Section 11

Effects of Exposure to Radiofrequency Waves from Mobile Phones on Neurophysiology and Cognitive Performance

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Summary

- The question posed in this section is whether there is convincing evidence of non-cancerous effects on the brain from exposure to radiofrequency (RF) waves from mobile phones.
- All of the primary studies cited by the five reviews referenced has assessed the effects of RF exposures to the head from mobile phones. Mention was made in one review of three recent negative studies of base-station exposures.
- There is no evidence to date that exposure to RF from mobile phones has adverse effects on cognitive performance as measured by neurobehavioral tests of memory and attention.
- A consistent effect on brain physiology was of enhanced alpha brain wave activity.
- Among studies with positive effects, it was the pulsed modulation of second generation GSM mobile phone system that was associated with neurophysiologic changes.
- The positive results of some of the newer neurophysiologic techniques, such as measurement of increased brain glucose metabolism in the area of the brain near the RF-emitting antenna, suggest the possibility of subtle effects on brain physiology from exposure to RF, although the significance of such findings on behaviour or health is unclear.

11.1 Introduction

A major concern about exposure to RF is whether there are adverse effects on cognitive function. The highest personal exposures to RF are from mobile phones held to the head. Such symptoms as impaired concentration, tiredness, irritability and headache, are common complaints associated with exposure to sources of RF, as elicited through cross-sectional surveys.[1] Whether there is a physiological basis for these symptoms is unknown. Persons who suffer health problems attributed to exposure to RF are referred to as having "electrohypersensitivity" or "idiopathic environmental intolerance attributed to electromagnetic fields." This syndrome and studies of symptomatic complaints associated with RF are described in Section 12.

The perception and reporting of health symptoms is a subjective process. Although more objective invasive measurement techniques can be done on animals and using cell lines, it is problematic to extrapolate these findings to humans. Therefore only studies of human brain activity and cognitive performance ascertained through non-invasive physiological provocation techniques and neurobehavioral testing will be considered in this section. Provocation studies, which comprise an experimental (exposure) and sham (with no exposure) condition, ideally with double-blinding so neither the subject or investigator are aware of the exposure condition, are appropriate for determining acute effects of RF fields. A discussion of biological effects, including results of animal studies are offered in Section 6. The focus of this section is to assess recent literature reviews concerning the effects of RF exposure on human neurophysiology and cognitive performance of healthy normal volunteers, with reference to representative studies.

Personal exposure to RF is highest for mobile phone use (see Section 5). As such, almost all of the studies on brain activity and behaviour are strictly on exposures from mobile phones. The question addressed is: "Is there convincing evidence of non-cancerous effects on the brain from exposure to RF from mobile phones?"

11.2 Methods

11.2.1 Article search strategy

Recently published scientific articles were searched through the OvidSP Medline database and with Google Scholar from 2009 to 2011. With Medline, the following search terms were used: electromagnetic fields/ radiowaves/ cellular phone/ microwaves, along with the keywords "radiofrequency," "radiation" and "EMF"; these were combined individually with the search terms: neurobehavioral manifestations/ cognition/ and keywords "cognitive function," "psychomotor performance" and "neurophysiological." Of 318 articles found, 267 remained when limits of "human" and "English" were applied; further limits to publication years 2009 to 2011 resulted in 28 scientific articles. After reading through titles and abstracts for review articles which presented an overview of mobile phone effects on human neurophysiology or cognitive performance, three published review articles were found (van Rongen et al., 2009[2]; Regel and Achermann, 2011[3]; Habash et al., 2009[4]), supplemented by Google Scholar search results of two additional review articles (Kwon and Hamalainen, 2011[5]; Valentini et al., 2010[6]). Findings from a condensed master's thesis (Brouwer, 2010[7]) was cited in the text. Illustrative study examples were chosen from the review reference lists and literature searches of more recent publications.

11.2.2 Included published review studies

A description of the characteristics of the five review studies which were published in peer-reviewed journals is given in Table 1.

