsal RF exposure for 45 minutes was consequently applied, while exposure frequencies, power densities and modulation varied between the studies. For the highest frequencies (450 and 2450 MHz), the dorsal part of the head, trunk and upper arms, representing about 34% of the total skin, was exposed. Power densities at 450 MHz were 180 or 240 W/m^2 (Adair et al., 1998) and at 2450 MHz 270, 350, 500 and 700 W/m^2 (Adair, Mylacraine & Cobb, 2001a; b). Whole body exposure was achieved in the studies with 100 and 220 MHz exposures. In these studies the power densities were 40, 60 and 80 W/m^2 (100 MHz, (Adair, Mylacraine & Allen, 2003)) and 90, 120 and 150 W/m^2 (220 MHz, (Adair et al., 2005)). Six or seven healthy adult volunteers participated in the different studies; all included both men and women. In addition to objective measures of thermoregulation (see Section 9.2.1), all assessed the volunteers' perception of thermal sensation and comfort. The total thermal exposure influenced thermoregulation and sensed temperature. With no RF exposure, the ambient temperature of 24 °C was judged as "slightly cool", 28 °C as close to "neutral" and 31

°C as "warm". RF exposure at 450 or 2450 MHz increased the sensation of warmth. Especially in the higher ambient temperatures, the thermal comfort decreased with RF exposure concomitant with a preference to reduce the temperature. By exposure to the lowest frequencies, 100 and 220 MHz, with significantly less superficial absorption of the energy, judgement of thermal sensation changed little with exposure level, but the thermal comfort deteriorated. This was most prominent at the highest ambient temperatures and exposure levels (Adair, Mylacraine & Allen, 2003; Adair et al., 2005). [As noted, however, no statistical tests of these effects were reported].

Table 5.2.10. Studies with other exposures assessing symptoms, wellbeing or related subjective endpoints

Endpoint and Volunteers	Exposure[a]	Response	Comment[b]	Reference
Detection of warming 15 male healthy volunteers (45.2 ± 6.0 years)	Far field microwaves with E-field parallel to the volunteer's longitudinal axis, emitted 20–70 cm from the back of volunteers (stimulated area: 0.0327 m^2), 2.45, 7.5, 10.0, 35 and 94 GHz Power density 0–30 mW/cm^2 (0–300 W/m^2). Threshold for detection determined using a staircase procedure with 20 equally-spaced stimulus levels for each frequency 10 s or until warming from exposure was perceived	Thresholds (power density in W/m^2) by frequency: 63.1 (2.45 GHz), 19.5 (7.5 GHz), 19.6 (10 GHz), 8.8 (35 GHz), 4.5 (94 GHz).	Single blind, randomized, cross-over. Threshold corresponded to 70.7% probability of detection in a standard psychometric function.	(Blick et al., 1997)
Pain threshold 10 healthy volunteers (31–70 years; 7 males, 3 females)	Far field microwaves at 94 GHz, PM at 1 kHz (duty circle: 50 – 90%) directed at participant's back, 4 cm beam diameter. Power density 900– 1750 mW/cm^2 (900–17.5 kW/m^2) Threshold determined using a staircase procedure with power density varied in steps of 50 mW/cm^2 (0.5 kW/m^2) . Exposures lasted 3 s	Thresholds required for pain was 12.5 ± 0.5 kW/m^2.	Single blind, randomized, cross-over. Threshold corresponded to 29.9% probability of pain in a standard psychometric function.	(Walters et al., 2000)

Abbreviations: PM: pulse modulated; E-field: electric field.

[a] SAR with relevant averaging volume (e.g. SAR_{10g}) is specified if included in the paper.

[b] Unless explicitly noted, studies did not report a priori power calculations, or use pre-registered protocols.

Excluded papers

(Hocking & Westerman, 2002)

(Zhang, Clement & Taunton, 2000)

5.3 Animal studies

5.3.1 Cognitive performance

Based mainly upon studies investigating changes in operant behaviour, WHO (1993) concluded that RF fields could cause disruption in cognitive performance in animals following exposures at thermal levels. These effects were considered to be consistent with responses to increases in core body temperature of about 1 °C or more. Effects on performance in both rodents and primates were less well defined with exposures that did not cause hyperthermia, although it was also noted that exposure to fields with very high-peak-power pulses could affect ongoing behaviour in exposed mice, if specific energies per pulse exceeded the threshold for auditory perception.

However, neither of these excludes the possibility that long-term or low level exposure of adult animals may also engender subtle behavioural or cognitive changes under specific circumstances, due to the paucity of appropriate data. Since then, more studies have been published, particularly investigating the effects of mobile phone signals on spatial memory function in adult rodents. This review focuses on papers published in 1992 and later.

The present search resulted in 46 papers, 1 of which one was excluded since no sham group was included. Of the remaining 45 papers, 10 are not included in the analysis because of missing information or issues with the design.

5.3.1.1 Place learning and spatial memory

A number of studies have investigated the effects of RF fields on spatial memory and place learning tasks in adult rodents.

Lai, Horita and Guy (1994) exposed groups of 8 Sprague Dawley rats for 45 min per day on 10 consecutive days to pulsed circularly polarized 2450 MHz EMF at an whole-body SAR of 0.6 W/kg; the SAR in the brain was calculated to range from 0.5 to 2.0 W/kg. The exposure was without measurable impact on colonic temperature. Immediately after each daily exposure session the spatial memory function of the animals was tested in a 12-arm radial maze. In this task, animals learn to forage for food rewards placed at the end of each of the arms. Exposed animals consistently made more errors in the maze than sham-exposed controls ($p<0.005$). [Cassel et al. (Cassel et al., 2004) noted that there were differences in performance between the groups already on the first day of the tests, indicating possible differences in anxiety or motivation. However, since the tests were performed after the exposure, it cannot be excluded that there was already a very early response.] When the animals were treated with the cholinergic agonist physostigmine or the opioid antagonist naltrexone before each daily exposure, no difference in performance between real and sham-exposed groups was observed. Pre-treatment with another opioid antagonist, naloxone, resulted in similar differences between real and sham-exposed groups ($p<0.005$) as in the RF-alone treated animals. [Taking into account a duty factor of 0.001 for the pulse sequence used in these studies (2 µs at 500 pps), the spatially averaged whole-body SAR of 0.6 W/kg corresponds to a peak SAR of 600 W/kg, and the spatially averaged power density of 1 mW/cm^2 (10 W/m^2) corresponds to a peak power density of 1 W/cm^2 (10 W/m^2). Chou et al. (1985) showed that for the circular polarized waveguide used in these studies, the threshold for auditory responses in the rat would be an energy density per pulse of 1.5–3 $\mu J/cm^2$ (15–30 mJ/m^2) for pulses <30 µs, corresponding to a peak power density of 0.75–1.5 W/cm^2 (7.5–15 kW/m^2). This means that with the peak power density of 1 W/cm^2 (10 kW/m^2) used in the Lai et al. (1994) study it cannot be excluded that a hearing effect occurred.]

Two groups (Cassel et al., 2004; Cobb, Jauchem & Adair, 2004) tried to replicate the radial arm maze study performed by Lai, Horita and Guy (1994). Cobb, Jauchem and Adair (2004) also pretreated the animals with physostigmine, naltrexone or naloxone. They included seven to eight Sprague Dawley rats in each group and used similar experimental procedures to those of Lai, including restricted access to distal spatial cues normally used to perform the task. No effect of exposure was observed in this study and unlike Lai et al. (1994) they did not observe any effect of naloxone. Lai (2005) proposed that methodological differences between studies may have explained these outcomes: among other differences, Lai limited the number of choices his animals could make each day to 12, whereas Cobb allowed an unlimited number of choices (both within a 10 minute trial duration) which would support increased performance of the task. [An inspection of the data does not suggest that the animals used by Cobb showed over-learning compared with those of Lai, and so they were unlikely to have been more resistant to any field-induced disruptions in acquisition. Also the rates at which both sets of animals reduced errors in the task were very similar, suggesting equivalent rates of learning in both studies.]

In a series of studies with Sprague Dawley rats (n=12 per group), Cassel and colleagues reported that exposure at either 0.6 W/kg (Cassel et al., 2004) or 2 W/kg (Cosquer et al., 2005b) had no significant effect on maze performance. The radial arm maze used in these studies had small, transparent side walls, and so provided access to distal visual cues, but using a maze with high opaque walls (as originally used by Lai) did not affect the result (Cosquer, Kuster & Cassel, 2005). Cassel speculated that the results reported by Lai may have been more attributable to stress or anxiety; however, exposure had no significant effects on behavioural anxiety (Cosquer et al., 2005a).

Wang and Lai (2000) further investigated their previous observations using a Morris water maze and 11–12 Sprague Dawley rats for each the exposure condition. They placed rats in the water maze immediately after being exposed to pulsed 2.45 GHz at 1.2 W/kg for 1 h. The animals had to learn to escape from the water by locating a submerged, non-visible platform. In the training sessions, exposed animals took longer to find the platform than the sham-exposed and cage-control animals ($p<0.05$), and, in contrast to the control animals, spent much time trying to climb the side walls of the maze. In the probe trial without the platform being present, the exposed animals spent less time swimming in the quadrant of the maze that should have contained the platform ($p<0.05$). Therefore, it was concluded that exposure had disrupted spatial reference memory functions and that the exposed animals had to use less efficient learning strategies to locate the platform. [Statistical analysis of the probe trial data by one-way ANOVA revealed no significant treatment effect, but post-hoc analysis using the Newman-Keuls test showed a statistical difference between the exposed and control groups.]

In an extension of these results, Lai (2004) reported on the effects on task performance of simultaneous exposure to RF EMF and a temporarily incoherent magnetic field. In this study, groups of eight Sprague Dawley rats were exposed for 1 h to a continuous wave 2450 MHz field using a cylindrical waveguide system placed inside a set of Helmholtz coils. These coils were used to generate a ‘magnetic noise’ that consisted of a highly complex magnetic signal with frequencies between 30 and 100 Hz at a flux density of 6 µT. After exposure to the RF field only the time taken to locate the escape platform was significantly increased ($p<0.001$). Following simultaneous exposure to RF and the magnetic noise the increase was less, but still significant ($p<0.016$); magnetic noise alone had no effect. During the probe trial, the animals exposed to the RF field alone also spent significantly less time in the quadrant of the maze that previously held the platform compared with the other treatment groups ($p<0.05$).

Sienkiewicz et al. (2000) exposed C57BL/6J mice for 45 min dialy during 10 days to a pulsed 900 MHz field at an SAR of 0.05 W/kg. They observed no difference between five exposed and five sham-exposed animals in performance in a radial arm maze. Animals were tested immediately after exposure or following delays of 15 or 30 minutes. In both the exposed and sham-exposed animals tested without delay there was a slightly larger variability in the time to complete the task, possibly due to some mild stress associated with the exposure situation, but the two groups did not differ.

Dubreuil, Jay and Edeline (2002) exposed Sprague Dawley rats (n=8 per goup) to GSM-type pulsed 900 MHz fields for 45 min using a head-only exposure system. Exposure was given daily immediately preceding behavioural trials. These were either searching for food in a radial arm maze (10 subsequent days) or a food-rewarded navigation task in an open field arena, equivalent to a dry-land version of the Morris water maze (14 days). Different groups of animals were used for the two tasks. No significant effects on the performance of either task were seen using average SARs in the brain of either 1 or 3.5 W/kg.

In a follow-up of this study, Dubreuil, Jay and Edeline (2003) found no effect of a similar exposure on the performance of two more complex versions of the radial arm maze task with 9 or 12 Sprague Dawley rats in each group. In the first version of the task (lasting 12 days) there was a 10 s confinement period between arm choices; while the other version (lasting 16 days) also introduced a 15 min delay after four correct responses had been made on the last 7 days of testing. Animals were returned to their home cages during the delay. [This study is also discussed in Section 5.3.1.2 Non-spatial tasks and behaviour.]

Spatial reversal learning in a T-maze was reported by Yamaguchi et al. (2003) following exposure of 15–28 Sprague Dawley rats to pulsed 1439 MHz PDC signals for either 4 days or 4 weeks. In the 4-day experiment, the animals were exposed for 1 h per day (brain SAR = 7.5 W/kg, whole-body SAR = 1.7 W/kg), or 45 min per day (brain SAR = 25 W/kg, whole-body SAR = 5.7 W/kg) immediately preceding memory testing. In the 4-week experiment daily exposures of 1 h at the lower SAR level were given for 5 days per week during 4 weeks. In the 4th week each daily exposure was followed by memory testing. No effect was observed after either the 4-day or 4-week exposures at the lower SAR level, that had no effect on intraperitoneal temperature. However, performance was significantly impaired after exposures at the higher SAR level (p = ?), that increased core body temperature by up to 2 °C. [It cannot be excluded that a brain SAR of 7.5 W/kg, with a peak of 11 W/kg, caused a (local) increase in brain temperature, but even if this occurred it obviously had no effect on spatial learning.]

The previous studies investigated effects of acute exposure to RF fields. Ammari et al. (2008b) explored in groups of eight Sprague Dawley rats the effects on maze performance of long-term exposure to 900 MHz GSM signals. The animals were locally exposed to the brain for 45 min per day at an average brain SAR of 1.5 W/kg, or for 15 min per day at a brain SAR of 6 W/kg, 5 days per week, for 8 or 24 weeks before testing. After the exposure period, performance testing took place. No significant differences in performance with sham-exposed groups were seen following either schedule. There was some evidence of poorer performance in the animals in the cage-control group which was attributed to the lack of daily handling of these animals.

Li et al. (2008) exposed five Wistar rats to pulsed 2450 MHz RF EMF for 3 h per day during 30 days in the presence of or without the glucocorticoid receptor antagonist RU468. The whole-body SAR was 0.2 W/kg. The SAR of the brain was reported as 0.7 W/kg [it is difficult to conceive this as accurate, since the animals could move freely]. Twentyfour hours after the last exposure the water maze testing started with 6 daily training session followed by a pobe trail on the 7th day. The escape latency in the training phase of the water maze test was increased on days 4–6 ($p<0.01$) in the RF-only treated group, while in the group treated with RF and RU468 it was increased on the 6th day only ($p<0.01$) [correction for multiple testing was applied]. Memory in the RF-exposed groups was impaired ($p<0.01$), but not affected by RU468 treatment. [This study is also discussed in Section 7.3.2 Other hormones.]

Daniels et al. (2009) exposed six newborn Sprague Dawley rats for 3 h per day from day 2–14 after birth to an 850 MHz field at a power density of 60 μW/m^2. At an age of 58 days the animals were tested in a Morris water maze. No effects of exposure were observed on memory function, but in males an increased freezing behaviour was seen, which was considered indicative for mood disturbance. This is discussed below in Section 5.3.1.2. [This study is also discussed in Section 7.3.2 Other hormones.]

Takahashi et al. (2010) exposed pregnant rats during gestation and the progeny during lactation to 2140 MHz RF EMF for 20 h per day. Two exposure levels were used. At the higher exposure level, the average SAR was 0.066–0.093 W/kg for the dams and 0.068–0.146 W/kg for the foetuses and the progeny. At the lower level, the SARs were about 43% of these. A number of variables was measured, including memory function of the first generation offspring. Memory in the water maze was tested at an age of 9 weeks; no effect of exposure on performance was observed. [This study is also discussed in sections 5.3.1.2 (Non-spatial tasks and behaviour) and 11.3.3 (Studies addressing both fertility and developmental effects).]

Studies not included in the analysis

Other studies have also investigated effects of RF fields on spatial memory, but these studies suffer from methodological or other weakness that make them unsuitable for risk analysis.

Narayanan et al. (2009) placed a 900 MHz mobile phone in silent but vibratory mode beneath a cage containing Wistar rats. Each day for 4 weeks, these animals were exposed to the fields associated with 50 missed calls and then their spatial learning capabilities were tested using a water maze. Significant differences in behaviour were seen. Exposed animals initially took far longer to locate the escape platform during acquisition trials and, although their latencies improved, they remained slower than controls. During the probe trial, the exposed animals took significantly longer to reach the target quadrant and spent less time in that quadrant. [No estimate of the induced SAR was given. The emissions from the phone would be at maximum output power only for the first few seconds of each call and then adjusted to a (much) lower level during the call up time depending on the connection with the base station. Between calls the would be negligible (Hansson Mild, Bach Andersen & Pedersen, 2012).While a mobile phone offers a readily available source of RF fields, it does not allow any knowledge or control of individual exposures, particularly in a group of freely moving animals. The authors conceded that the vibrations made by the phone could have been responsible for the observed responses.]

Fragopoulou et al. (2010) reported subtle deficits in a water maze task in young adult BALB/c mice exposed to fields from a commercial mobile phone sending a continuous audio signal; sham exposed animals were exposed to the same sound from a radio. Animals were exposed for 1 hour before testing, for 15 minutes between each of four training trials, and again for 2 hours between the last training trial and the probe trial. No overall changes were observed in latency to find the hidden platform or in the mean distance swam for all days, but both latency and distance were significantly increased in the first training trial on days 2, 3 and 4, and exposed animals did not show the expected preference for the target quadrant during the probe trial. [There are a number of caveats with this study. The same start position was used for the first trial each day. Moreover, the actual exposure level of the animals is not clear. The authors measured a variation in power density of 0.05–0.2 mW/cm^2 (5–20 W/m^2), but much less variation in electric field strength (23–36 V/m), which they used to calculate brain SARs of 0.41–0.98 W/kg. It is not clear whether the variation in electric field strength includes the spatial variation of the power density, or merely reflects variations due to the varying sound level (they played music from a radiostation through the phone and the output level depended on the sound level). Since the animals could move freely in the cages, the variation in brain SAR might have been much larger then indicated.]

Table 5.3.1 Animal studies on effects of exposure to RF fields on place learning and spatial memory.

Endpoint, animals, number per group, age at start	Exposure: source, schedule, level, freely moving or restrained	Response	Comment	Reference

12-arm radial maze task, assessed after each daily exposure Rat: Sprague Dawley (n=8) 250–300 g	2450 MHz, pulsed; 2 µs pulses at 500 pps 45 min/day, 10 days WBA SAR 0.6 W/kg Brain SAR 0.5-2.0 W/kg With/without treatment before exposure with physostigmine (cholinergic agonist), naltrexone or naloxone (opioid antagonists) Restrained	RF alone: more errors than sham. Pre-treatment with physostigmine or naltrexone: no difference exposed/sham. Pretreatment with naloxone: no effect.		Lai, Horita & Guy (1994)
12-arm radial maze task Rat: Sprague Dawley (n=7 or 8) 250–300 g	2450 MHz pulsed; 2 µs pulses at 500 pps 45 min/day, 10 days WBA SAR 0.6 W/kg With/without treatment before exposure with physostigmine, naltrexone or naloxone Restrained	No effect on performance and no effect of pre-treatment with physostigmine, naltrexone or naloxone.	Did not confirm Lai, Horita & Guy (1994)	Cobb et al. (2004)
12-arm radial maze task Rat: Sprague Dawley (n=12) 3 months, 270–320 g	2450 MHz pulsed; 2 µs pulses at 500 pps 45 min/day, 10 days WBA SAR 0.6 W/kg Restrained	No effect on performance in maze with access to distal spatial cues.	Did not confirm Lai, Horita & Guy (1994).	Cassel et al. (2004);;
12-arm radial maze task Rat: Sprague Dawley (n=12) 3 months, 270–320 g	2450 MHz pulsed; 2 µs pulses at 500 pps 45 min/day, 10 days WBA SAR 2 W/kg Restrained	No effect on performance in maze with access to distal spatial cues.	Did not confirm Lai, Horita & Guy (1994).	Cosquer et al. (2005b)
12-arm radial maze task Rat: Sprague Dawley (n=12) 3 months, 270–320 g	2450 MHz pulsed; 2 µs pulses at 500 pps 45 min/day, 10 days WBA SAR 2 W/kg Restrained	No effect on performance in maze with reduced access to distal spatial cues.	Did not confirm Lai, Horita & Guy (1994).	Cosquer, Kuster & Cassel (2005)
12-arm radial maze task Rat: Sprague Dawley (n=12) 3 months, 270–320 g	2450 MHz pulsed; 2 µs pulses at 500 pps 45 min/day, 10 days WBA SAR 2 W/kg Restrained	No effect on anxiety.		Cosquer et al. (Cosquer et al., 2005a)
Water maze task Rat: Sprague Dawley (n=11, 12) 2–3 moths, 250–300 g	2450 MHz pulsed; 2 µs pulses at 500 pps 60 min 2x/day, 3 days WBA SAR 1.2 W/kg Restrained	Increased escape times, no effect on speed; less time in correct quadrant during probe trial.	Differences in probe trial not significant using one-way ANOVA , but significant in post-hoc analysis with Newman-Keuls test .	Wang & Lai (2000)
Water maze task Rat: Sprague Dawley (n=8) 2–3 months, 250–300 g	2450 MHz CW 60 min 2x/day, 3 days WBA SAR 1.2 W/kg Temporally incoherent magnetic noise at 6 µT Restrained	Increased escape times, less time in correct quadrant during probe trial; smaller changes after co-exposure with magnetic noise.	Magnetic noise alone had no effect.	Lai (2004)

8-arm radial maze task Mouse: C57BL/6J (n=5) 12 weeks	900 MHz pulsed at 217 Hz 45 min/day, 10 days WBA SAR 0.05 W/kg Tested immediately or 15 or 30 min after exposure Restrained	No effects on performance.	Animals tested immediately took longer to complete task both after RF and sham exposure.	Sienkiewicz et al. (2000)
8-arm radial maze task; spatial task in open field Rat: Sprague Dawley (n=8) 150 g	900 MHz pulsed at 217 Hz 45 min/day, 10 days (radial maze) or 14 days (spatial task) Brain SAR 1 or 3.5 W/kg Restrained	No effect.	Head-only exposure.	Dubreuil, Jay & Edeline (2002)
Two versions of 8-arm radial maze task Rat: Sprague Dawley (n=12 or 9) 120 g	900 MHz pulsed at 217 Hz 45 or 60 min/day, 4, 12 or 16 days Brain SAR 1 or 3.5 W/kg Restrained	No effect.	Head-only exposure. For non-spatial tasks and behaviour see Section 5.3.1.2.	Dubreuil, Jay & Edeline (2003)
T-maze reversal learning task Rat: Sprague Dawley (n= 15–28) 670 g	1439 MHz pulsed 6.7 ms pulses at 50 pps 45 or 60 min/day, 4 days or 60 min/day, 4 x 5 days Brain SAR 7.5 or 25 W/kg Restrained	No effect on performance at lower SAR, decreased performance at higher SAR resulting in increased core temperature.	Head-mainly exposure (animals positioned with head towards antenna).	Yamaguchi et al. (2003)
8-arm radial maze task over 10 days with further 8 days with 45 min inter trial delay after 4 correct responses Rat: Sprague Dawley (n=6) 6 weeks	900 MHz GSM 45 min/day at average brain SAR 1.5 W/kg or 15 min/day at brain SAR 6 W/kg, 5 days/week, 8 or 24 weeks before testing Restrained	No effects.	Head-only exposure.	Ammari et al. (2008b)
Water maze task Rat: Wistar (n=5) 3 months	Pulsed 2450 MHz ± glucocorticod receptor antagonist RU468 3 h/day, 30 days Brain SAR 0.7 W/kg; WBA SAR 0.2 W/kg Free	RF: increased escape latency on day 4-6; RF + RU468: only on day 6. RF exposure: impaired memory, no effect RU468.	Correctness brain SAR doubtful. For hormones see Section 7.3.2.	Li et al. (2008)
Water maze task Rat: Sprague Dawley (n=6) 2 days	840 MHz 3 h/day, 12 days Power density 60 $\mu W/m^2$ Free	No effect.	Increased freezing behaviour in males (mood disturbance); For Open field test see Section 5.3.1.1. Also discussed in Section 7.3.2.	Daniels et al. (2009)

Water maze task Rat: CR1:CD(SD) (n=4) Adults: 10 weeks + 5 days acclimatization Offspring: 4 days	2140 MHz, WCDMA 20 h/day, from day 7 of gestation to delivery and day 4–21after birth Dams: WBA SAR 0.066–0.093, 0.028–0.04 W/kg; Foetuses/progeny: WBA SAR 0.068–0.146, 0.029–0.067 W/kg Free	No effect in water maze test at 9 weeks of age.	For non-spatial tasks and behaviour see Section 5.3.1.2 and for fertility and developmental effects see Section 11.3.3.	Takahashi et al. (2010)

"No effect" means no statistically significant effect

5.3.1.2 Non-spatial tasks and behaviour

The effects of exposure to RF EMF on other measures of cognitive performance apart from spatial memory have also received some attention. These studies include investigations on effects on operant behaviour, spontaneous exploration of novel environments, and object recognition memory. Frequencies investigated include high-peak-power microwaves, ultrawideband (UWB) and mobile phone signals. Several studies that were published before 1992 but were not included in the previous WHO report (WHO, 1993) are also described.

Operant behaviour

High-peak-power microwave pulses are used in a number of military applications. Generally, while peak output powers are very high, average whole-body SARs are low due to the short pulse duration and long inter-pulse intervals. The possibility that such exposure could affect cognitive function has been studied using operant conditioning techniques. D'Andrea, Cobb and De Lorge (1989) exposed five juvenile rhesus monkeys to pulsed 1.3 GHz high peak-power fields, with 3 µs pulses and a 2–32 Hz repetition frequency. The peak power in the pulses was 131.8 W/cm^2 (1.32 kW/m^2), and the specific absorption (SA) 280 mJ/kg per pulse [this is above the auditory stimulation threshold, so it cannot be excluded that microwave hearing occurred]. The overall SAR to the head was 0.09–1.44 W/kg and the whole-body averaged SAR 0.05–0.80 W/kg. The animals had been trained to a differential-reinforcement-of-low-rate (DRL) schedule with limited hold, a time discrimination schedule or a fixed-interval schedule. They were exposed and tested for 1 hour per day, 5 days per week during 12 weeks. The performance during exposure did not differ from that during non-exposure.

Akyel et al. (1991) observed that high-power pulsed 1.25 GHz microwaves only had a disruptive effect on the behaviour of Wistar rats if exposure caused a substantial elevation in core temperature. Eight animals were exposed for 10 min to 10 µs pulses each of which produced a whole-body SA of 2.1 J/kg. Whole-body SARs were 0.84, 2.5, 7.6 or 23 W/kg by using different pulse repetition frequencies. Each animal received each of these four levels with a week interval in random order. Immediately following exposure, the rats were tested on three operant schedules: a fixed-ratio, a variable interval, and a DRL schedule. Exposure at the highest SAR induced a rise in core temperature of the animals of 2.5 °C. Under these conditions, cessation of all responses ("work stoppage") was observed in all behaviour schedules for about 13 minutes, by which time the core temperatures in the animals had returned to less than 1 °C above their starting values. Responding then resumed, albeit at somewhat reduced levels of efficiency. There was no carry-over effect to the next session. No behavioural effects were seen following exposure at the lower SARs.

Raslear et al. (1993) investigated the effects of high-peak-power microwave pulses on the performance of a time perception and discrimination task in eight Sprague Dawley rats. Animals were trained to distinguish between two light stimuli (0.5 s or 5 s in length) by performing appropriate lever responses. The effects of exposure to 3 GHz pulses (80 ns pulse width) at a five different SAs varying from 0.0058 to 580 mJ/kg per pulse for 25 min (resulting in a maximum whole-body SAR of less than 0.1 W/kg) were investigated by examining the responses to presentations of stimuli intermediate in length to the training stimuli. Changes in behaviour were observed following exposure: the time taken to complete a session of 300 trials increased with increasing levels of exposure ($p<0.05$), as did the number of null responses made (defined as a lack of a response within 10 s of the end of a stimulus) ($p<0.05$). This suggests that low-level exposure had affected cognitive function and impaired the ability of the animals to make decisions. [The authors indicate that for the three highest power levels the SA per pulse was above the auditory stimulation threshold. Thus, an effect of microwave hearing cannot be excluded.]

D'Andrea, Thomas and Hatcher (1994) exposed four rhesus monkeys for 20 min to pulsed 5.62 GHz fields at whole-body SARs of 2, 4 or 6 W/kg whilst they performed a variable interval, colour discrimination task. The three SAR levels and sham exposure were given to each monkey in random order on different days (within-subjects design). The monkeys were exposed to RF pulses with a pulse width of 2.8 μs at 100 pulses per second from military radar either with or without additional high-peak-power pulses (pulse width of 50 ns).The performance during exposure to the combined signal was identical to that during the radar signal alone. The total number of responses elicited, the choice reaction times and the numbers of rewards gained significantly decreased at 4 and 6 W/kg ($p<0.05$), which suggests these changes were due to heating. [The maximum power per pulse is above the auditory stimulation threshold, so it cannot be excluded that microwave hearing occurred.]

Sherry et al. (1995) reported that the acute exposure to UWB pulses had no effect on the performance of an overtrained, continuous balance task in rhesus monkeys. In this task, four animals manipulated a joystick to minimize random disturbance in pitch of the chair in which they were seated; large deviations resulted in the delivery of mild electric shock to the tail. Monkeys were exposed to UWB (60 pulses per second for 2 min at 250 kV/m); 1 h after exposure the task was tested. The whole-body SAR was calculated to be 0.005 mW/kg.

Bornhausen and Scheingraber (2000) exposed groups of 12 Wistar rats to 900 MHz GSM-type fields continuously during pregnancy. The power density was 1 W/m^2 and the estimated whole-body SAR 0.018–0.075 W/kg. The offspring were tested using nine tests of operant behaviour performance. No performance deficits were observed in the exposed animals. [This study is also discussed in Section 11.3 (Fertility, reproduction, development).]

Spontaneous exploration

As part of an extensive investigation in groups of 100 Sprague Dawley rats into the biological effects of long-term, low level exposure to pulsed 2450 MHz microwaves, Chou et al. (1992) found that near-continuous exposure for 2 years at up to whole-body SARs of 0.4 W/kg had no consistent effect on locomotory activity measured in an open field arena in either male or female rats, although the activity of the exposed animals was lower than that of the sham-exposed animals in the first session, 6 weeks after the start of exposure ($p=0.026$). Behaviour was assessed 14 times at 6-week intervals throughout the study. [This paper is also discussed in sections 10.3 (Immune system) and 12.2.2 (Cancer).]

Quock et al. (1994) used the mouse staircase test to investigate the interaction between radiofrequency fields and the anxiolytic and sedative actions of benzodiazepines. Twenty CD1 mice per group were exposed for 5 min to continuous wave 1.8 or 4.7 GHz fields at 4, 12 or 36 W/kg following pre-treatment with chlordiazepoxide in various concentrations, ranging from 8 to 32 mg/kg. Exposure without drug pretreatment had no effect on either the numbers of rears or steps ascended. Drug treatment at the two lower doses slightly increased the number of rears and steps climbed, while at the highest dose the numbers of rears and steps climbed were significantly lower than in vehicle-treated controls ($p<0.0001$). In general no effect of exposure was observed on the changes in the number of rears and steps ascended induced by the drug, except at the highest SAR with the 4.7 GHz field, where the reduction in the number of rears ($p<0.05$) and steps ascended ($p<0.016$) induced by the highest dose of the drug was significantly less than with sham exposure and the lower SARs. [In view of the level of SAR where effects were observed, 36 W/kg, a thermal effect is possible.]

Nittby et al. (2008b) exposed male and female Fisher 344 rats (n=16 per group) for 2 h per week during 55 weeks to an 900 MHz GSM signal. The whole-body SARs at the start of the exposures were 0.0006 and 0.06 W/kg. Due to the growth of the animals these were reduced to 59% of the initial values in males and 84% in females by the end of the treatments. Open field behaviour was tested on three consecutive days starting 3 or 4 weeks after the final day of exposure. No difference was observed between exposed and sham-exposed animals.

Mausset-Bonnefont et al. (2004a) exposed groups of 12 Wistar rats to a 900 MHz GSM signal for 15 min, with SAR in the brain of 6 W/kg and tested the behaviour of the animals immediately and 24 h after the end of exposure. They reported no significant changes in exploration or locomotor behaviour in an open field test and no significant changes in rearing or grooming. [With the SAR of 6 W/kg in the brain, mild thermal effects cannot be excluded. This study is also discussed in Section 5.3.4 (Neurotransmitters).]

Khirazova et al. (2012) exposed 10–12 week old rats in groups of 10 to an 905 MHz RF field for 2 h at a whole-body SAR of 1.67 W/kg. Five minutes and 24 h after exposure they tested the open field behaviour of the animals. At 5 min they observed increased activity and decreased anxiety in males, and reduced activity and increased anxiety in females (all $p<0.05$). At 24 h, the activity was decreased and anxiety increased in males, while in females anxiety was increased ($p<0.05$). [This study is also discussed in Section 7.3.2 (Other hormones).]

In a study discussed above in Section 5.3.1.1, Daniels et al. (2009) exposed six newborn Sprague Dawley rats for 3 h per day from day 2–14 after birth to an 850 MHz field at a power density of 60 μW/m^2. At an age of 58 days the animals were tested in a Morris water maze. In males (but not in females) an increased freezing behaviour was seen after the RF but not sham, which was considered indicative for mood disturbance. This was further tested in the open field test. This showed less locomotor activity and more grooming in males (both $p<0.05$) after the RF exposure. No effects of exposure were observed in females and on exploratory behaviour in both sexes. [This study is also discussed in Section 7.3.2 Other hormones.]

In a study described above in Section 5.3.1.1 (Place learning and spatial memory), Takahashi et al. (2010) exposed pregnant rats during gestation and the progeny during lactation to 2140 MHz RF EMF for 20 h per day. Two exposure levels were used. At the higher exposure level, the average SAR was 0.066–0.093 W/kg for the dams and 0.068–0.146 W/kg for the foetuses and the progeny. At the lower level, the SARs were about 43% of these. A number of variables was measured including behaviour in the first generation offspring, using the open field test at an age of 5 and 8 weeks. No effects were observed. [This study is also discussed in Section 11.3.3 (Studies addressing both fertility and developmental effects).]

Object recognition

Mickley et al. (1994) used a recognition memory task to investigate potential changes in working memory following exposure to RF EMF. Rats normally have a preference to explore less recently seen (older) objects or recently seen (familiar) objects in novel locations. Sprague Dawley rats (n=8–19 per group) were given 10 min to explore a previously unseen object in an arena before being exposed for 20 min to continuous wave 600 MHz at range of whole body SAR between 0.1 and 10 W/kg. After an inter-trial interval of 60 min, the animals were returned to the arena, which now contained the original (familiar) object and a novel object. Memory changes were evaluated by measuring the relative exploration times of these objects, with deficits in memory indicated by extensive re-exploration of the familiar object. SAR-dependent changes in object exploration were seen, with a significant impairment in discrimination of the objects following exposures of 9.3 W/kg and higher SARs ($p<0.05$). Exposures above 5 W/kg increased rectal and brain temperatures by at least 1°C; with 9.3 W/kg the brain temperature increase was 2 °C. [So it is possible that the effect on memory was thermally-induced. This paper is also discussed in Section 5.3.5 (Gene expression).]

In an extension of this study, Mickley and Cobb (1998) investigated the role of thermal tolerance on this response. They exposed 15 animals per group on two successive day for 20 min to the CW 600 MHz signal at a whole- body SAR of 9.3 W/kg. The second exposure resulted in a smaller increase in core body temperature than the first (thermal tolerance) ($p<0.05$). A similar trend was observed with brain temperature, but this was not significant. The object recognition after the second exposure did not differ from that of the sham-treated animals, while that after the first exposure was significantly impaired ($p<0.05$). A reduced memory impairment was observed when the opiate antagonist naltrexone was administered before exposure at a dose of 10 mg/kg, while 0.1 mg/kg had no effect.

Using a paradigm similar to that used by Mickley and colleagues, Dubreuil, Jay and Edeline (2003), in a study discussed above in Section 5.3.2.1, examined the effects of head-only exposure to 900 MHz GSM signal on the performance of an object recognition task. Sprague Dawley rats (n=12 per group) were exposed for 45 min at an average SAR in the brain of 1 or 3.5 W/kg either before they explored the objects for the first time, or before they explored the objects for the second time: the inter-trial interval was 15 or 60 min respectively. Exposure at either SAR had no effect on performance of the task.

In a study described above with the open field tests (see Spontaneous exploration), Nittby et al. (2008b) also investigated the effects of long-term (55 weeks) exposure to 900 MHz GSM signals at whole-body SARs of 0.0006 or 0.06 W/kg on object recognition memory of groups of 16 rats. A small deficit in recognition memory, independent of SAR, was observed in the exposed animals ($p=0.02$), although the magnitude of this effect was far smaller than that shown by the cage-control animals. Exposure had no effect on remembering object location, and all animals showed the expected preference to explore objects in novel locations.

Anxiety

Studies have addressed the possibility that RF fields might influence cognitive performance by increasing the levels of stress or anxiety in exposed animals. Elevated plus-maze is a much used behavioural model of anxiety in rodents. The maze takes the form of a cross, with one pair of opposing arms enclosed by high side walls and the other pair of arms have (very small or) no side walls. The maze is elevated above floor level on a central pedestal. Higher levels of anxiety are indicated by increased number of entries into the closed arms or by more time spent in those arms.

In a very thorough study, Cosquer et al. (2005a) exposed Sprague Dawley rats in groups of 12 to pulsed 2450 MHz fields at a whole-body SAR of 0.6 W/kg for 45 min. Then they were tested in the elevated plus-maze under conditions of low ambient light (2.5 lux) to reveal anxiogenic responses, or under high ambient light (30 lux) to reveal anxiolytic responses. In both conditions, exposure had no effect on either the number of open arm entries or time spent in those arms. Thus, EMF exposure had not significantly altered anxiety responses.