Table 1. Selected general reviews on neurophysiological and/or neurobehaviorial effects associated with exposure to RF from mobile phones (2009–2011)

	Kwon & Hamalainen (2011)[5]	Regel & Achermann (2011)[3]	Valentini et al. (2010)[6]	Van Rongen et. al. (2009)[2]	Habash et al. (2009)[4]
Type of Review	Narrative with search strategy	Systematic	Systematic, with meta-analysis	Narrative	Narrative with search strategy
General Topic	Brain physiology & behaviour	Neuro-behavioral	Neuro-behavioral	Brain physiology & behaviour	Health effects in general
Databases	Pubmed & Web of Science	Pubmed & Web of Science	Medline + 9 databases	Not given	Pubmed, Embase, Medline
# Studies	105	41	42	Not given	Not given
Period	1997–2009	1998–2009	Not given	Not given	2004–2007
Conclusion on RF Effects	No effects or inconsistent findings	Inconsistent findings; no mechanism	No effects	Minor effects of GSM on physiology, but not behaviour	Small effects on physiology but no auditory effects

The review by Habash et al. (2009)[4] encompassed a broad range of health effects, including results of neurobehavioral and neurophysiology tests. Only one review, Valentini et al. (2001),[6] presented a meta-analysis including a forest plot of the common risk estimate of the relationship between RF and specific neurobehavioral tasks. This publication had the most detail of the review process, including over 8000 studies screened, but only one reviewer assessed the studies, whereas two reviewers are recommended for systematic reviews.[8] Other reviews relied on a narrative approach, including critique of the selected studies (particularly for the review by Regel and Achermann (2011)[3]. For three of the five published reviews,[2,3,6] no descriptions were given of the physiological or neurobehavioral tests undertaken (other than naming them) or the rationale for their use.

11.2.3 Interpretation of study validity

Study design is an important consideration as to whether the findings are valid and reproducible. Experimental provocation studies with a sham (no exposure) condition are best suited for evaluation of cognitive function. Provocation studies typically comprise one or more experimental conditions of a genuine RF field exposure (such as different levels of intensity) and a sham exposure. A crossover double-blinded design where subjects serve as their own controls and are randomly assigned to a specific exposure order (including sham exposure) is preferable. Double blinding, such that neither the subject nor the investigator is aware of the type of exposure applied, helps to avoid bias. Adequate sample size is needed for good statistical power, which is the probability of detecting a change (at a selected probability level such as $p < 0.05$), given that a change has truly occurred.

For the majority of studies, exposures were from mobile phones with Global System for Mobile Communication (GSM) signals, typically having a frequency of 900 MHz with pulse modulated signals at 217 Hz. These systems have been widely used in second generation (2G) systems since the 1990s, and are still used in some of the third generation (3G) systems, particularly in Europe. A number of newer studies also evaluated the 3G Universal Mobile Telecommunications System (UMTS) introduced in the 2000s. It has a frequency of approximately 2100 MHz and uses the Code Division Multiple Access (CDMA) channel system which is characterized by a more continuous signal that is not pulsed (but with some amplitude variations at 1500 Hz due to adaptive power control).

Differences in exposure set up and dosimetry affect the amount of exposure of the cerebral cortex to RF.[3] Typically a modified commercial or generic mobile phone is used but there are differences between phone models and phone positioning (hand held or contacting the ear directly, right or left side of the head or both) and sometimes the only exposure is from the antenna. Carrier frequencies and pulse moderation affect the type of signal (e.g., GSM signals often use 900 Mz with 217 Hz pulse moderation). The strength of the field can be described as power in watts (W), power density (W/m^2) or specific absorption rate (SAR, the power absorbed per mass of tissue, measured in W/kg), which are difficult to compare. Relying on the peak SAR of the manufacturer does not give information on the degree to which the brain regions of interest are effectively exposed.

Often a single study involves the analysis of many different outcomes (and therefore testing of many hypotheses), particularly for neurobehavioral tasks. For example, if the probability against rejection of the null hypothesis is set at 5%, then one out of 20 comparisons could be significant on the basis of probability, when there is actually no statistically significant association between the studied variables. Whether or not to correct for multiple comparisons is controversial. According to Rothman, by adjusting for multiple comparisons (to reduce type I error, rejecting the null hypothesis of no effect), type 2 error is increased (accepting the null hypothesis, although the alternative hypothesis is true) leading to errors of interpretation and possibly missing important findings.[9]

11.3 Results

Findings from the recent reviews and examples of individual studies are organized according to “neurophysiology” (human brain activity) and “cognitive performance" ascertained through neurobehavioral testing.