Sinha (2008) reported that repeated, very low level exposure of Charles Foster rats (n=12 per group) to pulsed 2450 MHz resulted in changes in behaviour in both the elevated plus-maze and an open field arena. Free roaming animals were exposed for 2 h a day for 21 days at a whole body SAR of around 0.01–0.04 W/kg and behaviour was measured in each maze once every five days during the exposure period. It was found that the amount of time the animals spent in the open arms of the plus-maze decreased with time of exposure, becoming significantly different from the sham controls after day 11 ($p<0.05$); at the same time, the amount of centre-stay time increased and was significantly different after day 11 ($p<0.05$). Activity in the open field also changed, with significant increases in rearing after day 16 ($p<0.05$) and in locomotion on day 21 ($p<0.05$). [These results suggest that long-term, low level exposure may cause progressive changes in animals even with very low exposures. However, it is possible that other factors may have played a role, because the control animals maintained the same level of responsiveness throughout the experiment for all measured variables, and did not show the modifications in behaviour that might be expected with repeated testing. This raises some doubts about the validity of the results. This paper is also discussed in Section 7.3.2 (Other hormones).]

In a parallel study with similar exposures (SAR = 0.036 W/kg) in adult rats (n=5 per group), Sinha et al. (2008) reported on the open-field behaviour assessed after the exposure period. They observed higher activity in mobility ($p<0.01$) and rearing ($p<0.05$), but no effect in grooming. [This paper is also discussed in Section 7.3.2 (Other hormones).]

Shtemberg et al. (2001) conditioned animals to avoid the naturally sought dark environment in a space with an open illuminated and closed dark section. Entering the dark section evoked a painful stimulus in another rat (kept outside the testing space) which resulted in a stress response (vocal and movement) that was perceived by the tested rat. This resulted in three groups (10–18 animals in each) with different natural levels of stress conditioning. These groups were exposed to a 4200 MHz RF field, modulated at 20 Hz–20 kHz for 1 h (electric field strength = 150 mV/m^2). Subsequently they were tested using a conditioning paradigm in which, in a space with two sectors, in one sector a conditioning stimulus (light and sound) was accompanied by a small electric shock. Avoidance and escape reactions were recorded. The group with the highest level of excitability seemed to learn best to avoid the painful stimulus. [The statistical analysis of this complex set of experiments is not clear. This study is also discussed in Section 5.3.4 (Neurotransmitter function).]

Bouji et al. (2012) exposed groups of six 6-weeks and 12-months old Sprague Dawley rats to a 900 MHz GSM signal for 15 minutes locally to the head at a SAR of 6 W/kg. They observed no effect of the exposure on a conditioned fear response (an aversive reaction to an electric shock) and to memory in both the young and the old rats. [This study is also discussed in Section 7.3.2 Other hormones.]

Studies not included in the analysis

This includes several older studies that were not discussed in WHO (1993), but that showed up with the searches. It is considered useful to indicate why these studies are not included in the overall analysis.

Galloway (1975) exposed restrained rhesus monkeys weighing 4.5–5.5 kg to continuous 2450 MHz fields, using an applicator that exposed the head only. Four animals were trained to a lever-pressing task. In the first series this was a discrimination task and in a second series a repeated acquisition task (only two animals completed this due to technical problems with the exposure device resulting in skin burns). For the discrimination task, the four animals were each exposed for 2 min with an output power of 5, 10 ,15, 20 or 25 W, administered in random order and emitted by an applicator fixed on a helmet worn by the subject . The interval between exposures is not provided, but is probably days or weeks, since the exposures were stated to be given twice each over a 9-month period. Directly following each exposure the animals were tested. Exposures with 25 W output power all resulted in convulsions during exposure, and in some cases this also occurred with 20 and 15 W. In those cases the exposure was immediately discontinued and the test started. In a second series of experiments for this tasks, three of the four monkeys were exposed for 1 h with 10 W output power, using a 2 min on, 1 min off schedule. For the repeated acquisition task the exposures were for 2 min with output powers at 10 ,15, 20 or 25 W, each given at least twice each over a 100-day period. No effect of any of the 2-min or 1-h exposures on the discrimination task was observed. With the repeated acquisition task, the exposures with 25 W output power were stated to result in decreased performance. [It is not clear whether the data presented in the figures are from one animal or the means from the two animals. No statistical analysis of any data is performed, so in fact no conclusion on effects can be drawn. The exposure is not clear, since only the output power of the applicator is given. The number of subjects is very low.]

Mattsson and Oliva (1976) used one 12-kg rhesus monkey for exposures to broadband EMF (1 Hz – 1 GHz, primarily <30 MHz) from a pulse generator. The exposure was for 1 h at 5 pulses per second, with an average power density of 25.3 mW/cm^2 (253 W/m^2). The animal was restrained during exposure and trained for avoidance of electric shock by pressing a lever. The exposure had no effect on this behaviour. [This is a study on only a single subject.]

Jensh (1997) exposed pregnant Wistar rats throughout gestation to RF EMF with frequencies of 915 MHz at 10 mW/cm^2 (100 W/m^2), 2.54 GHz at 20 mW/cm^2 (200 W/m^2) or 6 GHz at 35 mW/cm^2 (350 W/m^2), each for 6 h per day. With 6 GHz exposures a decreased performance was observed in avoidance and memory tests in the offspring. No effects were found with the other frequencies. [No data or p-values are provided, therefore this study cannot be properly evaluated. This paper is also discussed in Section 11.2.3 (Fertility, reproduction and development).]

Narayanan et al. (2009) reported significant effects on passive avoidance learning in Wistar rats (n=6 per group) following exposure to the fields from a mobile phone associated with 50 missed calls each day for 4 weeks. A commercial 900/1800 MHz mobile phone was placed in their cage in silent (but vibratory) mode. Passive avoidance was tested using latency to enter a small, dark compartment from a large, bright one. The exposed animals took significantly longer to enter the dark compartment on the second and third of three habituation trials and during the retention trials performed 24 and 48 h after associating the small compartment with electrical foot shock. [No estimate of the SAR from the phone was given, and it is likely to have been very variable between animals. The contribution of the vibrations made by the phone was also not considered.]

Kumar et al. (2009) reported that exposure to a daily cohort of 50 missed calls from a 900/1800 MHz GSM mobile phone increased levels of anxiety in groups of 6 Wistar rats. Behaviour in an elevated-plus maze was measured both immediately and 24 h after the last exposure. At both time points, exposed animals spent significantly less time in the open arms of the maze and also defecated more than sham controls. [As in the study of Narayanan et al. (2009), no estimate of the SAR from the phone was given, and it is likely to have been very variable between animals. The contribution of the vibrations made by the phone was also not considered.]

Ntzouni et al. (2011) investigated the effects of GSM signals on the performance of an object recognition task in groups of 8 C57BL mice. The task was conducted in a dedicated arena, with animals exploring two identical objects on one trial, and after an inter trial interval of 10 min, the animals explored one of the objects from the previous trial as well as a new object. Animals were exposed using a working 1800 MHz GSM mobile phone that had been placed under the testing arena or home cage. The average SAR in the brain was reported to be 0.22 W/kg. No effect of exposures during the trials on object discrimination was observed. After an interval of 8 days with no procedures, the same animals were exposed in their home cages for 90 min each day for 17 days. Another object recognition task was conducted immediately after the animals had been exposed in their home cages for 60 min , and with addition exposures during the inter trial interval and for 20 min after testing. Under these conditions, the animals showed a significant reduction in discrimination. Daily home cage exposures of 90 min were reinstated for a further 11 days. One day later, a third object recognition task was begun, and this again showed no effect on object discrimination. [The complex exposure schedule (with animals being exposed either during a trial, during the inter trial interval, or before and after a trial) complicates interpretation of these data. Moreover, the actual exposure of the animals is not clear. The authors report an average electric field strength of 17 V/m and calculate an SAR of 0.22 W/kg from this, but they also refer to a previous study (Fragopoulou et al. (2010), described above) in which they report measuring a variation in power density of 0.05–0.2 mW/cm^2 (5–20 W/m^2), but much less variation in electric field strength (23–36 V/m), which they used to calculate brain SARs of 0.41–0.98 W/kg. It is not clear whether the variation in electric field strength reported in the previous study included the spatial variation of the power density, or merely reflects variations due to the varying sound level (they played music from a radiostation through the phone) and whether no such variation was present in the current study. Since the animals could move freely in the cages, it is unlikely that there were no variation in brain SAR, and these might have been much larger then indicated in the first study.]

Zhao et al. (2012) exposed Wistar rats (10 per group) to unspecified RF EMF for 6 min per day up to 1 month. Whole-body SARs of 1.05, 2.1 and 4.2 W/kg were employed. Memory was tested in a Morris water maze at various times between 1 day and 6 months after exposure. A significant decrease in learning and memory was observed at 7 and 14 days and 1 month after exposure in all three exposure groups ($p<0.01$–0.05). [Since the type of RF EMF and the exposure parameters were not specified, this study cannot be evaluated. This study is also discussed in Section 5.3.4 (Neurotransmitters).]

Aldad et al. (2012) exposed pregnant mice (39 exposed, 42 controls) to a 800-1900 MHz mobile phone placed above the animal cage at 4.5–22.3 cm from the mice. The animals were exposed 9, 15 or 24 h/d for 18 days. Hyperactivity and impaired memory was reported in the offspring. Differences were observed also in electrophysiological measurements. [Since the exposure level was not characterized, this study cannot be evaluated. It is also discussed in Section 11.3.2 (Developmental effects).]

Table 5.3.2. Animal studies on effects of exposure to RF fields on non-spatial tasks and behaviour

Endpoint, animals, number per group, age at start	Exposure: source, schedule, level, freely moving or restrained	Response	Comment	Reference
Operant behaviour				
Differential-reinforcement-of-low-rate with limited hold (DRL 8 LH4), time discrimination (TD) and fixed-interval (FI) schedules Rhesus monkey (n=5) Juvenile, 5–5.5 kg	1.3 GHz, pulsed (pulse width 3 µs, at 2–32 pps) SA 280 mJ/kg per pulse 60 min WBA SAR 0.05–0.8 W/kg, peak SAR 8.3 W/kg Restrained	No effect.	Within-subjects design. Animals previously used in other experiments. SA per pulse above the auditory perception threshold.	D'Andrea, Cobb & De Lorge (1989)
Fixed ratio, fixed interval or differential-reinforcement-of-low-rate schedule Rat: Wistar (n=4 per schedule) Adult, 185 g	1.25 GHz, pulsed (pulse width 10 µs) SA 2.1 J/kg per pulse 10 min WBA SAR 0.84, 2.5, 7.6 or 23 W/kg Restrained	No effects at lower SARs, but complete cessation of responding in all schedules for 13 min at 23 W/kg followed by decreased performance.	Within-subjects design. Exposure at 23 W/kg increased core temperatures by 2.5 °C.	Akyel et al. (1991)
Two choice, time perception and discrimination task Rat: Sprague Dawley (n=8) 12–15 weeks	3 GHz pulses, pulse width 80 ns, 0.125 pps for 200 pulses at SA of up to 580 mJ/kg per pulse 25 min WBA SAR up to 0.072 W/kg Restrained	Dose-dependent increase in session time and numbers of null response made; possible effect on discrimination.	Co-incidental noise (~57-89 dBA per pulse) or soft x-rays did not correlate with effects. SA per pulse above the auditory perception threshold.	Raslear et al. (1993)

Variable-interval schedule with choice reaction time task Rhesus monkey (n=4) 2 years, 5.5–5.8 kg	5.62 GHz, pulsed (radar pulse width 2.8 µs, with or without additional high-peak-power 50 ns pulses, at 100 pps 20 min WBA SAR 2, 4 or 6 W/kg Restrained	Decreases in numbers of responses made, rewards gained and in choice reaction time at 4 and 6 W/kg. No additional effect of high-peak-pulses. All changes temporary, only during exposure.	Within-subjects design. SA per pulse above the auditory perception threshold.	D'Andrea, Thomas & Hatcher (1994)
Performance in negatively-reinforced, primate equilibrium platform task Rhesus monkey (n=6) 3 months	UWB pulsed; peak field strength 250 kV/m, pulse band width 100 MHz to 1.5 GHz, 60 pps 2 min WBA SAR 0.000005 W/kg Restrained	Animals exposed twice, 6 days apart: no effects 1 h after exposure compared with day before exposure.	Within-subjects design. Animals previously used in other experiments.	Sherry et al. (1995)
Operant-behaviour performance after in utero exposure Rat: Wistar (n=12) 3 months	900 MHz, GSM 21 days WBA SAR 0.018–0.075 W/kg Free	No effects.	Also discussed in Section 11.3 (Fertility, reproduction, development).	Bornhausen and Scheingraber (2000)
Spontaneous exploration				
Open field behaviour Rat: Sprague Dawley (n=100) 8 weeks	2450 MHz, pulsed, 10 µs pulses at 800 pps, square-modulated at 8 Hz 21.5 h/day, 25 months WBA SAR 0.15–0.4 W/kg Free	Exposed animals less active only in the first of 14 sessions, 6 weeks after start of treatment.	SAR decreased with age. For immune system and cancer see Sections 10.3 and 12.2.2.	Chou et al. (1992)
Behaviour in staircase test following injection ip with chlordiazepoxide (8–32 mg/kg) Mouse: CD1 (n=20) 25–30 g	1.8 or 4.7 GHz, CW 5 min WBA SAR 4, 12 or 36 W/kg Restrained	No effect on number of stairs ascended or on rearing, except at 36 W/kg where effects of 32 mg/kg drug was reduced.	SAR used suggests a thermal effect.	Quock et al. (1994)
Open field behaviour; object recognition task Rat: Fischer 344 (n=16) 4-6 months	900 MHz, GSM 2 h/week, 55 weeks WBA SAR 0.0006 or 0.06 W/kg Free	No effects in open field. Small deficit in recognition memory, independent of SAR.		Nittby et al. (2008b)
Open field behaviour Rat: Wistar (n=12) Adult, 250 g	900 MHz, GSM 15 min Brain SAR 6 W/kg Restrained	No effects immediately or 24 h after exposure.	Head-only exposure. For neurotransmitters see Section 5.3.4.	Mausset-Bonnefont et al. (2004b)
Open field behaviour Rat (n=10) 10–12 weeks	905 MHz 2 h WBA SAR 1.67 W/kg Restrained	5 min after exposure: males: increased activity, decreased anxiety; females: reduced activity, increased anxiety 24 h after exposure: males: decreased activity, increased anxiety; females: increased anxiety.	For hormones see Section 7.3.2	Khirazova et al. (2012)

Open field behaviour Rat: Sprague Dawley (n=6) 2 days	840 MHz 3 h/day, 12 days 60 µW/m^2 Free	Increased freezing behaviour in Water maze in males (mood disturbance). Open field test: less locomotor activity, more grooming in males. No effect in females. No effect on exploratory behaviour.	Also discussed in sections 5.3.1.1. For hormones see Section 7.3.2	Daniels et al. (2009)
Open field test Rat: CR1:CD(SD) (n=4) Adults: 10 weeks + 5 days acclimatization Offspring: 4 days	2140 MHz, WCDMA 20 h/day, from day 7 of gestation to delivery and day 4–21after birth Dams: WBA SAR 0.066–0.093, 0.028–0.04 W/kg; Foetuses/progeny: WBA SAR 0.068–0.146, 0.029–0.067 W/kg Free	No effect in open field test at 5 and 8 weeks of age.	For fertility see Section 11.3.3	Takahashi et al. (2010)
Object recognition				
Object recognition task Rat: Sprague Dawley (n=8–19) 325–400 g	600 MHz CW 20 min WBA SAR 0.1–10 W/kg Restrained	Impaired memory at 9.3 W/kg and above.	Brain temperature increase 2°C at 9.3 W/kg. For gene expression see Section 5.3.5.	Mickley et al. (1994)
Object recognition task Rat: Sprague Dawley (n=15) 325–400 g	600 MHz CW 20 min, 1–2 days WBA SAR 9.3 W/kg With/without naltrexone (0.1, 10 mg/kg) Restrained	No impairment of memory after 2nd exposure. Impairment of memory after 1st exposure reduced after 10 mg/kg naltrexone.	Smaller core temperature increase after 2nd exposure. For gene expression see Section 5.3.5.	Mickley & Cobb (1998)
Object recognition task Rat: Sprague Dawley (n=12) 120 g	900 MHz, GSM 45 min Brain average SAR 1 or 3.5 W/kg Restrained	No effect.	Head-only exposure. Also discussed in 5.3.1.1.	Dubreuil, Jay & Edeline (2003)
Anxiety				
Behaviour in elevated plus-maze Rat: Sprague Dawley (n=12) 3 months	2450 MHz, pulsed (2 µs pulses at 500 pps) 45 min WBA SAR 0.6 W/kg Restrained	No effect with ambient light of 2.5 or 30 lux.		Cosquer et al. (2005a)
Behaviour in open field and elevated plus-maze Rat: Charles Foster (n=12) 4–5 weeks	2450 MHz square wave modulated at 1 kHz 2 h/day, 21 days WBA SAR 0.0098–0.036 W/kg Free	Progressive changes in activity in open field, and open arm entries in plus-maze.	For hormones see Section 7.3.2	Sinha (2008)
Behaviour in open field Rat: Charles Foster (n=5) 9-10 weeks	2450 MHz, square wave modulated 1 kHz 2 h/day, 21 days WBA SAR 0.036 W/kg Free	Higher activity in mobility and rearing, no effect on grooming.	For hormones see Section 7.3.2.	Sinha et al. (2008)

Conditioned avoidance reflex Rat: Wistar (n=10, 15, 18) 200-250 g	4200 MHz, modulated 20 Hz–20 kHz 1 h 15 µV/cm^2 (150 mV/m^2) Free	Learning seems to be affected by EMF, differently in different groups.	Statistical analysis not clear. For neurotransmitter functions see Section 5.3.4.	Shtemberg et al. (2001)
Conditioned avoidance reflex, memory Rat: Sprague Dawley (n=6) 6 weeks, 12 months	900 MHz GSM 15 min Brain SAR 6 W/kg Restrained	No effects.	For hormones see Section 7.3.2	Bouji et al. (2012)

Excluded studies

(Narayanan et al., 2009)

5.3.2 Brain electrical activity

[Please note that due to time constraints this section has not been reviewed and the table is missing.]

In the previous WHO monograph (1993), only a few investigations on brain electrical activity are reported. Exposures to low-levels of RF EMFs were found to alter electroencephalographic (EEG) rhythms in cats, rabbits and rats, but no effects were observed in monkeys and rats in another study.

In the present literature search, only 17 articles on this topic have been recognized. One of them (Sidorenko, 1999) has not been used in this analysis, as exposure levels were not sufficiently controlled and documented. Most of the 16 included articles are focused on EMF effects on EEG activity; other electrophysiological approaches have been used in 3 of them: in vivo extracellular recordings using microelectrodes pre-implanted in the brain under general anaesthesia (Chizhenkova, 2004; Prochnow et al., 2011), or in vitro extracellular field potential recording in hippocampal slices prepared from the brains of the exposed animals (Prochnow et al., 2011).

Thuróczy et al. (1994)(performed two series of experiments in anaesthetized adult F1-hybrid rats (n=5 perexperimental group), primarily aimed at evaluating the effect of MW EMFs on the EEG: whole-body exposure and brain localized exposure experiments. Before, during and after the exposure, electroencephalogram (EEG), rheoencephalogram (REG, as an index of cerebral blood flow), brain tissue DC impedance, and brain temperature were simultaneously recorded. Whole-body exposure for 10 min to 2.45 GHz CW EMF, at a measured average SAR in the brain of 25.1 ± 5.2 mW/g, was associated with a consistent (more than 40%, but significance is not indicated in the article) and persistent (still present 30 min after the end of the exposure) increase in EEG activity (sum of EEG wave frequency bands), and a slight increase in the delta rhythm (0.5–4 Hz). These changes are likely thermal effects, as more than 1°C increase was measured in the brain 1 min after the exposure, and no EEG changes were observed after exposure for 10 min to 2.45 GHz CW EMF at a calculated average SAR in the brain of 8.3 ± 1.7 mW/g, which did not alter the brain temperature. Brain localized exposure for 30 min to 4 GHz CW EMF, at a calculated average SAR in the brain of 42 ± 13.5 mW/g, was associated with a significant (shown in the article) increase in the delta wave band (0.5–4 Hz) only during the exposure period, and a slight (significance is not shown in the article) increase in the theta wave band (4.5–8 Hz) of the EEG. Also these changes are likely thermal effects, as more than 1.5 °C increase was measured in the brain after the exposure, and no EEG changes were observed after exposure for 30 min to 4 GHz CW EMF at a calculated average SAR in the brain of 8.44 ± 2.7 or 16.88 ± 5.4 mW/g, which did not alter the brain temperature. Moreover, brain localized exposure for 30 min to 4 GHz amplitude-modulated (16 Hz) EMF, at a calculated average SAR in the brain of 8.44 ± 2.7 mW/g (not altering the brain temperature), was associated with a significant (shown in the article) increase in the beta wave band (14.5–30 Hz) of the EEG, which persisted 1 min, but not 20 min, after the exposure. Surprisingly, the exposure to the same modulated EMF at twofold intensity (corresponding to a calculated average SAR of 16.88 ± 5.4 mW/g, not altering the brain temperature) was not associated with any change in the beta wave band (4.5–8 Hz) of the EEG.

Vorobyov et al. (1997) performed whole-body exposure experiments in unanaesthetized and unmyorelaxed adult male rats (n=8/experimental group) to study the effect of MW EMFs on EEG activity of symmetric brain areas. The rats were predominantly in a sleepiness state. Averaged EEG frequency spectra were studied before, during and after the exposure to a weak (power flux density of 0.1–0.2 mW/cm) 945 MHz EMF, amplitude-modulated (square form, 20-ms pulse duration) at 4 Hz, applied intermittently (1 min On, 1 min Off) for 10 min. Before the exposure, hemispheric asymmetry in frequency spectra (averaged data for 10 or 1 min) of EEG was characterized by a power decrease in the 1.5–3 Hz range on the left hemisphere and by a power decrease in the 10–14 and 20–30 Hz ranges on the right hemisphere. No differences between control and exposure conditions were found under these routines (10 or 1 min) of data averaging. When the 10-s period averaging of frequency spectra was used, significant elevations of EEG asymmetry in 10–14 Hz range were observed during the first 20 s after four from five onsets of the EMF field. Under neither control nor pre- and post-exposure conditions was this change observed.

To investigate if the effects of MW exposure and those of acupuncture zones stimulation are correlated, starting from previous evidences supporting the involvement of endogenous opioids in both processes, Vorobyov and Khramov (2002) studied in unanesthetized, restrained New Zealand male rabbits (n=3 per experimental group) the effect of the local exposure of various acupuncture zones to MW EMFs (55–75 GHz, 10 mW/cm^2, for 105 min) on frequency spectra of hypothalamic EEG. They found that chances of occurrence of significant ($p<0.05$) changes in the EEG spectra during exposure of "auricular", "cranial" and "corporal" zones versus sham exposures were equal to 31, 21 and 5%, respectively. Exposure of the "auricular" zone was associated with a reduction of the EEG power in narrow bands with central frequencies of 5.3 and 15.9 Hz, and an increase in those of 2.6, 3.2, 6.9, 7.9, 11.5 and 25.6 Hz. Exposure of the "cranial" zone was associated with a reduction of the EEG power in a narrow band with central frequency of 15.9 Hz, and an increase in that of 25.6 Hz. Exposure of the "corporal" zone was associated with negligible changes.

Marino et al. (2003) performed whole-body exposure experiments in ten (unanaesthetized, restrained, five males and five females) New Zealand rabbits to investigate the effect of cellular telephone radiation on brain electrical activity. EEG recording was performed before, during and after exposure to the radiation from a standard cellular telephone (TDMA technology, 824–849 MHz, nominal maximum radiated power 600 mW, but the actual exposure power was not measured) under conditions that simulated normal human use: the antenna was positioned 1 cm above its head. Exposure trials consisted in the application of the field to the rabbit for 2 s, followed by a field free period of 5 s (produced by switching the transmission path of the signal to a distant antenna; a minimum of 60 trials were run. EEG records were studied using a novel analytical method based on a nonlinear model: they were embedded in phase space, and local recurrence plots were calculated and quantified using recurrence quantisation analysis, to permit statistical comparisons between filtered segments of exposed and control epochs from individual rabbits. Significant EEG changes (increases of the randomness) associated with cell phone radiation exposure were found in nine of the ten animals studied; changes began about 100 ms after initiation of application of the field, and lasted about 300 ms. No EEG differences were found between exposed and control EEG epochs in any animal when a) the radiating antenna was repositioned from the head to the chest of the rabbit, or b) the experiment was repeated after the rabbits had been sacrificed (indicating that absorption of radiation by the EEG electrodes could not account for the observed changes).

Chizhenkova (2004)performed chronic neural spike activity recordings in unanaesthetized, restrained rabbits (using microelectrodes pre-implanted in the sensorimotor cortex under general anaesthesia) before, during and after 1-min microwave irradiation (wavelength 37.5 cm, power density 0.2–40 mW/cm^2). They observed shifts in mean values of interspike intervals and in the number of spike bursts associated with EMF exposure. The relation between the intensity of the exposure and the amplitude of the changes was not linear.

Vorobyov et al. (2004) compared the effect of scopolamine (an acetylcholine receptor antagonist) alone and after repeated exposure to low-level (average power flux density of about 0.3 mW/cm^2) 915 MHz EMF, amplitude-modulated (square form, 20-ms pulse duration) at 4Hz (see Vorobyov et al., (1997)) on EEG activity in nine adult male freely moving rats. The exposure to the EMF was intermittent: it consisted of three 10-min exposure sessions (1 min On, 1 min Off) with a 10-min non-exposure period between them. They observed a significant enhancement of the 18–30 Hz EEG rhythms associated with the exposure to EMF alone; this increase did not occur in subsequent sham-exposure experiments (in the same 9 rats) and in 11 radiation-naive animals. In the EMF exposed rats, scopolamine (0.1 mg/kg, subcutaneously) did not cause a slowing in the EEG that was observed in nonexposed rats. The scopolamine-induced effect on EEG in the EMF exposed rats was similar to that of physostigmine (enhancing the acetylcholine level in the brain) in radiation-naive animals.

In order to assess if the degenerated brain is more sensitive to EMFs, Barcal et al. (2005) investigated in anaesthetized Lurcher adult (10-12 week old) mutant mice (model of olivocerebellar degeneration) and in anaesthetized wild type healthy littermates (n=20 animals/experimental group) the effect of 880–890 MHz EMF (10 W power output) exposure for 2 min on cortical and hippocampal EEG activity. The following changes associated with the exposure to EMF were found: a shift to lower frequency components in wild type mice cortical EEG (minor changes were observed in Lurcher mice cortical EEG), and a shift to higher frequency components in hippocampal EEG components in both types of animals. [The absence of a statistical analysis makes the results of this paper questionable.]

Sallam (2006) investigated the effect of the EMF received or emitted by a mobile phone (935.2–960.2 MHz GSM signal, 8.36 mW, 41.8 mW/cm^2 power density) on cortical bioelectrical activity in adult albino rats (n=20 per experimental group), by means of extracellular electrophysiological recording (using a microelectrodes pre-implanted in the parietal cortex under general anaesthesia). Exposure times of 30 s and above (for irradiation received by, i.e. directed to the mobile phone) or 10 s and above (for signals emitted by the mobile phone) were associated with the appearance of a slow potential change defined “Cortical Spreading Depression” (CSD), whose percent of appearance and amplitude increased with the increase of the exposure time. A CSD appeared in 90% of the experiments at 50 s and 35 s exposure times for irradiation received or transmitted by the mobile phone, respectively. Further increases of irradiation time where associated with increases in duration of the slow potential changes, while amplitude and propagation speed remained approximately constant.

In a more recent study (Sallam, Mohamed & Dawood, 2008), the same research group investigated the effect on EEG activity of the exposure to the EMG emitted by the same mobile phone (935.2- 960.2 MHz GSM signal, 8.36 mW, 41.8 mW/cm2 power density) for 1 hour daily for 10 days, in adult albino mice (n=10 per experimental group). EEG recordings were performed before and after exposure to mobile phone EMF, 2% KCl, or both. It was observed a pronounced decrease in slow EEG components associated with all these exposures, which resulted in the appearance of slow potential changes; increases in the amplitude of spindle shaped firings were also observed: increases by about 87%, 17%, and 226% (compared to the control group of animals) were associated with the exposures to mobile phone EMF, 2% KCl, or both mobile phone and 2% KCl, respectively.

Crouzier et al. (2007a) investigated in free moving adult rats (n=10 per experimental group) the effect on EEG activity of the exposure to 1.8 GHz GSM signal (1.2 or 9 W/m2) for 24 hours. A spectral analysis of EEG was also performed and sleep stages were determined. No significant modification associated with EMF exposure was found. Moreover, the same research group (Crouzier et al., 2007b) investigated in 10 free moving adult rats the effect on EEG activity of the exposure to a 2.4 GHz, 1000 Hz pulsed signal (10 W/m^2) for 24 hours. Also in these exposure conditions, no significant modification associated with EMF exposure was observed.

Sinha et al. (2008) investigated in adult male rats (n=5 per experimental group) the effect of chronic exposure (2 hours daily for 21 days) to 1 kHz square wave-modulated 2450 MHz EMF (16.5 μW/cm^2) on EEG activity. EEG data were recorded during slow wave sleep, REM sleep and awake states. The following changes associated with the exposure to EMF were observed: during slow wave sleep, a decrease in percentage power of θ and α activity, and an increase in percentage power of β1 activity; during REM sleep and awake states, a decrease in percentage power of δ activity, and an increase in percentage power of β2 activity. EEG data were also analysed using an artificial neural network able to reveal even mild changes; the lower percentage of pattern identification agreement in the EMF exposed group in comparison to the control group suggests only mild effects of microwave exposure in these experimental conditions.

López-Martín et al. (2009) investigated in adult rats male rats (n=10 per experimental group) the effect of 2 hours exposure to 900 MHz GSM signal EMF (0.26 W, mean SAR in the brain: 0.03–0.05 W/kg) or continuous wave 900 MHz EMF (0.26 W, mean SAR in the brain: 0.26 W/kg) on EEG activity; in parallel, the same exposure protocol was applied in rats of the same age pre-treated with a sub-convulsive dose of picrotoxin. Nonpicrotoxin-treated rats exposed to GSM or to continuous wave did not exhibit any abnormal EEG activity. The EEG of picrotoxin-treated non-exposed rats showed isolated spikes or very short bursts of spikes, but no more than minimal signs of seizure. In these picrotoxin-treated rats, exposure to either GSM or continuous wave were associated with short duration polyspikes, continuous spike-and-wave discharges and seizures; some differences were observed between these changes, depending on the kind of exposure (GSM or continuous wave).

Vorobyov et al. (2010) investigated in freely moving adult rats (n=5 per experimental group) the effect on cortical and hypothalamic EEG activity of repeated (several times per day, for 5 consecutive days) 10 min exposures to low-level (average power flux density of about 0.3 mW/cm^2, 0.7 mW/g average SAR) 915 MHz EMF, amplitude-modulated (square form, 20-ms pulse duration) at 4 Hz, applied intermittently (1 min On, 1 min Off; see Vorobyov et al., 1997, 2004). Exposure to EMF was associated with an increase of β2 activity (17.8–30.5 Hz) in both cortical and hypothalamic EEG. In the first exposure sessions (days 2 and 3) this change was small in the cortex and much more pronounced in the hypothalamus; at day 5 it was very robust in both structures. The increase was observed after the first min of exposure and during the 10-min post-exposure period.

Prochnow et al. (2011) applied 2-GHz UMTS signal EMF (2 or 10 W/kg SAR average in the brain, computer controlled providing blind conditions) for 2 hours, in vivo, on full brain exposed male rats (n=7-10 per experimental group), in order investigate, by means of extracellular field potential recording, the effect on synaptic long-term potentiation (LTP) and depression (LTD) between Schaffer collateral pathway and CA1 neurons (electrophysiological hallmarks for memory formation) in hippocampal slices prepared after EMF exposure. LTP and LTD were similar in hippocampal slices from sham and SAR 2 W/kg-exposed animals, whereas in slices from SAR 10 W/kg-exposed animals the LTP-inducing protocol only induced the early phase of LTP, and the LTD-inducing protocol induced a significantly less pronounced LTD.

Pelletier et al. (2013) investigated in 13 juvenile male rats the effect on EEG activity of 5 weeks of continuous exposure to 900 MHz EMF (1 V/m; estimated SAR: 0.3 mW/kg for rats aged 3 weeks, and 0.1 mW/kg for rats aged 8 weeks), by comparing with EEG data from 11 non-exposed animals. No differences were observed.

Study not used in the analysis

Siderenko (Sidorenko, 1999) [The exposure levels were not sufficiently controlled and documented (description of the exposure: “millimetre waves” “in continuous and impulse modes”)].

5.3.3 Blood-brain barrier integrity

The blood-brain barrier is a dynamic, selectively permeable interface that actively regulates the composition of the cerebrospinal and interstitial fluids that bathe the tissues of the brain and spinal cord. The barrier consists of tight junctions between the endothelial cells which line the blood capillaries of the brain and spinal cord and epithelial cells which line the choroid plexuses of the ventricles of the brain. These characteristics restrict the exchange of molecules through extracellular pathways, enabling them to regulate the entry of high molecular weight or water soluble molecules. Increased passage through the barrier of otherwise impermeant molecules can produce severe and lasting adverse consequences, and may follow insults such as brain trauma, hyperthermia or immobilisation stress. Changes in permeability can be readily detected using immunohistochemical staining of endogenous albumin or using injected tracer dyes.

There has been considerable scientific debate surrounding the possible effect of RF fields on the integrity of the blood-brain barrier. Early studies, some of which were discussed in the previous WHO EHC (1993), reported that exposures of rodents to microwaves at even very low levels could alter the permeability of the barrier and cause leakage of molecules from the blood into the cerebrospinal fluid. However, other studies have not always been able to replicate these results, and consistent changes in permeability were only found using exposures that significantly elevated body temperature (WHO, 1993). This section contains several papers that were published before 1992, but that have not been discussed in the previous WHO EHC (1993). They are considered important, however, and are therefore included here. The present search resulted in 28 papers, of which three were in a language that could not be understood. Two papers were obtained from other sources. That left 27 papers to be extracted.

Neubauer et al. (1990) reported significant changes in blood-brain barrier function following short-term exposure of groups of 3–4 Sprague Dawley rats to pulsed RF fields. Animals under anaesthesia were exposed to pulsed 2450 MHz at whole-body SAR of 1 or 2 W/kg for up to 120 min using a far field exposure system, and uptake of a tracer complex present during the exposure by the capillary endothelial cells of the cortex was monitored using a fluorescence assay. Uptake was significantly increased with exposures at 2 W/kg for 30 min or more ($p<0.05$). It was suggested that the RF field had activated a pinocytotic-like uptake system because the observed effects were attenuated by pre-treatment with colchicine, which is a non-specific blocker of microtubular function.

Lange and Sedmak (1991) exposed Swiss-Cox mice that were previously injected with Japanese Encephalitis Virus (JEV) to continuous 2450 MHz microwaves at levels causing acute hyperthermia. Groups of 20–50 animals were exposed at whole-body SARs of 24 to 98 W/kg for 10 min a day on four days following inoculation, which resulted in short-term increases in rectal temperatures of between 1.5 to 7 °C. An increased lethality was observed ($p<0.05$) and it was suggested that exposure had increased the permeability of the blood-brain barrier and that this increased the uptake of JEV into the brain.

Using an interstitial microwave antenna placed in a lateral groove in the right hemisphere of the skull to cause highly localised exposure of the brain, Moriyama et al. (1991) exposed 21 Sprague Dawley rats to continuous 2450 MHz fields for 30 or 60 min at local brain SARs of up to 400 W/kg [these values were determined using temperature measurements; the volume is not specified]. They histologically observed increased permeability of the blood-brain barrier to horseradish peroxidase (HRP) only when the exposures had a hyperthermic effect, which did not occur when they used a water-cooled antenna.

A research group from Lund University has been actively investigating the effects of exposure to low-level 915 MHz GSM fields on the integrity of the blood-brain barrier for many years. Several of these publications suffered from a lack of adequate description of experimental data, including dosimetry, and are therefore listed under 'Studies not included in the analysis'. Some of the studies also included the analysis of so called 'dark neurons', neurons that were darkly stained in the procedure used by these investigators. The dark neurons were considered to be dying, and thus indicative of neuronal damage. That part of these studies is more extensively discussed in Section 8.2 (Animal studies on neurodeneration).

Belyaev et al. (2006) explored the effects of exposure to pulsed fields on gene expression profiles in the cerebellum of rats following exposure to 915 MHz GSM signals for 2 h at a whole-body SAR of 0.4 W/kg. Four Fisher 344 rats were exposed and a similar group received sham treatment. Immediately after exposure the brains were removed and the activity of 8800 genes was measured using a microarray. They found a modest up-regulation of 11 genes and one was down-regulated. There was little obvious commonality in function between these genes, but of particular interest here was the 1.5-fold increase ($p<0.0025$) in one gene, solute carrier family 6 (neurotransmitter transporter), member 6 (SLc6a6), that was ascribed a role in blood-brain barrier function. [This is an exploratory study with a low number of animals included and needs to be follow-up. It is also discussed in Sections 7.2 Neuroendocrine and 12.2.1 Genotoxicity.]

In a study measuring more directly effects on the blood-brain barrier, Eberhardt et al. (2008) reported that exposure of Fisher 344 rats (8 per group) to 915 MHz GSM signals for 2 h at whole body SARs of 0.12–120 mW/kg was associated with increased albumin extravasation at 14 days after exposure ($p=0.02$) and no effect on the occurrence of darkly stained neurons; at 28 days after exposure no effect was seen on albumin, but the occurrence of darkly stained neurons was increased ($p=0.02$). There was an indication of an inverse dose-response relationship, although no explanation could be offered for this result. [The quantification of the pathological effects in terms of numbers of dark neurons was very subjective and the numbers of brain slices scored per animal were not given. Also large weight variation of the animals (164–446 g) should be noted.]