11.3.1 Neurophysiology

11.3.1.1 EEG studies

A common method to evaluate human brain activity is by determining spontaneous base-line changes in electrical activity of the brain in the absence of a specific sensory stimulus through the application of electroencephalography (EEG), as recorded from electrodes positioned on the surface of the volunteer's scalp. Because there are wide variations between subjects in their EEG patterns, a crossover or "within-subject design" is necessary. Electrical activity occurring at the surface of the brain appears as waveforms of varying frequency and amplitude. Recording ongoing background activity of the brain is referred to as resting EEG, measured by calculating the power of each frequency band. Rhythmic brain activity is divided into different frequencies, consisting of the delta, theta, alpha, beta and gamma bands, which are bandwidths of increasing frequencies from <4 Hz (delta) to >30 Hz (gamma), obtained through spectral analysis of EEG signals. Most waves of 8 Hz and higher frequencies are normal findings in the EEG of an awake adult. Waves with a frequency of 7 Hz or less often are classified as abnormal in awake adults, although they normally can be seen in adults who are asleep. Sleep EEG is recorded continuously during sleep, using measurements of characteristic patterns of brain oscillatory activity for each phase of sleep. EEG waveforms of an appropriate frequency may be considered abnormal when they occur at an inappropriate scalp location or demonstrate irregularities in rhythm or amplitude.

The normal alpha rhythm has a frequency of 8–12 Hz and appears with eyes closed while relaxed. The alpha band is usually associated with cognitive inhibition and visual relaxation, including transition to sleep. Alpha activity disappears normally with attention (e.g., mental arithmetic, stress, opening eyes). Many of the studies on RF effects on EEG have been inconclusive. However, a relatively consistent finding from exposure to RF is enhanced alpha activity (at 8–12 Hz) in resting EEG, particularly in the older studies of 2G GSM exposures.[2,5] Enhanced spectral power (increased activity) in the alpha band in the sleep spindle frequency range (brain activity during stage 2 non-rapid eye movement sleep) has also been noted. No observed effect on resting EEG or during sleep has been found using 3G UMTS (non-pulsating) signals. While GSM signals resulted in minor effects on alpha and beta power during sleep, there was no effect on sleep latency, or any other indication of adverse health effects.[2] It was concluded by Habash and colleagues[4] in their update of the 1999 Royal Society of Canada report that, while there is some evidence to suggest that mobile phone RF exposure may lead to changes in brain activity, further research is needed to address study limitations and explore mechanisms underlying any effects.

This conclusion was supported by Marino and Carrubba[10] who undertook a thorough critical analysis of reports published prior to 2009 on RF effects on baseline EEG and on event-related potentials (a change in the EEG due to specific sensory or cognitive stimuli). They concluded that the question on the pathophysiology of mobile phone use as reflected in brain electrical activity not only remains unanswered but unaddressed. In general, the 55 reports had attempted to study a nonlinear phenomenon using linear methods without proper controls while failing to consider experimental artefacts (a spike at the input occurs each time the stimulus is applied or removed) or the role of chance. Non-linear analysis was seldom applied, yet real effects can disappear due to averaging with linear analysis (such as ANOVA) as the stimuli produce both increases and decreases in brain alpha, for example. Almost all reports assumed incorrectly that the brain was in equilibrium with its surroundings and failed to distinguish low frequency EMF effects (from mobile phone batteries) from RF. Of the 55 reports on brain electrical activity, 48 were funded partly or in whole by the mobile phone industry.

Examples of EEG studies: An objective of the study by Kleinlogel and colleagues (2008)[11] was to investigate the effects of the new 3G UMTS technology on resting EEG.

Methods: The randomised crossover design with double-blinding involved 15 healthy male subjects (age range 20–35 years) being tested in a shielded room after fixation of EEG electrodes. The subjects were regular mobile phone users, without reported sensitivity to EMF and had normal hearing and vision and no history of major medial, neurological or psychiatric disorders nor head injury or substance abuse. Alcohol and mobile phone use were prohibited 12 hours before testing, while coffee and smoking were not allowed two hours prior.

After vigilance controlled resting EEG (eyes either closed or open while pressing the mouse key to a random tone) either the sham-exposure or the specific RF exposure was applied. RF signals were from an antenna, with either 2G GSM-exposure or 3G UMTS-exposure at weak (no modulation) and at high levels.

Results: There was no main effect of short-term exposure differences by type of exposure on vigilance control resting EEG (with frequency bands combined) before, at the start, at the end, or after exposure. The alpha1 band for the comparison of conditions was closest to being significantly lower at the start of exposure to the UMTS (weak) model (p=0.08). It was concluded that the study provided no evidence of short term effects of pulsed GSM 900 MHz or UMTS 1950 MHz EMF on resting EEG. The authors acknowledge limitations of small sample size, which allowed only strong effects to be detected and the pulsed test signal not conforming to that of a typical GSM-EMF mobile phone.

The study by Croft and colleagues (2010)[12] was the first to consider effects of RF on the EEG of different age groups.