To complement the previous studies of the Lund group, Nittby et al. (2009) examined the effects of exposure to GSM signals on the blood-brain barrier after an interval of 7 days. Groups of 8 (exposed) or 16 (sham) Fisher 344 rats were exposed to 915 MHz GSM signals at whole body SARs of 0.12–120 mW/kg and albumin extravasation and the occurrence of darkly stained neurons were assessed. It was reported that exposure overall was associated with an increased albumin leakage, although only values for 12 mW/kg were significantly different from their control values ($p=0.007$).

In contrast to the other studies from the Lund group using shorter exposures, Grafström et al. (2008) reported no increase in albumin extravasation (or other histopathological changes) following long-term, low-level exposure of Fisher 344 rats to a GSM 900 MHz signal. Animals were exposed at an average whole-body SAR of 0.6 or 60 mW/kg (n=16 each) for 2 h once per week for 55 weeks in a TEM cell, although the SARs had decreased to 0.4 and 40 mW/kg at the end of the exposure period, to correct for the growth of the animals. [The quantification of the pathological effects in terms of numbers of dark neurons was very subjective and the numbers of brain slices scored per animal were not given.]

Overall, this series of studies from Lund University provide some provocative and intriguing data, but despite regularly reporting field-related changes, they failed to provide compelling evidence for a consistent effect on blood-brain barrier function, largely because of omissions or unanswered questions regarding methodology or analysis. Nevertheless, the potential importance of these results prompted three independent attempts to replicate the key findings. These investigations used the same strain of rat, similar exposure parameters, and two used the same type of exposure system as used previously. They also avoided some of the technical limitations in the original studies, which included using rats of both sexes and widely different ages, and poorly characterized dosimetry. In addition, the new studies habituated their animals to their exposure systems to reduce any effects of stress associated with exposure.

McQuade et al. (2009) exposed male Fisher 344 rats (n=24–42 per group) for 30 min to 915 MHz RF EMF, either continuous or pulsed at 16 or 217 Hz, over a very wide range of whole-body SARs (from 0.0018 to 20 W/kg). No increases in albumin extravasation were found at any intensity compared to sham exposed or cage-control animals. The lack of albumin extravasation at 20 W/kg was attributed to an insufficient temperature rise in the brain. Positive controls (infused urea or RF-induced high body temperature (43 °C) caused massive staining indicative of albumin extravasation.

Another replication of the Lund studies was carried out by Masuda et al. (2009). This study aimed to determine, using improved staining techniques, whether albumin leakage and dark neurons were present in rat brains 14 and 50 days after a single 2-h exposure to a 915 MHz EMF. Groups of 8 male Fisher 344 rats (12 weeks old) were exposed at an whole-body SAR of 0, 0.02, 0.2 or 2 W/kg in a TEM cell following the same protocol as the Lund studies. In this study the dose received by each rat was assessed in real time during the experiment through the power balance method. The SAR data showed rather large variations, mainly due to movement of the animal within the plastic holder used for the exposures. No effect on albumin extravasation was observed in the exposed groups.

Finally, Poulletier de Gannes et al. (2009) exposed 12-weeks old male Fisher 344 rats in groups of 8 at SAR levels averaged over the brain of 0.14 and 2.0 W/kg. Sham and cage-control animals were included, as well as positive control groups (n=10). The animals were restrained in order to allow local exposure of the brain, which was carried out using an exposure apparatus consisting of a printed loop antenna, so this differs from the Lund studies. The full dosimetry of this study was published in a previous paper (Leveque et al., 2004), that included a comparative analysis of human and rat brain exposure. The results were collected at 14 and 50 days after exposure. Albumin leakage was only reported in the positive controls. [This study thus failed to replicate the results of the Lund studies. Although the exposure conditions (restrained, head-only exposure) differ from those of the Lund group (whole-body exposure in a TEM cell), the dosimetry in this study is more carefully performed and the highest exposure level was 10 times higher than the maximum level in the Lund studies.]

Using a head-only exposure system, Fritze et al. (1997a) exposed Wistar rats to 900 MHz GSM signals for 4 h at local SARs in the brain of 0.3 or 1.5 W/kg, or to a 900 MHz continuous signal at 7.5 W/kg (n=10; sham and cage-controls: n=20). The leakage of albumin across the blood–brain barrier was examined using immunohistochemical staining either at the end of exposure or 7 days later. Small increases in permeability were observed in all groups immediately after exposure, but this only reached significance with the CW exposure at 7.5 W/kg ($p<0.05$). No increases in permeability were observed 7 days after exposure, and there were no indications of neuronal damage.

Tsurita et al. (2000) exposed the heads of Sprague Dawley rats to a pulsed 1439 MHz TDMA signal for 1 h a day, 5 days a week, for 2 or 4 weeks using a carousel exposure system (n=6 per group). The peak SAR in the brain was 2 W/kg. Permeability was assessed using immunohistochemical staining for endogenous albumin and after injection with Evans blue dye immediately after the last exposure. Exposure had no observable effect on permeability, but no quantitative data are provided, only the description of observations. Exposure also did not have any effect on body weight or on the numbers of Purkinje cells in the cerebellum. [No statistical analysis is provided, but the absence of effect is obvious from the graphs..] As positive controls, both local cold injury of the skull or 2 h irradiation at 20 W/kg produced increases in leakage of albumin.

Finnie et al. (2001) exposed 30 C75BL/6NTac mice to 898 MHz GSM signals for 60 min at whole-body SAR of 4.0 W/kg using a purpose-built, whole-body exposure system. This system consisted of a cylindrical parallel plate with the animals restrained in clear acrylic tubes arranged radially around a dipole antenna. Exposure had no significant effect on permeability to endogenous albumin, as assessed using immunohistochemical staining immediately after exposure. Where leakage had occurred, it was mainly confined to the leptomeningeal blood vessels which have no recognised blood-brain barrier.

A similar pattern of responses was reported by the same group (Finnie et al., 2002; Finnie & Blumbergs, 2004) using long-term, repeated exposures in the same exposure system. In this study, groups of 23–39 C75BL/6NTac mice were exposed to 900 MHz GSM signals for 60 min a day, 5 days a week for 104 weeks at whole body SARs of 0.25, 1, 2 or 4 W/kg. Small numbers of albumin extravasations were observed in the brains of exposed, sham-exposed and freely moving control animals; statistical analysis was not considered necessary.

A further analysis of material from these two studies (Finnie et al., 2001; 2002) was presented in Finnie et al. (2009a), in which an effect on vascular permeability in the adult mouse brain was studied by measuring the water channel protein, aquaporin-4 (AQP-4), using immunohistochemistry. The amount of immunostaining was assessed independently by two pathologists and after neither the acute not the protracted exposure an increase in AQP-4 was found compared to sham-exposed or cage-control animals.[Quantitative data from the assessment were not presented.]

Kuribayashi et al. (2005) investigated the effects of repeated exposure to pulsed 1439 MHz TDMA signals on the blood-brain barrier function in groups of 5 immature (4 week old) and young (10 week old) Fisher 344 rats. Permeability to dextran was measured quantitatively, as was the expression of three genes which are associated with barrier function (regulating transmembrane drug transport, water homeostasis and tight junction integrity). Exposure of the head at 2 or 6 W/kg for 90 min per day for 6 days per week for 1 or 2 weeks had no effect on either permeability or gene expression at either age. In addition, no histopathological changes, such as gliosis or degenerative lesions, were seen in the brain.

Cosquer et al. (2005b) assessed the effects of microwaves on barrier function using a rat behavioural model. The performance of Sprague Dawley rats in a win-shift radial arm maze task was measured following daily exposure for 45 min to a pulsed 2450 MHz field at a whole-body SAR of 2 W/kg and injection of scopolamine methylbromide (groups of 12 animals were used). This derivative of scopolamine only poorly crosses the blood-brain barrier and exerts minimal effects on task performance. Injection of the derivative either before or after exposure had no significant effect on task performance, suggesting that the permeability of the blood-brain barrier had not been affected. In addition, exposure was not associated with increased leakage of albumin as measured using Evans blue dye.

Finnie et al. (2006b) studied the effects of daily exposure to a 900 MHz GSM signal throughout gestation on the blood-brain barrier in foetal BALB/c mice. Ten pregnant mice were exposed from day 1 to day 19 of gestation for 1 h per day at a whole-body SAR of 4 W/kg. When examining 30 foetuses immediately prior to birth, no effects on the permeability to endogenous albumin were seen in any of the regions of the brain examined, including the cerebral cortex, thalamus, basal ganglia, hippocampus, cerebellum, midbrain and medulla. A second study investigated the effects of exposure on neonatal BALB/c mice (Finnie et al., 2006a). Here, 10 newly born animals were exposed for 1 h per day for the first 7 days to 900 MHz GSM fields at a whole-body SAR of 4 W/kg. No effects were seen on the permeability of the blood-brain barrier to albumin.

As part of a larger behavioural study, Kumlin et al. (2007) found that repeated exposure of immature Wistar rats to 900 MHz GSM signals had no effect on extravasation of injected Evans blue dye. Groups of 18 freely-moving animals were exposed at a whole body SAR of either 0.3 or 3.0 W/kg for 2 h per day, 5 days per week from 3 to 8 weeks of age.

One group has used the closed cranial window model to observe the effects of acute and sub-chronic exposure to RF fields on cerebral microcirculation directly in Sprague Dawley rats (Masuda et al., 2007a; b). In these studies, neither single, nor repeated exposures over 4 weeks to pulsed TDMA signals produced any significant effects on blood-brain barrier permeability as measured using injections of two types of fluorescent dyes in groups of 4–6 animals. The heads of the animals were exposed to 1438 MHz TDMA signals for either 10 min at average SARs in the brain of 0.6, 2.4 or 4.8 W/kg, or for 60 min a day, 5 days per week for 4 weeks at 2.4 W/kg.

Sirav and Seyhan (2009) exposed groups of 8–9 anaesthetised male and female Wistar rats to continuous 900 or 1800 MHz RF EMF at 12–13 V/m for 20 min. After exposure to both types of field they found an increased blood-brain permeability to Evans blue dye, which binds to albumin, in males only ($p<0.01$). Similar results ($p<0.05$) were found in a follow-up study that used lower power densities (Sirav & Seyhan, 2011), where the average SARs in the brain were calculated to be 4.3 mW/kg at 900 MHz and 1.5 mW/kg at 1800 MHz. Eight rats were exposed to each condition. [It is possible that the changes seen in the exposed males are attributable to a depressed value for the sham-exposed controls.]

Studies non included in the analysis

Persson et al. (1992) observed increased leakage of endogenous albumin in the brains of Fisher 344 rats that had been exposed to either continuous or pulsed fields, with greater amounts of leakage seen using fields modulated at 8–125 Hz. Animals were exposed using a tuned transverse electromagnetic transmission line (TEM) cell. [This report suffers from a number of limitations, with insufficient description of the experimental and exposure protocols used and a lack of dosimetry.]

In a more recent paper from the same group, Salford et al. (2003) reported that single, brief exposure of juvenile Fisher 344 rats to 915 MHz GSM signals for 2 h at SARs of 0.002, 0.02 or 0.2 W/kg was associated with long lasting increases in blood–brain barrier permeability to albumin (measured 50 days after exposure) and neuronal damage throughout the brain (indicated by darkly staining neurons; discussed in Section 8.2). Quantification of albumin leakage was not performed. [There are a number of caveats with this study. These include the wide age range of the rats used (12–26 weeks) and insufficient descriptions of the experimental procedures, exposure protocols and dosimetry in the TEM cells used. The dosimetry is not described in Salford et al. (2003), but in Martens et al. (1993). However, SAR variations due to animal size, position and age were not dosimetrically analysed.The quantification of the pathological effects in terms of numbers of dark neurons was very subjective and the numbers of brain slices scored per animal were not given.]

Table 5.3.4. Effects of exposure to RF fields on blood-brain barrier function in animals

Endpoint, animals, number per group, age or weight at start	**Exposure: source, schedule, level, freely moving or restrained**	**Response**	**Comments**	**Reference**
Uptake of rhodamine-ferritin (Rh-F) tracer complex by capillary endothelial cells in cortex Rat: Sprague Dawley (n=3–4) 200–300 g	2450 MHz, pulsed (10 µs pulses at 100 pps) 5–120 min WBA SAR 1, 2 W/kgAnaesthetized	Increased uptake of tracer after 30 min or longer at 2 W/kg. Uptake reduced by pre-treatment with colchicine (i.v. injection 0.4 mg/kg).	Animals anaesthetised with sodium pentobarbital (30 mg/kg i.p.).	Neubauer et al. (1990)
Lethality following inoculation i.p. with Japanese Encephalitis Virus (JEV) Mouse: Swiss-Cox (n=20–50) 20–25 g	2450 MHz, CW 10 min on day 1,2, 4 and 8 after JEV WBA SAR 24–98 W/kg Free	SAR-dependent increase in lethality and mean time to death. Response not altered by pre-exposure to 2450 MHz. No effect of RF exposure alone.	Thermal response: rectal temperatures increased by 1.5–7.2 ^{o}C after exposure. Similar increase in lethality using 60 min exposures to elevated CO_2 levels.	Lange and Sedmak (1991)
Staining of injected horseradish peroxidase (HRP, 1 mg/20 mg) in brain by histochemistry Rat: Sprague Dawley (n=21) Age or weight not reported	CW 2.45 GHz using interstitial antenna placed in lateral groove in right hemisphere of skull 30, 60 min Local SAR in brain approx. 100–400 W/kg, determined by temperature measurements Anaesthetized	Increased HRP extravasation with local brain temperatures of 42.5 ^{o}C for 60 min, and above 44.4 ^{o}C for 30 min. No effects when using water-cooled antenna.	Thermal response only. Left hemisphere of animal served as own control. Animals anaesthetised with sodium pentobarbital (50 mg/kg i.p.).	Moriyama et al. (1991)
Gene expression profiles in cerebellum by RNA microarray immediately after exposure Rat: Fischer 344 (n=4) 12 weeks	915 MHz GSM 2 h WBA SAR 0.4 W/kg Free	11 genes up-regulated 1.34–2.74 fold , one gene down-regulated 0.48-fold, SLc6a6 increased 1.56-fold .	Small group sizes. Also discussed in 7.2 Neuroendocrine and 12.2.1 Genotoxicity.	Belyaev et al. (2006)

Staining for endogenous albumin in brain by immunohistochemistry, dark neurons by cresyl violet 14 or 28 days after exposure Rat: Fischer 344 (n= 8 or 16) 164–446 g	915 MHz GSM 2 h WBA SAR 0.12–120 mW/kg Free	Increase in albumin extravasation after 14 days, but not after 28 days; increase in dark neurons only after 28 days.	No clear dose-response, lower SARs tended to give larger responses. Subjective quantification of dark neurons. Numbers of brain slices scored per animal not given.	Eberhardt et al. (2008)
Staining for endogenous albumin in brain by immunohistochemistry, dark neurons by cresyl violet 7 days after exposure Rat: Fischer 344 (n= 8 or 16) 169–293 g	915 MHz GSM 2 h WBA SAR 0.12–120 mW/kg Free	Albumin extravasation only at 12 mW/kg, no effect on dark neurons.	No data values presented. Subjective quantification of dark neurons. Numbers of brain slices scored per animal not given.	Nittby et al. (2009)
Staining for endogenous albumin in brain by immunohistochemistry, 5–7 weeks after exposure Rat: Fischer 344 (n= 16) 200–545 g (males) 200–304 g (females)	915 MHz GSM 2 h once per week, 55 weeks WBA SAR 0.6, 60 mW/kg, corrected for growth Free	No effect.	Same animals as used in Nittby et al. (2008a).	Grafström et al. (2008)
Staining for endogenous albumin in brain by immunohistochemistry, 10–15 min after exposure Rat: Fischer 344 (n= 24–42) 250–300 g	915 MHz CW or pulsed at 16 or 217 Hz 30 min WBA SAR 1.8 mW/kg to 20 W/kg Free	No effects on albumin extravasation.	Positive controls (infused urea or RF-induced high body temperature (43 ^{o}C) caused massive staining.	McQuade et al. (2009)
Staining for endogenous albumin by immunohistochemistry, dark neurons by cresyl violet, haematoxylin and eosin in brain 14 or 50 days after exposure Rat: male Fischer 344 (n= 8) 12 weeks	915 MHz GSM 2 h WB SAR 0.02, 0.2, 2.0 W/kg Free	No effect.	Injection of kainic acid (10 mg/kg) or cold injury (positive controls) caused large effects.	Masuda et al., (2009)
Staining for endogenous albumin by immunohistochemistry, dark neurons by cresyl violet, Fluoro-Jade B, apoptosis by NeuroTACS II in brain 14 or 50 days after exposure Rat: Fischer 344 (n= 8 or 10) 12 weeks + 1 week acclimatization	915 MHz GSM 2 h Brain local SAR 0.15, 2 W/kg	No effect.	Acute cold injury and TACS-Nuclease (positive controls) caused large effects.	Poulletier de Gannes et al. (2009)
Staining for endogenous albumin in brain by immunohistochemistry immediately or 7 days after exposure Rat: Wistar (n= 10 or 20) 250-300 g	900 MHz, CW or GSM 4 h Brain SAR GSM: 0.3, 1.5 W/kg; CW: 7.5 W/kg Restrained	CW: Modest increase in albumin permeability seen only immediately after exposure at 7.5 W/kg. No neuronal damage. GSM: no effect.	Small changes in permeability in rats immobilised for 4 h, and after cold injury (positive control).	Fritze et al. (1997a)

Staining for endogenous albumin in brain by immunohistochemistry or injected Evans blue dye Rat: Sprague Dawley (n=6) Age or weight not provided	1439 MHz TDMA 1 h per day, 10, 20 days Peak brain SAR 2.0 W/kg Restrained	No effects on albumin or Evans blue permeability, but responses not quantified. Numbers of Purkinje cells in granular layer of cerebellum not changed.	Modest group sizes. No statistical analysis. Cold injury and single 2 h exposure at 20 W/kg used as positive controls.	Tsurita et al. (2000)
Staining for endogenous albumin in brain by immunohistochemistry immediately after exposure Mouse: C75BL/6NTac (n=10 (controls) or 30 (exposed)) 8 weeks	898 MHz GSM 1 h WBA SAR 4.0 W/kg Restrained	No effects on albumin permeability: any leakage mainly confined to leptomeningeal vessels.	Clostridium toxin (positive control) increased permeability.	Finnie et al. (2001)
Staining for endogenous albumin in brain by immunohistochemistry within 2 h after exposure Mouse: C75BL/6NTac (n=23, 37 or 39) 8 weeks	900 MHz GSM 1 h per day, 5 days per week, 104 weeks WBA SAR 0.25, 1.0, 2.0, 4.0 W/kg Restrained	No effects on albumin permeability; formal statistical analysis not considered necessary.	Clostridium toxin (positive control) increased permeability.	Finnie et al. (2002), Finnie and Blumbergs (2004)
Expression of aquaporin-4 (AQP-4) and endogenous albumin in brain by immunohistochemistry after exposure Mouse: C75BL/6NTac (n=10 or 39) 8 weeks	900 MHz GSM 1 h or 1 h per day, 5 days per week, 104 weeks WBA SAR 4.0 W/kg Restrained	No effect.	No quantitative data presented. Clostridium toxin (positive control) increased AQP-4 expression and albumin permeability. Same samples as Finnie et al. (2001; 2002).	Finnie et al. (2009a)
Staining for FITC-dextran in brain by immunohistochemistry, and for expression of p-glycoprotein, AQP-4 and claudin-5 by RT-PCR after exposure Rat: Fischer 344 (n= 5) 4 or 10 weeks	1439 MHz TDMA 90 min per day, 6 days per week, 1 or 2 weeks Head SAR 2, 6 W/kg Restrained	No effect.	Modest group sizes. Injection of 1,3-dinitrobenzene (positive control) increased permeability of albumin and decreased protein levels of 3 genes.	Kuribayashi et al. (2005)
Performance in a 12-arm radial maze and injection i.p. of scopolamine methylbromide (MBR, 0.5 mg/kg) and staining for albumin by injected Evans blue dye in brain before or after exposure Rat: Sprague-Dawley (n=12) 270–320 g	2450 MHz pulsed; 2 μs pulses at 500 pps 45 min per day, 10 days WBA SAR 2.0 W/kg, brain SAR 3.0 W/kg	No effect on performance with injection of MBR 2 min before or 1 min after exposure. No increased leakage of albumin.	Injection with Scopolamine hydrobromide (positive control) caused significant deficits in performance. Cold injury (positive control) increased permeability.	Cosquer et al. (2005b)

Staining for endogenous albumin in foetal brain by immunohistochemistry after exposure on day 19 of pregnancy Mouse: BALB/c (n=30, from 10 dams) Foetal	900 MHz GSM 1 h per day from day 1–19 of pregnancy Maternal WBA SAR 4 W/kg Dams restrained	No effect.	Subcutaneous injection of cadmium chloride (2 mg/kg) at birth (positive control) increased permeability.	Finnie et al. (2006b)
Staining for endogenous albumin in brain by immunohistochemistry after exposure on postnatal day 7 Mouse: BALB/c (n=10) 1 day	900 MHz GSM 1 h per day from postnatal day 1–7 WBA SAR 4 W/kg Free, but motionless during exposure	No effects.	Subcutaneous injection of cadmium chloride (2 mg/kg) at birth (positive control) increased permeability.	Finnie et al. (2006a)
Staining for injected Evans blue dye in brain after exposure Rat: Wistar (n=18) 8 weeks	900 MHz GSM 2 h per day, 5 days per week, 5 weeks WBA SAR 0.3, 3.0 W/kg	No effect.	Used 35 µm coronal sections.	Kumlin et al., (2007)
Leakage of injected sodium fluorescein or FITC-dextran, by fluorescence microscopy via closed cranial window (CCW) for 20 min immediately after exposure Rat: Sprague Dawley (n= 4 or 6) 364–408 g	1439 MHz TDMA, 6.7 ms pulses at 50 pps head-mainly exposure 10 min Brain SAR 0.6, 2.4, 4.8 W/kg Anaesthetized	No effects on permeability, pre-exposure values used as controls.	CCW implanted at least one week prior to exposure. Animals anaesthetised with ketamine (100 mg/kg) and xylazine (10 mg/kg) and with pentobarbital (25 mg/kg) throughout.	Masuda et al. (2007b)
Leakage of injected sodium fluorescein or FITC-dextran, by fluorescence microscopy via CCW for 30 min, prior to exposure, 24 h after completing exposures Rat: Sprague-Dawley (n= 3 or 6) 368–440 g	1439 MHz TDMA, 6.7 ms pulses at 50 pps, head-mainly exposure 60 min per day, 5 days per week, 4 weeks Brain SAR 2.4 W/kg Anaesthetized	No effects on permeability.	CCW implanted at least one week prior to exposure. Animals restrained during exposure, anaesthetised during observation with ketamine (100 mg/kg) and xylazine (10 mg/kg) and with pentobarbital (25 mg/kg) .	Masuda et al. (2007a)
Staining for injected Evans blue dye measured by spectrophotometry in whole brain immediately after exposure Rat: Wistar (n= 8 or 9) 192–310 g	900 or 1800 MHz CW 900 MHz: 13. 5 V/m 1800 MHz: 12.6 V/m 20 min Anaesthetised	Increased staining in males at both frequencies, no effect in females.	Animals anesthetised with ketamine (45 mg/kg) and xylazine (5 mg/kg).	Sirav and Seyhan, (2009)

Staining for injected Evans blue dye measured by spectrophotometry in brain immediately after exposure Rat: Wistar (n= 9) 193–284 g	900 or 1800 MHz CW 20 min WB SAR 4.3 (900 MHz), 1.5 mW/kg (1800 MHz) Anaesthetised	Increased staining in males at both frequencies, in whole brain or cerebellum only, no hemispheric differences. No effect in females.	Animals anesthetised with ketamine (45 mg/kg) and xylazine (5 mg/kg)	Sirav and Seyhan, (2011)

5.3.4 Neurotransmitter function

In the previous RF EHC (1993) reference was made to three studies of Lai and coworkers, leading to the conclusion that RF might act as a mild stressor and more research would be needed to confirm this. No general conclusion on the effect of RF EMF on neurotransmitters was made.

The present search resulted in 28 papers, of which 12 were in a language that could not be understood. That left 16 papers to be extracted.

In a series of papers, Lai and co-workers investigated the effects of exposure to pulsed 2450 MHz fields (2 µs pulses, 500 pulses per second) on the brain of Sprague Dawley rats. The exposure times and schedules varied, but the exposure level was always the same: a whole-body SAR of 0.6 W/kg, that resulted in a SAR in the brain of 0.5–2 W/kg in the free roaming rats. [It is noted in Section 5.3.1 that the pulses used in these studies resulted in peak SARs of 600 W/kg and a specific absorption (SA) of 1.2 mJ/kg during one single pulse, which is around the threshold for auditory perception of short pulses (< 30 µs). It is thus the question whether the effects of the RF exposure can be attributed to a direct effect on the brain, or an indirect effect resulting from microwave hearing.]

In the first experiment (Lai et al., 1990) the animals (n=9–12) were exposed for 45 minutes and immediately killed afterwards. The authors measured a decrease in the sodium-dependent choline uptake in the frontal cortex and hippocampus ($p<0.01$). No change was observed when the corticotropin-releasing factor antagonist α-helical-$CRF_{9\text{-}41}$ was administered before the exposure. This indicates an effect of the pulsed RF EMF on the central cholinergic system in the brain through activation of corticotropin-releasing factor. [This study has not been discussed in WHO (1993) and is therefore included here.]

In a follow-up study, Lai et al. (1992b) subjected rats in groups of 8–9 to an identical treatment as in the previous study to investigate the effect of opioid-receptor antagonists on the cholinergic response. They again observed a decrease in the sodium-dependent choline uptake in the frontal cortex and hippocampus ($p<0.01$). No effect of administration of µ-, δ- or κ-receptor blockers before the RF exposure was observed in the cortex, with the choline uptake still being reduced ($p<0.01$). In the hippocampus, however, after administration of each of the three receptor blockers, RF exposure did not result in a decreased choline uptake. This means that in the hippocampus endogeneous opioids mediate the cholinergic effect of the pulsed RF EMF exposure, but this mechanism is not present in the cortex.

In a third study, Lai et al. (1992a) investigated the effect of a single or ten daily 45-min exposures to the same type of pulsed RF field on benzodiazepine receptors in the rat brain, using groups of 6–9 rats. They observed an increased number of benzodiazepine receptor sites ($p<0.02$) in the cortex after single, but not after repeated exposure, and no effect in the hippocampus and cerebellum. The affinity of the receptors was not changed. Since benzodiazepine receptors are involved in anxiety responses, the authors hypothesize that the RF exposure might induce a stress response, to which adaptation occurs after multiple exposures.

In a further study, also discussed in Section 5.3.1 Cognitive performance, Lai, Horita and Guy (1994) observed decreased learning after a single 45-minute exposure to the pulsed RF field ($p<0.01$) (n=8 rats per group). This effect was not observed when the cholinergic agonist physostigmine or the opiate antagonist naltrexone were administered before the RF exposure, while the peripheral opiate antagonist naloxone methiodide did not influence the effect of RF exposure on learning. This indicates that both central cholinergic and opioid neurotransmitter systems are involved in an effect of pulsed RF EMF on learning ability. [As stated in Section 5.3.1, there were differences in performance between the groups at the start of the task, indicating possible differences in anxiety or motivation (as noted by (Cassel et al., 2004))].

In a study specifically focussing on the action of opioids in the hippocampus, Lai et al. (1996) reproduced in groups of 8 rats the decrease in sodium-dependent choline uptake in the hippocampus ($p<0.01$). When the μ-opioid-receptor blocker β-funaltrexamine was administered before the RF exposure, the effect was not observed. This confirms the role of the opioid system in the response to pulsed RF EMF.

Inaba et al. (1992) exposed groups of 5 Wistar rats to 2450 MHz for 1 hour at a power density of 5 or 10 mW/cm^2 (50 or 100 W/m^2), i.e. 5 or 10 times the ICNIRP exposure level. At the lower level they measured an increase in colonic temperature of 2.3 °C and no effect on noradrenaline, dopamine, dihydroxyphenyl acetic acid (DOPAC, a metabolite of dopamine) and serotonin in the brain. Exposure to the higher power level resulted in a temperature increase of 3.4 °C and a decrease of noradrenaline in the hypothalamus ($p<0.05$). No effects were observed on dopamine and serotonin, but an increase in DOPAC was found in the pons and the medulla oblongata after exposure to the higher power level ($p<0.01$) and an increase in 5-HIAA (5-hydroxyindoleacetic acid, a metabolite of serotonin) was found in the cortex after both exposure levels ($p<0.05$). [All statistical analyses were corrected for multiple exposures. It is not completely clear whether the controls were sham or cage controls: the authors mention that they 'were not exposed to microwaves'. Most likely this means that they were sham exposed and had been trained, as the RF exposed animals, to stay in the holders used to immobilize the animals during exposure. This was obviously a thermal experiment and thus not necessarily relevant for normal human exposure situations.]

Mason et al. (1997) exposed Sprague Dawley rats to a pulsed 5.02 GHz EMF for 40 minutes (n=7–8). The SAR to the left side of the brain was 40 W/kg and to the right side 29 W/kg. They measured an increase in the neurotransmitters aspartic acid, serine and glycine in the hypothalamus and the caudate nucleus ($p<0.05$), but no effect on glutamic acid and glutamine. [This was obviously a thermal experiment. Since the animals were anaesthetized, this could have influenced the responses.]

Shtemberg et al. (2001) conditioned animals to avoid the naturally sought dark environment in a space with an open illuminated and closed dark section. Entering the dark section evoked a painful stimulus in another rat (kept outside the testing space) which resulted in a stress response (vocal and movement) that was percepted by the tested rat. This resulted in three groups with different natural levels of stress conditioning. These groups were exposed and directly after exposure the levels of noradrenaline, dopamine, adrenaline, serotonine and 5-hydroxyindolacetic acid (5-HIAA) were determined in the motor cortex of the brain. In the group with the highest level of exitability an increased level of dopamine and serotonin was observed ($p<0.01$), no changes in any parameter were observed in the group with the lowest level of exitability, while in the intermediate group the level of 5-HIAA was changed. [The direction of this change is not given, nor a p-value. This study is also discussed in Section 5.3.1 (Cognitive function).]

Mausset et al. (2001) exposed groups of 12 Wistar rats to a 900 MHz RF field, GSM modulated or CW, for 2 hours. The SARs in the brain were 4 W/kg for the GSM signal and 32 W/kg for the CW field. They used immunohistochemistry and image analysis to detect γ-aminobutyric acid (GABA, the chief inhibitory neurotransmitter) in the cerebellum. Exposure to the GSM signal did not result in an effect on GABA in the cerebellum as reflected in the mean optical density, but a 16% reduction in the area of stained processes of Purkinje cells ($p<0.01$) was observed. With CW exposure 28% reduction of GABA in the molecular layer, 32% in the Purkinje layer and 27% in the granular layer (all $p<0.001$) were measured. Also a 17% decrease in the area of stained processes in the Purkinje layer ($p<0.01$) and a 13% decrease in the stained area in the molecular layer ($p<0.05$) were observed. For the CW exposure thermal effects could not be excluded. [The number of microscopic fields analysed per animal, 6 per layer, was rather small.]

Mausset-Bonnefont et al. (2004a) exposed Wistar rats (n=4–18) to a 900 MHz GSM signal for 15 min, with an SAR in the brain of 6 W/kg. They then analysed the binding properties of various excitatory and inhibitory neurotransmitter receptors and transporters in three parts of the brain: the cortex, striatum and hippocampus. For the excitatory N-methyl-D-aspartate receptors (NMDAR) they observed a 10% decrease of binding activity in the cortex ($p<0.01$), and a 15% decrease in the striatum ($p<0.05$). They also found a reduced expression of NMDAR subunits on the postsynaptic membrane: the NR1 subunit was reduced in the cortex ($p< 0.05$), the NR2A subunit in the cortex ($p<0.01$) and the hippocampus ($p<0.001$), and the NR2B subunit in the striatum ($p<0.05$). Binding of the inhibitory GABA receptors was decreased by 15% in the hippocampus ($p<0.001$), and that of the modulatory dopamine transporters by 20% in the cortex ($p<0.05$), while these were increased by 30% in the striatum ($p<0.001$). They also observed an increased hypertrophy and/or hyperplasia of astrocytes ($p<0.001$–0.05). These changes in neurotransmitter function obviously had no effect on behaviour, since behavioural test did not reveal any differences between real and sham-exposed groups (see Section 5.3.1). [With the SAR of 6 W/kg in the brain, mild thermal effects can not be excluded.]

Hata et al. (2005) used a 1439 MHz TDMA signal for a 4-h exposure of Sprague Dawley rats. The brain SAR was 7.5 W/kg and the whole-body SAR 1.9–2.0 W/kg. The main purpose of the study was to investigate the influence of RF EMF exposure on melatonin synthesis, and therefore the level of serotonin in the pineal gland, as a precursor of melatonin, was also determined. The 64 animals were exposed in the dark, and exposure to light was included as a positive control (n=16). No effect of EMF exposure on pineal serotonin level was observed, while the light exposure resulted in a 2–3 fold increase ($p<0.001$). [Serotonin is a substance that has many functions in the body, including neurotransmission. The pineal level of serotonin is less relevant, in this respect, also because serotonin is not produced in the pineal gland. This paper is also discussed in Section 7.2.1 Neuroendocrine effects / melatonin. With a brain-SAR of 7.5 W/kg thermal effects can not be excluded.]

Belyaev et al. (2006) exposed Fisher 344 rats (n=3–4) for 2 h to a 915 MHz mobile phone signal at an whole-body SAR of 0.4 W/kg. The main topics of this study were effects on DNA and gene regulation. Therefore it is also discussed in the sections on gene expression (5.3.5) and genotoxicity (12.2.1), but also with neuroendocrine effects (7.2) and blood brain barrier function (5.3.3). Microarray techniques revealed that 11 genes were modestly up-regulated and one was down-regulated. There was little obvious commonality in function between these genes, but relevant for this section is the significant ($p<0.0025$) 1.56-fold upregulation of solute carrier family 6, member 6 (SLc6a6), a gene coding for a protein that is involved in the regulation of transport of neurotransmitters.

Crouzier et al. (2007b) exposed Sprague Dawley rats to 2450 MHz RF EMF pulse modulated at 1 kHz for 24 h. Two exposure levels were used, 10 and 50 W/m^2, resulting in whole-body SARs 0.31 ± 0.07 and 1.58 ± 0.62 W/kg, respectively , and SARs in the head of 0.46 ± 0.12 and 2.34 ± 0.97 W/kg. Acetylcholine levels in the hippocampus were measured by an implanted catheter. No effect of exposure was observed. [This study is also discussed in Section 5.3.2 (Brain electrical activity).]

Studies not included in the analysis

Wang et al. (2009) exposed groups of 5 Wistar rats to unspecified microwaves for 5 min at an whole-body SAR of 14.1 W/kg. They observed complex time and location-dependent changes in synaptic vesicle-associated proteins in the brain. [Although the authors state that the temperature was not increased directly after exposure, there may be a delayed effect of core temperature with this SAR level, so thermal effect cannot be excluded. It is not clear at what time points the sham controls were assayed, probably only at one point. The variation in the results could be due to variations in assays. Also the type of microwaves is not specified. Because of these issues the study cannot be evaluated.]

From the same group, Zhao et al. (2012) exposed Wistar rats (6 per group) to unspecified microwaves for 6 min per day up to 1 month. Whole-body SARs of 1.05, 2.1 and 4.2 W/kg were employed. They determined the levels of a number of neurotransmitters at various time points. The levels of glutamate, asparctic acid, glycine and GABA in the hippocampus were increased at 6 h, 14 days and 2 months with exposure to 1.05 W/kg and at 14 days and 2 months with exposure to 2.1 W/kg. A decrease in GABA was observed at 6 h, and for asparctic acid and glycine at 2 months with exposure to 4.2 W/kg. [Since it is not clear whether the time points of the neurotransmitter assays were calculated from the first or the last exposure, and since the microwaves were not specified, this study cannot be evaluated. This study is also discussed in Section 5.3.1 Cognitive function.]

Noor et al. (2011) exposed 1 and 4 month-old albino rats to 900 MHz EMF for 1 hour per day, once or during 1, 2 or 4 months; group size was 5–7. The whole-body SAR was reported to be 1.165 W/kg. They observed time, age and location-specific changes in inhibitory (GABA, glycine and taurine) and excitatory amino acid neurotransmitters (glutamic acid, aspartic acid and glutamine) in the brain, but without a clear pattern. [No correction for multiple comparisons was applied. The units of concentration are not provided and they used an unusual assay parameter, the equilibrium ratio percent, which is not explained.]

Jing et al. (2012) exposed pregnant Wistar rats to the signal from a mobile phone for 3 times 10, 30 or 60 minutes per day during the full 20 days of pregnancy. They observed an increase in noradrenaline and dopamine in the 10-min group, and a decrease in the 60-min group ($p<0.05$). No effect on 5-hydroxyindole acetic acid was observed in either group. [No data on exposure level are provided; therefore these results cannot be interpreted. The study is also discussed in Section 5.3.5 Gene expression and oxidative stress.]

Dogan et al. (2012) exposed Wistar rats to the signals from a mobile phone transmitting 1900–2200 MHz fields, for 40 minutes per day during 20 days. The exposures simulated actual phone conversations, but exposure levels were not provided. After the last exposure the animals were sacrificed and the brains removed.

No effect of any of the exposures was observed on the choline/creatinine, N-acetylaspartate/creatinine and N-acetylaspartate/choline ratios. [Also in this study no data on exposure level are provided, therefore these results cannot be interpreted. The study is also discussed in Section 5.3.5 Gene expression and oxidative stress.]