Methods: The subjects were 41 adolescents (13–15 years of age), 42 young adults (the typical group studied, 19–40 years of age) and 20 older adults (55–70 years). All were healthy volunteers (those who were smokers, had substance abuse, hearing problems, head injuries, or history of personal or family psychiatric disorders were excluded). For 24 hours prior to testing, no alcohol or caffeinated beverages were to be consumed.

A double-blind, counterbalanced, crossover design (recommended for experimental human studies) was used, with each subject tested in a shielded room under Sham, 2G pulsed (GSM) and 3G (UMTS) conditions. Two cognitive tasks were undertaken with order counterbalanced across subjects either for an auditory oddball discrimination paradigm (responding to auditory stimuli that are dissimilar to the majority of auditory stimuli presented) or n-back test (indicating when the current stimulus matches the one from n steps earlier in the sequence), each followed by resting EEG, cessation of exposure, and a further resting EEG. The 2G exposure was through a Nokia 6110 mobile phone (using GSM technology) with the speaker removed to avoid audible sound and there was 50 dB background white noise generated. The 3G exposure was through use of a dummy model shaped like a typical mobile phone.

Results: Alpha power was greater in the 2G compared to Sham condition in the young adults (p=0.043). There was no increase in the 2G alpha power for adolescents (p=0.619) or older adults (p=0.47). For the 3G exposure compared to Sham, there was no main effect in adolescents (p=0.274), young adults (p=0.577) or older adults (p=0.557)). The authors concede that study limitations include low statistical power, given the small effect size. They concluded that the study supported the observation that effects on brain activity (alpha power) were more marked from the pulsed (2G) than the continuous (3G) RF exposures. However, it is unknown what the functional significance would be for an increase in alpha power in young adults.

Commentary on the studies by Kleinlogel et al. (2008)[11] and Croft et al. (2010)[12]: Both used appropriate experimental designs and included exposures from GSM and UMTS RF. Kleinlogel et al. included smokers (unlike Croft et al.) but purposely chose subjects without sensitivity to EMF. Combining the EEG bands for initial analysis does not allow any speculation as to physiological mechanisms since each band is associated with different properties. A further limitation of this study was not using actual mobile phones. Their version of the UMTS "weak" phone was found to affect the alpha1 band (of a narrower frequency range), unlike the more powerful UMTS "high" exposure model. This result puts into question the adequacy of the surrogate exposure. Prior to Bonferroni correction for multiple comparisons, this association would have been statistically significant and difficult not to emphasize. Croft et al. tested males and females but did not determine if there were sex differences and used less powerful non-parametric data analysis methods; however, the unique contribution of their study was demonstrating age group differences, as typically, studies use young adults only (such as Kleinlogel et al.'s). On balance, the study findings of Croft et al., which showed an increase in alpha power of young adults exposed to 2G RF, appeared to be more convincing.

11.3.1.2 Auditory and vestibular organ studies

The inner ear's receptor structures of auditory and vestibular organs absorb most of the radiation energy from the antenna of the mobile phone. The inner ear, being in closest proximity to the mobile phone, would be expected to have a high absorption rate of RF leading to higher energy deposition in the cochlea. Findings of effects on otoacoustic emissions (sound signal generated from the cochlea to the outer hair cells) and auditory brainstem response (electrical response evoked from the brainstem by a sound stimulus) were mostly negative, based on short-term exposures to RF.[2,5]

Examples of Auditory Processing Studies: The aim of the study by Paglialonga and colleagues (2007)[13] was to assess subtle changes in cochlear function by measuring transiently evoked otoacoustic emissions (TEOAE, a standard validated method to determine cochlear outer hair cells functionality through measurement of dynamic changes) after exposure from GSM EMF signals.

Methods: Participants were 17 males and 12 females 23–30 years of age with no hearing disorders as determined by testing and questionnaire. A within-subjects double-blind study design was done, using a sham exposure and a commercially available GSM phone (NOKIA 6310) at 900 MHz and 1800 MHz. Using a phantom model, maximum SAR values of 0.41 and 0.19 W/kg were found for the 900 MHz and 1800 MHz frequencies respectively, which were much lower than the 2 W/kg limit.

Results: No significant differences were shown for the TEOAE parameters of mean energy and latency contrasting sham versus exposed conditions to a GSM mobile phone. Any observed changes in the parameters were suggested as random variation and not attributed to exposure.

Concern about possible auditory system effects of UMTS RF phones (as opposed to GSM mobile phones) was the basis for the study by Parazzini and colleagues (2009).[14]

Methods: Men (n=61) and women (n=73) 18–30 years of age had to have no evidence of hearing or hearing disorders based on testing and questionnaire responses, from which data was recorded using the ear with the best auditory results. Glasses and earrings were removed. A within-subject double-blind counterbalanced design was used. Auditory function measurements were in the following order:

- pure tone audiometry (PTA measures hearing threshold level, thus enabling the determination of the degree, type and configuration of hearing loss)
- auditory evoked potentials (AEP is a recording of brain electric voltage potentials from auditory frequent non-target and infrequent target stimuli)
- distortion product otoacoustic emission (DPOAE uses stimuli of two pure tones and two sound levels to record otoacoustic emissions that indicate cochlear or inner ear health)
- contralateral acoustic stimulation during transiently evoked otoacoustic emissions (CAS effect on TEOAE uses a brief acoustic click in the contralateral ear, allowing functional exploration of the auditory efferent system synapsing with the cochlear outer hair cells).

Speech at conversational level was delivered through an insert earphone (not through the mobile phone handset) to one ear and a UMTS mobile phone (Nokia 650) at another. SAR measurements made by phantom using the touch position of the phone, resulted in a level of 69 mW/kg for the 1947 MHz frequency of the UMTS phone at a 30 mm distance (approximately to the cochlea), which is well below the standard of 2 W/kg.

Results: After exposure to UMTS, the hearing threshold limit was increased particularly at 500 Hz (p=0.02) and at 2–8 Hz averages (p=0.03), but this was no longer statistically significant with statistical adjustment for multiple comparisons. The findings of all other audiometric tests showed no statistically significant differences and therefore there was a lack of corroboration. It was concluded that there were no general effects on the human central or peripheral auditory system due to short-term (20-minute) exposure of a UMTS phone. This study had an adequate sample size, supported by a priori sample calculations, and excellent protocols, similar to the previous study by the same authors on the possible effects of GSM phone signals on auditory function, which also concluded that there were no effects of RF on the audiological measures.

Commentary on the studies of Paglialonga et al. (2007)[13] and Parazzini et al. (2009)[14]: The study by Paglialonga and colleagues was the first to look at effects of exposure to RF on energy and latency of TEOAE. However, by only presenting one type of auditory test, there is no chance to simultaneously evaluate other tests of cochlear function. The sample size was small (n=29) and the exposure duration of 10 minutes was relatively short in duration. Despite applying two different frequencies of GSM, any differences in results were not presented. The authors were careful to assess whether the data was normally distributed and not skewed and applied appropriate transformations to each parameter and then used MANOVA, which is ideal for repeated measures designs with more than one dependent variable. However, the limited sample size (especially if 50% of the subjects had a different exposure to RF) puts into question whether this powerful type of analytical tool was appropriate; as well, no “F” statistic nor p-value was given. The study by Parazzini et al. presented an analysis of a number of tests of auditory function. The sample size was larger (n=127) and exposure duration was longer, at 20 minutes. A negative aspect is the statistical analysis. Unlike the findings of Paglialona et al., all measures were regarded as “approximately” normally distributed and therefore a simple paired t-test was used to compare the sham and exposure conditions for all outcomes. Because each subject only underwent a sham and exposure trial, this analysis is reasonable, however correlations between outcomes complicates the analysis. The Parazzini et al. study presents a more convincing demonstration of the lack of effect of UMTS RF on auditory function.

11.3.1.3 Studies of cerebral blood flow and volume

Positron emission tomography (PET) scans (nuclear imaging technique for producing 3D images of functional processing, including cerebral blood flow), magnetoencephalography (measurement of magnetic field, produced by brain electrical activity) and transcranial magnetic stimulation (which induces weak electrical currents in the brain with rapidly changing magnetic fields) and near infrared spectroscopy (NIRS) (a noninvasive optical imaging technique which measures hemoglobin concentration changes in the brain and changes in regional cerebral blood volume) are among the newer neurophysiological techniques employed to assess the effect of mobile phones on brain physiology. However, these have shown mixed results (e.g., cerebral blood flow either increased and/or decreased in specific brain areas) and the positive findings (such as altered event-related magnetic fields, reduced short intracortical inhibition and increased intracortical facilitation) are difficult to interpret.[2,5] For instance, in a much publicized recent study by Volkow et al. (2011)[15] PET scans were used on subjects exposed to cellular phones with CDMA (G3) modulation. They concluded that: "In healthy participants and compared with no exposure, 50-minute mobile phone exposure was associated with increased brain glucose metabolism in the region closest to the antenna. This finding is of unknown clinical significance."

Examples of PET studies: The purpose of the study by Aalto and colleagues (2006),[16] was to determine the main effects of RF on regional cerebral blood flow (rCBF) using positron emission tomography (PET) imagery.