Table 5.3.5. Animal studies on effects of exposure to RF fields on neurotransmitter function

Endpoint, animals, number per group, age or weight at start	Exposure: source, schedule, level, freely moving or restrained	Response	Comments	Reference
Na-dependent choline uptake in frontal cortex & hippocampus Rat: Sprague Dawley (n=9–12) 250–300 g	2450 MHz pulsed; 2 µs pulses at 500 pps 45 min WBA SAR 0.6 W/kg, brain regions 0.5–2 W/kg Free	Decreased Na-dependent choline uptake in frontal cortex & hippocampus , not observed after administration of corticotropin-releasing factor antagonist before exposure.	Peak exposure around the threshold for auditory perception of short pulses.	(Lai et al., 1990)
Na-dependent choline uptake in frontal cortex & hippocampus Rat: Sprague Dawley (n=8–9) 250–300 g	2450 MHz pulsed; 2 µs pulses at 500 pps 45 min WBA SAR 0.6 W/kg, brain regions 0.5–2 W/kg Free	Decreased Na-dependent choline uptake in frontal cortex & hippocampus, not observed in hippocampus after administration of by µ-, δ- and κ-receptor blockers before exposure.	Peak exposure around the threshold for auditory perception of short pulses.	(Lai et al., 1992b)
Benzodiazepine receptor sites in frontal cortex & hippocampus Rat: Sprague Dawley (n=6–9) 250–300 g	2450 MHz pulsed; 2 µs pulses at 500 pps 45 min/day, 1 or 10 days WBA SAR 0.6 W/kg, brain regions 0.5–2 W/kg Free	Increased number of benzodiazepine receptor sites after single, not after repeated exposures in cortex, no effect in hippocampus and cerebellum; no effect on receptor affinity.	Peak exposure around the threshold for auditory perception of short pulses.	(Lai et al., 1992a)
Effect of neurotransmitter (ant)agonists on learning Rat: Sprague Dawley (n=8) 250–300 g	2450 MHz pulsed; 2 µs pulses at 500 pps 45 min WBA SAR 0.6 W/kg, brain regions 0.5–2 W/kg Free	Decreased learning after RF alone, not observed after administration of cholinergic agonist physostigmine, or opiate antagonist naltrexone before exposure. No effect of peripheral opiate antagonist naloxone methiodide.	Peak exposure around the threshold for auditory perception of short pulses. Possible differences between groups in anxiety or motivation. Also discussed in 5.3.1 Cognitive effects.	(Lai, Horita & Guy, 1994)
Effect opioids on Na-dependent choline uptake in hippocampus Rat: Sprague Dawley (n=8) 250–300 g	2450 MHz pulsed; 2 µs pulses at 500 pps 45 min WBA SAR 0.6 W/kg, brain regions 0.5–2 W/kg Free	Decreased Na-dependent choline uptake in hippocampus, not observed after administration of β-funaltrexamine (µ-opioid-receptor blocker) before exposure.	Peak exposure around the threshold for auditory perception of short pulses.	(Lai et al., 1996)

Effect on neurotransmitters in 7 brain regions Rat: Wistar (n=5) 250–320 g	2450 MHz 1 h 5, 10 mW/cm^2 (50, 100 W/m^2) Restrained	Low level: no effect on noradrenaline, dopamine, dihydroxyphenyl acetic acid (DOPAC, metabolite of dopamine) and serotonin. High level: decreased noradrenaline in hypothalamus. No effects on dopamine and serotonin, increase in DOPAC in pons and medulla oblongata. Both levels: increase in 5-HIAA (metabolite of serotonin) in cortex.	Increase in colonic temperature: thermal experiment.	(Inaba et al., 1992)
Effect on neurotransmitters in hypothalamus and caudate nucleus Rat: Sprague Dawley (n=7–8) Age / weight not provided	5.02 GHz, pulsed; 10 µs pulses at 1000 pps 40 min SAR right brain 29 W/kg, left brain 40 W/kg Restrained, anaesthetized	Increase in aspartic acid, serine and glycine in hypothalamus and caudate nucleus, no effect on glutamic acid and glutamine.	Thermal experiment. Anaesthesia could have influenced response.	(Mason et al., 1997)
Neurotransmitters in motor cortex Rat: Wistar (n=10, 15, 18) 200-250 g	4200 MHz, modulated 20 Hz–20 kHz 1 h 15 µV/cm^2 Free	Highest level of exitability group: increased dopamine and serotonin; lowest level of exitability group: no effects; intermediate group changed level of 5-hydroxyindolacetic acid.	Incomplete reporting of results. Also discussed in 5.3.1.2.	Shtemberg et al. (2001)
Effect on γ-aminobutyric acid (GABA) in cerebellum Rat: Wistar (n=12) 180 g	900 MHz GSM, CW 2 h Brain SAR: GSM 4 W/kg CW 32 W/kg Restrained	GSM: no effect on GABA in cerebellum, except reduction in area Purkinje processes. CW: reduction in GABA in molecular, Purkinje, granular layers; decrease in area of stained processes in Purkinje layer, decrease in stained area in molecular layer.	Number of fields analysed (6/layer) rather small. Possibly thermal effect for CW.	(Mausset et al., 2001)
Effect on neurotransmitters in cortex, striatum, hippocampus Rat: Wistar (n=4–18) 250 g	900 MHz, GSM 15 min Brain SAR 6 W/kg Restrained	N-methyl-D-aspartate receptors (excitatory): decrease binding in cortex, and striatum, reduced expression postsynaptic; GABA receptors (inhibitory): decreased binding in hippocampus; dopamine transporters (modulatory): decreased binding in cortex, increased in striatum; increased astrocyte hypertrophy/hyperplasia.	Also discussed in 5.3.1 Cognitive effects.	(Mausset-Bonnefont et al., 2004a)
Effect on pineal serotonin Rat: Sprague Dawley (n=64) 8–10 weeks	1439 MHz TDMA 4 h SAR brain 7.5 W/kg WBA 1.9-2.0 W/kg Restrained	No effect.	Pineal serotonin less relevant because serotonin is not produced in the pineal gland. Also discussed in 7.2.1 Neuroendocrine effects / melatonin.	(Hata et al., 2005)

Effect on gene expression Rat: Fisher 344 (n=3-4) 12 weeks	900 MHz, GSM 2 h WBA SAR 0.4 W/kg Free	1.56-fold upregulation of solute carrier family 6, member 6 (SLc6a6), gene coding for protein involved in regulation of transport of neurotransmitters.	Also discussed in 5.3.5 Gene expression, 12.2.1 Genotoxicity, 7.2 Neuroendocrine effects and 5.3.3 Blood brain barrier function.	(Belyaev et al., 2006)
Acetylcholine in hippocampus Rat: Sprague Dawley (n=10, 14) 300-350 g	2450 MHz pulsed at 1 kHz 1 day WBA SAR 0.31±0.07, 1.58±0.62 W/kg Head SAR 0.46±0.12, 2.34±0.97 W/kg Free	No effect.		Crouzier et al. (2007b)

Abbreviations: 5-HIAA: 5-hydroxyindoleacetic acid; CW: continuous wave; DOPAC: dihydroxyphenyl acetic acid ; GABA: γ-aminobutyric acid; GSM: Global System For Mobile Communication ; pps: pulses per second; TDMA: Time Division Multiple Access; WBA SAR: whole-body averaged SAR

5.3.5 Gene expression and oxidative stress

[Due to time constraints only a list of retrieved papers is provided.]

(Singh et al., 1994)

(Fritze et al., 1997b)

(Morrissey et al., 1999) [This paper is also discussed in Section 9.3.1 (Cardiovascular system and themoregulation – Animal studies).]

(Stagg et al., 2001) [This paper is also discussed in Section 7.3.2 (Neuroendocrine system – Animal studies).]

(Mausset-Bonnefont et al., 2004a) [This paper is also discussed in Section 5.3.1.2 (Non-spatial tasks and behaviour).]

(Paulraj & Behari, 2004)

(Finnie, 2005)

(Kuribayashi et al., 2005) [This paper is also discussed in Section 5.3.3 (Blood-brain barrier).]

(Belyaev et al., 2006) [This paper is also discussed in sections 5.3.4 (Neurotransmitter function) and 12.2.1 (Genotoxicity).]

(Köylü et al., 2006)

(Finnie et al., 2006c)

(Paulraj & Behari, 2006)

(Brillaud, Piotrowski & de Sèze, 2007)

(Kim et al., 2008)

(Ammari et al., 2008a)

(Yilmaz et al., 2008)

(Lee et al., 2008)

(Paparini et al., 2008)

(Sokolovic et al., 2008)

(Finnie et al., 2009a) [This paper is also also discussed in Section 5.3.3 (Blood-brain barrier).]

(Finnie et al., 2009b)

(López-Martín et al., 2009) [This paper is also discussed in Section 5.3.2 (Brain electrical activity).]

(Kesari & Behari, 2009) [This paper is also discussed in Section 12.2.1 (Genotoxicity).]

(Guler et al., 2010)

(Maskey et al., 2010a)

(Maskey et al., 2010b)

(Ammari et al., 2010)

(Finnie et al., 2010)

(Jorge-Mora et al., 2011)

(Aryal et al., 2011)

(Carballo-Quintás et al., 2011)

(Watilliaux et al., 2011) This paper is also discussed in Section 10.3 (Immune system and haematology – Animal studies).]

(Avci et al., 2012)

(Bouji et al., 2012) [This study is also discussed in section 5.3.1.(Cognitive fucntion) and 7.3.2 (Other hormones).]

(Paulraj & Behari, 2012)

(Daşdağ et al., 2012)

(Fragopoulou et al., 2012)

(Maskey et al., 2012)

Not to include in analysis

(Irmak et al., 2002)

(Ilhan et al., 2004)

(Meral et al., 2007)

(Kesari, Kumar & Behari, 2011)

(Jing et al., 2012) [This paper is also discussed in Section 5.3.4 (Neurotransmitters).]

(Dogan et al., 2012)

5.4 In vitro studies

Experimental studies performed in in vitro neuronal preparations were focused to examine the effect of RF EMF exposure on either functional or morphological parameters. In this section, in vitro studies on non-mammalians, regarded as model systems, have been also included.

In the previous WHO monograph (WHO, 1993), a scanty number of in vitro investigations on this topic are reported. In most cases, the effects of RF EMF exposure, when present, are ascribed to heating. In the present literature search, 33 articles dealing with in vitro studies have been recognized. Among them, ten were in a language that could not be understood. One was excluded because it did not meet the inclusion criteria for in vitro studies due to the lack of sham-exposed samples, and the reference is reported at the end of this section.. Two papers did not completely comply with the quality criteria for inclusion, and are only presented in the text. The remaining twenty papers have been described in the text and summarized in Tables 5.4.1.1, 5.4.1.2 and 5.4.2.1. Unless specifically mentioned, papers did not report on blinding of the investigators to the exposure conditions.

5.4.1 Functional parameters

These studies are focused on various functional parameters, including normal and epileptiform bioelectrical activity, synaptic transmission and plasticity, ion currents through membrane ion channels, Ca^{2+} dynamics, membrane input resistance and blood-brain barrier permeability.

5.4.1.1 Neuronal cell function

Brain slice preparations are widely used in neurophysiology to study the electrophysiological mechanisms underlying the functions of the nervous system. Tattersal et al. (2001) exposed rat hippocampal slices for 5, 10 or 15 min to 700 MHz (CW) at a calculated SAR of between 0.0016 and 0.0044 W/kg during extracellular field potential recording. They observed SAR-dependent changes in synaptic transmission (population spike amplitude) in the Cornu Ammonis 1 (CA1) region that were bidirectional (increases or decreases of up to 120 and 80%, respectively), and generally reversible ($p<0.05$). RF-induced rises in temperature were too small to be detected even using a thermistor with a resolution of 0.1 °C, and imposed temperature changes of up to 1 °C failed to mimic the effects of RF exposure. To eliminate the possibility of RF-induced artefacts due to the metal stimulating electrode, the effect of RF exposure on spontaneous epileptiform activity induced in CA3 neurons by 4-aminopyridine, that blocks potassium membrane channels, was also investigated. In four out of the eleven slices tested, the highest field intensity (71.0 V/m) produced a transient increase in the frequency of epileptiform bursting, accompanied by a decrease in the amplitude of the bursts; this was followed by a long-lasting decrease of bursting, which recovered slowly when the field was turned off. No effect was observed in six sham-exposed slices. Positive controls have not been included in the study design. [In this investigation thermal effects cannot be excluded].

Xu et al. (2006) exposed primary cultures of rat hippocampal neurons for 15 min per day for 8 days to 1800 MHz, GSM, (average SAR of 2.4 W/kg). Using whole-cell patch-clamp recording combined with immunocytochemistry, to evaluate synaptic functionality, in three independent experiments they found a selective decrease in the amplitude of alpha-amino-3-hydroxy-5-methyl-4-soxazole propionic acid (AMPA) miniature excitatory postsynaptic currents (mEPSCs) ($p<0.05$), whereas the frequency of AMPA mEPSCs and the amplitude of N-methyl-d-aspartate (NMDA) mEPSCs did not change. The exposure also decreased the expression of the protein postsynaptic density 95 (PSD95), which is involved in excitatory synapse maturation and in synaptic plasticity ($p<0.05$). Positive controls have not been included in the study design. [The authors stated that “all these changes found in our study were non-thermal effects because the irradiation used in our study did not increase the temperature of cell cultures”, but they did not describe how the temperature was monitored].

Using ion-sensitive fluorescent dyes for the real-time measurement of intracellular calcium ion concentrations ($[Ca^{2+}]i$), Green et al. investigated the effect of Terrestrial Trunked Radio signals (TETRA, 380.8875 MHz, pulse modulated at 17.6 Hz, 25% duty cycle) in cultured rat cerebellar granule cells (Green et al., 2005). Exposure to SARs of 0.005–0.4 W/kg induced no significant changes in resting $[Ca^{2+}]i$. Although increases in $[Ca^{2+}]i$ in response to potassium-induced depolarization in TETRA-exposed cells were different from sham controls, the majority of the differences was attributable to initial biological variation between cell cultures. The results of six to nine independent experiments showed no evidence of any consistent or biologically relevant effect of TETRA fields on $[Ca^{2+}]i$ in granule cells at any of the SARs tested. In this study, carried out blinded, positive controls have not been assessed. [Indication about the homogeneity of the SAR distribution is not given. The study is also reported in Section 12.3.2 (Intracellular Calcium).]

Whole-cell current-clamp and single-channel recording was used by Marchionni et al. (2006) to study the effect of 900 MHz CW EMF on rat dorsal root ganglion neurons (four to nine independent experiments). Exposure at a SAR value of 1 W/kg for 10 s did not modify the frequency of action potentials, and did not affect the L-type Ca^{2+} current and the Ca^{2+}-activated K^+ current, which are involved in the control of the interspike interval. Positive controls have not been included in the study design. [For dosimetric analysis the authors refer to a previous report (Liberti et al., 2004). The study is also reported in Section 12.3.2 (Intracellular Calcium).]

Platano et al. (2007) investigated the effect of 900 MHz exposure on Ba^{2+} currents through voltage-gated Ca^{2+} channels in primary cultures of rat cortical neurons. They found that 1–3 periods of 90-s exposure at a SAR of 2 W/kg (CW or GSM modulated) during patch-clamp whole-cell recording did not alter the current amplitude or current-voltage relationship (three to seven experiments). Samples treated with $CdCl_2$, a specific blocker of voltage-gated calcium channels, were used as positive controls and gave positive findings. The results are consistent with a previous study by Linz et al. (1999) on isolated rat and guinea pig ventricular myocytes, in which no effects on voltage-gated Ca^{2+} channels were found using CW or GSM exposure (180 MHz, 900 MHz, or 1800 MHz) with SAR values up to 0.88 W/kg for 2 min. The study by Linz et al. (1999) has been described in details in Section 12.3.2. This study is also reported in Section 12.3.2 (Intracellular and intercellular signalling).]

In contrast to these latter negative results, Rao and co-workers (2008) observed changes in neuronal cells derived from mouse embryonal P19 carcinoma. Using fluorescent dyes, they found that during exposure for 60 min to 70–1100 MHz (SAR 0.5 to 50 W/kg) the number of spontaneous $[Ca^{2+}]$i spikes significantly increased ($p<0.05$) in three to four independent experiments. The effect was dependent on the frequency (with a peak effect at 800 MHz) but not on the SAR in the range 0.5 to 5 W/kg. When 50 W/kg was tested, the change was significantly lower than with the lower SAR values and accompanied by a temperature increase (>5°C), which may have introduced thermally-induced alterations in Ca^{2+} dynamics. In sham-exposed cells, spontaneous Ca^{2+} spiking could be blocked by ω-conotoxin GV1A (a selective blocker of the N-type voltage-gated Ca^{2+} channels) or U73122 (a phospholipase C inhibitor); no effect of RF exposure at 0.5 W/kg was observed. These findings indicate that N-type voltage-gated Ca^{2+} channels and phospholipase C are involved in intrinsic Ca^{2+} spiking, and may be modulated by RF. [This study has been also described in Section 12.3.2, (Intracellular and intercellular signalling) and 12.3.6.1 (Cell differentiation).]

O'Connor et al. (2010) monitored intracellular Ca^{2+} in primary cultures of hippocampal neurons and PC12 cells during 30 min exposure to 900 MHz, GSM (SAR 0.012–2 W/kg) performed blinding, and found that neither basal Ca^{2+} homeostasis nor Ca^{2+} signals were affected with respect to sham-controls. No positive controls were included. [The number of independent experiments carried out is unclear. In this study, also described in Section 12.3.2 (Intracellular and intercellular signalling, similar findings were reported in human endothelial cells.]

Three papers deal with the effect of EMFs at higher frequencies.

Using extracellular field potential recording in rat hippocampal slices, Pakhomov et al. (2003) found a fully reversible decrease in synaptic transmission (population spike amplitude) in the CA1 region during exposure to brief (0.5–2.0 μs) extremely high power (peak SAR of up to 5x108 W/kg) microwave pulses at a repetition rate of 0.5 to 10 Hz, with a 9.3 GHz carrier frequency ($p<0.05$). Microwave heating of the preparation ranged from 0.5 °C (at 300 W/kg time-average SAR) to 6.8 °C (at 3600 W/kg time-average SAR). The effect on synaptic transmission was only due to temperature increase, as it was proportional to the temperature rise but not to any specific parameter of the microwave pulses, and the same effect could also be induced by a CW irradiation or conventional heating. Moreover, they found that neither microwave pulses nor CW irradiation affected 2 s, 50 Hz tetanus-induced long-term potentiation of synaptic transmission (LTP), a form of synaptic plasticity believed to underlie long-term memory formation (10 to 14 independent experiments). Positive controls were not included in the study design.