Methods: Healthy right-handed male volunteers (n=12) abstained from caffeine, nicotine and alcohol for 24 hours prior to the study, and from mobile phone use that day. An MRI was undertaken to exclude those with brain structural abnormalities. A double-blind counterbalanced within-subject design was conducted with subjects performing a simple neurobehavioral (memory) task during the PET scans and sham conditions. The 1-back memory task involved responding to a "yes" key to a particular letter on the computer screen (if it was the same as the previous letter); otherwise the "no" key was pressed. A factory model GSM phone was used with both the loudspeaker and battery removed, as previously it was noted that even subliminal noise might induce a change in rCBF in the auditory cortex. The subject also had an earplug in the left ear to avoid noise from the operation of the phone. The SAR measurements, using a phantom was 0.743 W/kg for 10 g tissue, with an extrapolated peak value of 1.51 W/kg.

Results: A decrease in rCBF was found during RF exposure at the site of peak EMF in the brain, while an increase in rCBF was seen in other lobes of the brain. The RF had no effects on reaction times (p=0.56) or accuracy of responses (P=0.37). The authors speculated that frontal cortex changes in rCBF may reflect changes in neuronal activity but would not be related to facilitation in cognitive performance. They conclude that "our results do not provide any evidence to suggest that use of mobile phones would be more harmful to brain tissue than normal cognition, which is also always accompanied by intense temporary changes in neural activity and rCBF."

The aim of the study by Volkow and colleagues (2011)[15] was to determine whether acute mobile phone exposure affects brain glucose metabolism, measured by using PET with injection of fluorodeoxyglucose (FDG). The rationale is that brain glucose activity is a better marker of neuronal activity than using PET alone to measure cerebral blood flow.

Methods: Analysis was done on 47 healthy paid volunteers screened for absence of medical, psychiatric or neurologic diseases or addiction. Urine testing confirmed no psychoactive drug use. The within-subject crossover randomized design was blinded only for the subjects. FDG uptake was through sampling of arterial blood. Two mobile phones (Samsung model SCH-U310 mobile phones with code division multiple access modulation, 3G, were used). Exposure from the right mobile phone was started 20 minutes prior to FDG injection and maintained 30 minutes after. The mobile phones were then removed and participants underwent emission and transmission PET scans using whole body tomography.

Results: Whole-brain glucose metabolism showed no differences in glucose metabolism, however there were significant regional effects. In the region closest to the cellular phone antenna, there was an increase in glucose metabolism and no decreases were noted. They concluded that the human brain is sensitive to the effects of RF from acute mobile phone exposure and brain absorption of RF may enhance the excitability of brain tissue in regions close to the antenna, as measured by increases in glucose metabolism.

Commentary on the studies by Aalto et al. (2006)[16] and Volkow et al. (2011)[15]: Both studies evaluated subtle acute effects of mobile phone RF on brain physiology. In the study by Aalto et al., double blinding was used and scans were taken during the EMF or sham modes, all done while a simple memory task was used to minimize random variation in rCBF. In addition, they set out to determine if the physiological measures were associated with task performance (they were not). The results were inconclusive in that both decreases and increases in rCBF were found, similar to what would be seen in normal cognition. On the other hand, the 2011 study by Volkow et al. used FDG to evaluate glucose metabolism as a more direct and longer lasting indicator of brain activity. Negative aspects were not calculating SAR using phantom modelling, but just reporting the model specifications and not removing the phone battery, as done by the Aalto study. PET measurements were done after exposure, and not during. However, the results were more consistent with all measurements showing increased glucose metabolism when exposed to RF from the cellular phone.

11.3.2 Neurobehavioral testing

Neurobehavioral tests typically are non-invasive computer administered tests used to describe cognitive function constructs such as “attention” and “working memory.” Tests of attention require vigilance and focus when responding to changing visual presentations, while tests of memory require short-term recall of a previous visual presentation. As with neurophysiological studies, there are mixed findings on cognitive performance measures attributed to exposure to RF. Regel and Achermann[3] conducted a systematic review of 41 provocation studies (1998–2009) on mobile phone exposures between 1998 and 2009. For over one half of the studies concerning exposure to mobile phone RF, no behavioural changes were found; six of the studies noted improvements in performance speed, whereas seven showed decreases in performance. Accuracy of performing the test was worse in two studies, but improved in four studies.