Pikov et al. (2010) exposed rat neocortical slices for 1 min to 60.125 GHz at 0.3–8 mW/m^2 and recorded the bioelectrical activity of single cortical layer 2/3 pyramidal neurons by whole-cell patch-clamp. They found that 1 min of exposure at high power levels (7–8 mW/m^2) reduced the firing rate to one third of the pre-exposure level in four out of eight examined neurons ($p<0.05$). The width of the action potentials was narrowed to 17% of the baseline value, and the membrane input resistance decreased to 54% of the baseline value across all neurons ($p<0.05$). These effects were short lasting (2 min or less) and were accompanied by exposure-induced 3 °C heating of the bath solution. Comparison of these results with previously published data on the effects of general bath heating of 10 °C indicate that exposure-induced effects cannot be fully attributed to heating and may involve specific interaction of EMF with the tissue. Blocking of the intracellular Ca^{2+}-mediated signalling did not significantly alter the RF-induced neuronal responses, suggesting that RF interacted directly with the neuronal cellular membrane. Positive controls have not been included in the study design.

Titushkin et al. (2009) observed an increase in Ca^{2+} spiking frequency and nitric oxide (NO) production (about 2 fold increase; $p<0.05$) in mouse embryonic stem cell-derived neuronal cells exposed to 94 GHz at 18.6 kW/m nominal power density ($p<0.05$). The detailed dosimetry for the experimental system employed is reported in a later paper (Pickard, Moros & Shafirstein, 2010). The N-type calcium channels, phospholipase C enzyme, and actin cytoskeleton appeared to be involved in this effect (2 to 4 independent experiments). The authors observed up to 8 °C temperature rise during exposure, but reported that not all cellular responses were similar to thermally-induced effects. For example, exposure-induced nitric oxide (NO) production could not be reproduced by thermal heating of the cells up to 42 °C from about 22 °C. [The experiments were performed at room temperature, without any forced convection cooling.]

Two studies have been carried out on neurons from molluscs.

Partsvania et al. (2011) exposed single neurons of molluscs to 900 MHz, GSM (SAR 0.63 W/kg) for 60 min. The results obtained on 31 neurons showed that the average firing threshold of the action potentials was not changed with respect to sham-controls, but the average latent period was reversibly decreased ($p<0.01$). Positive controls have not been included in the study design.

Field et al. (1993) studied the effects of 45 min exposure to pulsed microwaves (2.45 GHz, 10 µs, 100 pps, time average SAR 81.5 W/kg) on membrane input resistance and action potential intervals in spontaneously active ganglion neurons of *Helix aspersa*. Six independent experiments were performed and comparison with sham-exposed neurons revealed a significant ($p<0.05$) and persistent (still present 45 min after the end of the exposure) increase in the mean membrane input resistance of neurons exposed to pulsed microwaves, whereas the action potential frequency was not affected. [The possibility that the increase in input resistance represents a thermal effect seems unlikely, since a constant temperature of 20.8 ± 0.07 °C within the recording chamber was maintained by a thermostatic system, and the same research group previously found that the threshold temperature variation for changes in input resistance is ± 0.63 °C, and that temperature elevation exceeding this threshold is associated with an opposite change (decrease) in input resistance (Ginsburg, Lin & O'Neill, 1992).]

Table 5.4.1. In vitro studies assessing effects of RF EMF exposure on various functional parameters in neuronal cells

Cells Number of independent experiments*	Biological endpoint	Exposure conditions	Results	Comment	Reference
CA1 or CA3 neurons in rat hippocampal slices n=5–12 n=11	Synaptic transmission (CA1) 4-aminopyridine-induced epileptiform activity (CA3)	700 MHz, CW SAR 0.0016–0.0044 W/kg 5–15 min	SAR-dependent increase and decrease in synaptic transmission. Changes in epileptiform bursting.	Possible localized temperature increase at tips of stimulating electrodes in synaptic transmission experiments. No information on blinding of staff.	Tattersal et al. (2001)

Primary cultures of rat hippocampal neurons n=3	Ion currents through AMPA and NMDA synaptic receptors Postsynaptic density 95 (PSD95) expression in dendrites	1800 MHz, GSM SAR 2.4 W/kg 15 min/day for 8 days	Decrease of AMPA receptor current. No effect on NMDA receptor current. Decrease of PSD95 expression in dendrites.	No information on blinding of staff.	Xu et al. (2006)
Rat cerebellar granule cells n=6–9	Intracellular Ca^{2+} concentration	380.89 MHz (TETRA), pulse-modulated at 17.6 Hz SAR 0.005–0.4 W/kg 10 min	Increase in intracellular Ca^{2+} concentration following K+-induced depolarization.	Effect due to biological variation between cultures. No information on blinding of staff.	Green et al. (2005)
Primary cultures of dorsal root ganglion neurons n=4–9	Frequency of action potentials L-type Ca^{2+} current Ca^{2+}--activated K+ current	900 MHz, CW SAR 1 W/kg 10 s	No effect.	No information on blinding of staff.	Marchionni et al. (2006)
Primary cultures of rat cortical neurons n=3–7	Ba^{2+} currents through voltage-gated calcium channels	900 MHz, CW or GSM SAR 2 W/kg 90 s, 1–3 times	No effect.	No information on blinding of staff.	Platano et al. (2007)
Neuronal cells derived from mouse embryonal P19 carcinoma cells n=3–4	Ca^{2+} spike frequency	70–1100 MHz SAR 0.5–50 W/kg 60 min	Increase in Ca^{2+} spike frequency at SAR from 0.5 to 5 W/kg.	For cell proliferation and differentiation see 12.3.6. No information on blinding of staff.	Rao et al. (2008)
Primary cultures of rat hippocampal neurons PC12 cells n not clear	Basal Ca^{2+} homeostasis Ca^{2+} signals	900 MHz, GSM Average SAR 0.012–2 W/kg 30 min	No effect.	For results on human endothelial cells see 12.3.2.1.	O'Connor et al. (2010)
CA1 neurons in rat hippocampal slices n=10–14	Synaptic transmission	9.3 GHz pulsed (0.5–2 μs pulses at 0.5–2.0 pps) Average SAR 300–3600 W/kg 2–7 min	SAR-dependent decrease in synaptic transmission. No effect on long-term potentiation.	Thermal effect on synaptic transmission. No information on blinding of staff.	Pakhomov et al. (2003)
Neurons in rat neocortical slices n=2–6	Action potential frequency and width input resistance	60.125 GHz Power density 0.3–0.8 mW/m^2 1 min	Decrease in action potential frequency and width. Decrease in membrane input resistance.	No information on blinding of staff.	Pikov et al. (2010)
Mouse embryonic stem cell-derived n=2–4	Ca^{2+} spike frequency NO production	94 GHz Nominal power density 18.6 kW/m^2 30–60 min	Increase in Ca^{2+} spike frequency and in NO production.	No information on blinding of staff.	Titushkin et al. (2009)
Studies on non-mammalian cells					

Mollusc single neurons n=31	Action potential threshold Latent period	900 MHz, GSM Average SAR 0.63 W/kg 60 min	No effect on action potential threshold. Decrease of latent period.	No information on blinding of staff.	Partsvania et al. (2011)
Ganglion neurons of *Helix aspersa* n=6	Membrane input resistance Action potential frequency	2.45 GHz pulsed (10 µs pulses at 100 pps) Average SAR 81.5 W/kg 45 min	Increase in membrane input resistance. No effect on action potential frequency.	No information on blinding of staff.	Field et al. (1993)

*When cell cultures are examined, n refers to the number of independent experiments carried out. In the case of experiments carried out on slices/single neurons, n refers to single samples (slices/neurons)

"No effect" means no statistically significant effect

Abbreviations: AMPA: alpha-amino-3-hydroxy-5-methyl-4-soxazole propionic acid; CA: Cornu Ammonis; CW: continuous wave; GSM: Global System for Mobile Communication; NMDA: N-methyl-d-aspartate; NO: nitric oxide; PDS: postsynaptic density; SAR: specific absorption rate; TETRA: Terrestrial Trunked Radio signals

5.4.1.2 Blood-brain barrier permeability

The blood-brain barrier is an important dynamic interface between the circulating blood and the brain extracellular fluid, that protects the brain from potentially harmful chemicals while regulating transport of essential molecules and maintaining a stable environment; it is absent in a small number of brain areas whose function depends on unrestricted access to the blood. The barrier is formed by highly specialized endothelial cells that line brain capillaries; these cells are connected to each other by tight junctions, which restrict the permeability for hydrophilic and charged molecules. The barrier also includes pericytes, astrocytic endfeet and thick basement membranes. Cells of the barrier allow the diffusion of small hydrophobic molecules, and actively transport metabolic products such as glucose and amino acids by means of specific transporter proteins. An increase in the normally low permeability for hydrophilic and charged molecules could potentially be detrimental for the brain.

Schirmacher et al. found that after two and four days of exposure to 1800 MHz, GSM (SAR 0.3 W/kg) sucrose permeation in an in vitro model of blood-brain barrier made up by a co-culture of rat astrocytes and porcine brain capillary endothelial cells had increased by a factor of two with respect to sham-controls, but the sucrose permeation of control cell cultures was already about two orders of magnitude higher than the in vivo sucrose permeation ($p=0.002$ and $p<0.001$ for two and four days exposure, respectively) (Schirmacher et al., 2000). Positive controls were not included in the study design. In a following study, the research group improved the model's barrier tightness and came very close to the low in vivo permeability. Then cell cultures were exposed for one–five days in the same electromagnetic conditions and they did not observe any increase in permeability (Franke, Ringelstein & Stogbauer, 2005). Treatments with mannitol as positive control gave positive results. [It should be noted that, since the exposure system employed in these studies was not designed to include a temperature probe, temperature control of the exposed cells was not carried out.] In a further study (Franke et al., 2005), the same research group investigated the influence of a generic UMTS signal at 1966 MHz. The cell cultures were exposed, in blind condition, continuously for up to 84 h at an average electric field strength of 3.4–34 V/m (maximum SAR 1.8 W/kg) ensuring non-thermal conditions. They did not find any evidence of RF field-induced disturbance of the function of the cells: after and during exposure the tightness of the barrier remained unchanged compared to sham-exposed cultures. Permeation of transporter substrates as well as the localization and integrity of the tight-junction proteins occludin and ZO1 were not affected either. Heating of the incubator at 45 °C was used as positive control and gave positive findings. [In this study the authors employed a different exposure system with respect to the previous investigations (Franke, Ringelstein & Stogbauer, 2005; Schirmacher et al., 2000), with integrated online monitoring of temperature and EMF parameters].

Studies not included in the analysis

Leszczynski et al. (2002) found that 1 hour exposure of the human endothelial cell line EA.hy926 to a 900 MHz GSM signal (SAR = 2 W/kg) caused a transient increase in heat shock protein (hsp)27 phosphorylation (which was prevented by a specific inhibitor of p38 mitogen-activated protein kinase, p38MAPK), and in p38MAPK expression. The temperature of the cell cultures remained at 37 ± 0.3 °C throughout the exposure period. Phosphorylated hsp27 stabilizes endothelial cell stress fibres, due to the increased actin polymerization; the stabilization of stress fibres causes several changes in endothelial cells physiology, including cell shrinkage and opening of spaces between cells, increase in permeability of the endothelial monolayer, and increase in pinocytosis. Based on the known functions of hsp27, the authors hypothesized that mobile phone radiation-induced activation may cause an increase in blood-brain barrier permeability. [The absence of a statistical analysis makes the conclusion of this paper questionable. This study has been also described in Sections 12.3.2 (intracellular and intercellular signalling), 12.3.3 (gene and protein expression) and 12.3.4 (apoptosis).]

Liu et al. (2011) investigated the possible protective effects of green tea polyphenols against RF EMF in cultured rat cortical neurons exposed for 24 h to 1800 MHz. A mobile phone in the “on” mode was employed, while sham exposures were carried out in the “stand-by” mode. They found that RF exposure induced cell death, evaluated with the MTT (3-(4,5-dimethylthiazole-2-yl)-2,5-diphenyl-tetrazolium bromide) and terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) assay. A protective effect of green tea polyphenols on the RF exposed cortical neurons was demonstrated by testing the content of Bcl-2 associated X protein (Bax), as assessed by the immunoprecipitation assay and Western blot assay. [There is an inadequate description of the RF exposure system and dosimetry. Use of a mobile phone in “on” mode as the exposure source does not provide appropriate control of the exposure level. Moreover, it is questionable whether placing the mobile phone in stand-by mode is an appropriate sham control, and therefore whether the study fulfilled the inclusion criteria. This study has been also reported in Section 12.3.4, where the effect of RF exposure on apoptosis has been described.]

Table 5.4.2 In vitro studies assessing effects of RF EMF exposure on blood-brain barrier permeability

Cells Number of independent experiments	Biological endpoint	Exposure conditions	Results	Comment	Reference
Porcine brain capillary endothelial cell cultures n=2	Blood-brain barrier permeability	1800 MHz, GSM Average SAR 0.3 W/kg 2 and 4 days	Increased permeability of ^{14}C-sucrose.	Too high permeability in control conditions compared to in vivo values. No temperature control. No information on blinding of staff.	Schirmacher et al. (2000)
Porcine brain microvascular endothelial cell cultures n=3–13	Blood-brain barrier permeability	1800 MHz, GSM Average SAR 0.3 W/kg 1 -5 days	No effect on ^{14}C sucrose permeability.	No temperature control. No information on blinding of staff.	Franke, Ringelstein & Stogbauer (2005)
Porcine brain microvascular endothelial cell cultures n=4	Blood-brain barrier permeability	1966 MHz UMTS SAR up to 1.8 W/kg for up to 84 h	No effect on ^{14}C-sucrose or serum albumin permeation.		Franke et al. (2005)

“No effect” means no statistically significant effect

Abbreviations: GSM: Global System for Mobile Communication; SAR: specific absorption rate; UMTS: universal mobile telecommunications system

5.4.2 Cell morphology

French et al. (1997) found marked alterations in the cell shape of the human astrocytoma cell line U-87 MG exposed to 835 MHz (0.081 ± 0.03 or 0.4 ± 0.15 kW/m^2) for 20 minutes, 3 times per day for 7 days. In order to minimize the interference of RF-induced heating, the cells were cooled to room temperature before the exposure: the temperature fell from 37 °C to 26 ± 0.6 °C in sham-control, to 27.0 ± 0.9 °C in cells exposed to 0.081 kW/m^2, and to 34.0 ± 0.1 °C in cells exposed to 0.4 kW/m^2. Following the exposure to both power densities, the spherical morphology disappeared, and the cells adopted a flattened, spread shape but no change was seen among the sham exposed cells; moreover, the cells lost the actin-containing cell surface projections observed in sham-exposed cells. Following the higher exposure, the flattened cells also exhibited actin aggregates (blebs) localized at specific sites on the cell membrane; the authors suggest that this effect may be related to the higher temperature increase induced by this exposure, although the temperature remained below 37 °C. Positive controls were not included in the study design. [Only descriptive results (morphological analysis) were provided in the paper and no statistical analysis was made. This study has also been described in Section 12.3.6 (cell proliferation).]

Aran et al. dissected out the organs of Corti (OC) from 15 new-born (postnatal day 3–4) rats. For each animal, one OC was exposed for 24 h to a 900 MHz GSM signal (SAR = 1 W/kg), and the other was sham-exposed. After 2–3 days of culture they were observed under light microscopy. The study was carried out blinded. No differences were found between exposed and sham-exposed organs: the pattern of organization of the hair cell population appeared completely normal at this stage of development (Aran et al., 2004). Positive controls have not been included in the study design. [This study has also been described in Section 6.4.1 (auditory and vestibular functions).]

Using a blind design Ning et al. (2007) exposed primary cultures of rat hippocampal neurons from the sixth in vitro day to 1800 MHz, GSM modulated (SAR = 2.4 W/kg) for 15 min per day for 9 days. They observed a decrease in the density and mobility of dendritic filopodia at the third days of exposure, and in the density of mature spines by the end of exposure compared to sham controls ($p<0.01$); in addition, the average length of dendrites per neuron at the fourth day and by the end of exposure was decreased, while the dendritic arborization was not altered. In contrast, no significant changes were found in the neurons exposed to 0.8 W/kg using the same protocol. Positive controls were not included in the study design.

Del Vecchio et al. (2009a) exposed from the first in vitro day the murine cholinergic cell line SN56 for 3 days, and from the second in vitro day a primary culture of rat cortical neurons for 5 days. Both cell lines were exposed to GSM 900 MHz (SAR = 1 W/kg). They found a reduction of the number of neurites generated by both cell systems ($p<0.05$). The experiments were performed blinded. This alteration correlates to increased expression of the mRNA of β-thymosin, an actin-sequestering protein involved in the molecular pathway regulating branching, outgrowth and sprouting. [The exposure system set up employed in this paper is described in detail in Del Vecchio et al. (2009b).]

Samsonov and Popov (2013) investigated the influence of a 94 GHz EMF on the assembly/disassembly of neuronal microtubules in *Xenopus* spinal cord neurons. Since the microtubule array is regulated by a large number of intracellular signalling cascades, it may serve as a sensitive reporter for the biochemical status of neuronal cytoplasm. They found that exposure for up to 60 min increased the rate of microtubule assembly ($p<0.01$; 24 experiments), and concluded that the effect was entirely attributable to the rapid EMF-elicited temperature jump. They reported that the intensity of the incident beam was measured with a power-calibrated crystal detector, and that each 1 mW of the forward radiation launched a wave with a nominal power density of 310 W/m^2 into the cell layer under the waveguide aperture. Positive controls were not included in the study design.

Table 5.4.3. In vitro studies assessing effects of RF EMF exposure on cell morphology

Cells Number of independent experiments	Biological endpoint	Exposure conditions	Results	Comment	Reference
Human astrocytoma cell line U-87 MG n not reported	Cell shape	835 MHz 0.081 ± 0.03 or 0.4 ± 0.15 kW/m^2 20 min, 3 times/day for 7 days	Flattened spread shape, loss of cell surface projections.	For cell proliferation see 12.3.6. No information on blinding of staff.	French et al. (1997)
Hair cells of the organ of Corti from newborn rats (postnatal day 3–4) n=15	Cell shape	900 MHz, GSM Average SAR 1 W/kg 24 h	No effect.	For auditory functions see 6.4.1.	Aran et al. (2004)

Primary cultures of hippocampal neurons n=3	Neuronal phenotype maturation	1800 MHz, GSM Average SAR up to 1.8 W/kg Up to 84 h	Decrease in dendritic development at the highest SAR.		Ning et al. (2007)
Mouse SN56 neural cells Primary cultures of cortical neurons n=3	Neuronal phenotype maturation	900 MHz, GSM Average SAR 1 W/kg Up to 5 days	Reduction in the number of new neurites.	Increased expression of mRNA of β-thymosin.	Del Vecchio et al. (2009a)
Studies on non-mammalian cells					
Xenopus spinal cord neurons n = 24	Assembly/disassembly of neuronal microtubules	94 GHz Nominal power density 310 W/m^2 1 mW forward radiation	Increase in the rate of microtubule assembly.	Thermal effect. No information on blinding of staff.	Samsonov and Popov (2013)

"No effect" means no statistically significant effect

Abbreviations: GSM: Global System for Mobile Communication; SAR: specific absorption rate

Excluded References

(Inoue et al., 2008)

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