According to Valentini and colleagues[6] it is only the tasks involving reaction time that appear to be affected by RF exposure, but this finding was weak, with the more recent studies showing negative outcomes when attempting replication of previous positive results or applying stricter statistical methods. They cited a previous meta-analysis[17] which showed the most consistent finding to be decreases in reaction time (improved performance) in a subtraction task.

There were no significant effects of 3G UMTS signals in any of the cognitive performance tasks as reviewed by Kwon and colleagues.[5] As well, Valentini et al.[6] did not find positive studies of neurobehavioral effects with longer-term exposure to RF such as testing with two-hour daily exposure over three weeks. In general, studies of cognitive function have generally found no correspondence between cognitive performance and changes in neurophysiological parameters.

All studies focused on RF exposure from actual or constructed mobile phones, with the exception of Kwon et al. (2011),[5] who cited three recent studies of base station-like exposure (far-field RF). Exposures to RF fields from base stations are usually much lower than exposures from mobile phones. These studies fulfilled basic inclusion criteria of having controlled exposures, being double blinded and having a sham exposure. All findings were negative for any effects of either GSM or UMTS exposures on a variety of neurobehavioral task results, when compared to sham exposures. An example is the study by Regel et al. (2006) (cited in Kwon and Hamalainen[5]). They used a controlled randomized double-blinded crossover design to evaluate cognitive performance after exposure to a UMTS base station-like signal at two different strengths and a sham condition. While they did observe some slight but significant differences in speed of the choice reaction time and in reduced accuracy of a separate task (out of 44 tests) at the higher level of exposure, this was no longer significant upon adjustment for multiple comparisons. They concluded that the marginal effects found may be due to chance. Prior studies had problems with poorly defined exposure, inconsistencies in cognitive outcomes and differences in design (such as not taking into account circadian rhythm effects), blinding, study population and sample size.

Examples of studies on neurobehavioral testing: The study by Cinel and colleagues (2008)[18] evaluated effects of mobile phones on short-term memory and attention at two cognitive loads, using a randomized double blinded design.

Methods: A large number of male (n=160) and female (n=168) subjects took part (most being university students) in two experiments. The mobile phone was positioned on the left side of the head for half the subjects and the right side for the others.

For experiment 1, subjects were tested in a manner performing a vigilance task (deciding whether one of three designated letters was shown earlier as a single or string of letters) and n-back task (a short-term memory task choosing a current stimulus which was shown earlier in the sequence; letters and faces were used). In experiment 2, 168 volunteers performed a Stroop attention task (used to study suppression of automatic responses by naming the number of items per string), a Sternberg task (short-term memory, in which four or six black and white pictures were followed by a simple arithmetic calculation, and then a previous picture was shown) and a visual search attention task (random display of 5, 15, or 30 coloured letters, indicating if a target letter was present). The exposure was either to a GSM modulated signal from a mobile phone, to unmodulated signals also having 888 MHz, or to sham. The average SAR (calculated, not measured) was 1.4 W/kg for both phones, but for the GSM mode the peak was 11.2 W/kg.

Results: For experiment 1, the only significant results were related to cognitive load, e.g., the reaction times in the 2-back tasks were faster than the 3-back task. There were no effects of RF exposure on performance for any task (reaction times and accuracy). The authors concluded that there were no significant effects from exposure to RF detected in any of the six tasks used in either the low or high cognitive load conditions. They discounted the results for one task, the Stroop task under a low cognitive condition, where there were faster reaction times in the control condition (i.e., slower times when exposed, although no indication of phone type was given). Accuracy of performance showed an opposite pattern of improvement when exposed to RF. The authors speculate that other aspects of cognitive function, apart from short-term memory and attention, may respond to RF and that longer-term exposure may have an effect on cognitive function.

The aim of the study by Unterlechner and colleagues (2008)[19] was to evaluate the cognitive effects of RF from UMTS signals (as opposed to GSM mobile phones, which were studied previously).

Methods: Young adults (20 men and 20 women; mean age 26 years) had to have no evidence during selection and at each test day of physical or mental illness; physical or psychological overwork; sleep disorders or chronic sleep deprivation; excessive use of caffeine, nicotine or alcohol; or medications. The subjects underwent four different computer tests measuring reaction time and attention under three exposure conditions (high, low, and sham) while in a shielded experimental room.

- The Vienna reaction test registers selective attention through a specific combination of presenting two coloured lights and a tone, given individually or simultaneously.
- The vigilance test measures sustained attention by subjects tracking a leap movement of a shiny point moving clockwise on a circle.
- The Vienna determination test registers divided attention, with the subject reacting to displays of coloured lights and tones.

- The flicker and fusion frequency test registers the optic fusion threshold by determining the frequency when a flickering light becomes constant, and vice-versa.

The order of tests was “pseudo-random” and testing was double-blinded. Exposure was from a generic 3G UMTS signal representing a wideband code division multiple access signal, given at two exposure levels. For the high exposure condition, maximum 10 g-averaged SAR in the brain cortex of the temporal lobe was 0.37 W/kg. Low exposure was 1/10th as much. Subjects sat in a shielded exposure cabin with RF absorbing material on the inner surfaces.

Results: The exposure levels (high, low, and sham) had no effect on any of the different components of attention, as determined by the reaction time, motor activity time and the number of correct and false responses, nor on mean flicker frequency or fusion frequency, nor was there an effect of gender. The authors concluded that a UMTS mobile phone-like exposure does not have an acute effect on attention or reaction time, but the results did not pertain to other cognitive parameters or to long-term effects.

Commentary on the studies by Cinel et al. (2008)[18] and Unterlechner et al. (2008)[19]: The studies used neurobehavioral testing paradigms, which included constructs of attention and vigilance. Cinel et al. added a short-term memory (n-back) task while Unterlechner et al. also evaluated CNS function through testing of the optic fusion threshold. Both studies gave a good description of the tests and their rationale. Positive aspects of the Cinel et al. study were the large sample size and the two levels of “cognitive load” difficulty of the neurobehavioral tasks. However, the conclusion was generalized to there being no significant effects from exposure, despite the data showing that there was a faster reaction time on average in the control condition for the Stroop test; that is, performance was worse during the mobile phone exposure. As well, the rationale given for discounting the Stroop test findings (that it did not correspond to the reaction time results), is not necessarily appropriate, since they may indicate different cognitive functions. In addition, the stringent exclusion criteria such as psychological overwork and taking of medications would affect generalizability of their findings to a large segment of the population.

In the Unterlechner et al. study, testing was done each time in the same period of the afternoon, a voiding possible circadian rhythm effects, but no power calculations were presented as to the choice of only 20 subjects of each sex, which appears to be statistically underpowered. It would have been of interest to use the same protocol but with the GSM exposure as a comparison. Both studies end the discussion with the same caution that other aspects of cognitive function and long-term exposure effects were not assessed and may not have the same findings with regard to the lack of effect of RF.

11.4 Discussion

Widespread and increasing use of wireless technologies has raised concerns about possible health effects associated with exposure to EMF. Canadian and international standards for exposure limits are based on evidence of thermal effects on the human body. The potential for subtle cognitive effects of RF at levels below exposure limits based on thermal mechanisms is controversial. As stated by a scientific panel on EMF health risks[20]: "Life on earth did not evolve with biological protections or adaptive biological responses to these EMF exposures."

Are there neurophysiological and behavioural effects that can be attributed to exposure to RF?

The general conclusions of the five reviews of provocation studies involving acute exposure to RF (as shown in Table 1) is that there are either no effects or inconsistent results on neurobehavioral parameters and possible minor but inconsistent effects on brain physiology. There is little evidence of acute effects of exposure to RF from mobile phones on cognitive performance or auditory function. Confirmatory research using large representative samples is needed to establish possible effects of exposure to RF on human brain physiology and on cognitive function and performance.

Validity of the laboratory measurements is an important consideration. Have researchers measured appropriate surrogates of cognitive activity? Is an "abnormal" response associated with symptoms or illness? Neurobehavioral tests developed to discriminate differences between "normal" and "neurologically impaired" subjects may not be sensitive in distinguishing more subtle differences in response. On the other hand, effects judged to be harmless when experienced transiently following isolated acute exposures in the laboratory setting may have implications in real-life circumstances, particularly after long-term cumulative exposure to RF.[3]

A further consideration is whether an underlying biological mechanism can be identified to explain effects on brain activity and cognitive performance attributable to exposure to RF. Proposed hypotheses for non-ionizing effects on the brain from RF exposure include interference with brain electric oscillatory activity by pulsed GSM signals and activation of extracellular-signal related kinase (involved in cell signalling).[7] Currently, a mechanism by which RF from mobile phones and other communication devices may interact with neurologic tissue and function is unclear.

A wide variety of neurobehavioral tests have been applied as indicators of such cognitive constructs as short-term memory and attention; yet they lack reliability to sensitively measure the effects of RF exposure. In addition to timing, order and duration of tasks, performance is affected by circadian rhythms and handedness of subjects. Additionally, learning effects may override any treatment effects.[3] More objective measures, such as the EEG, are susceptible to artifacts which can occur with eye or body movements. Not only has the alpha rhythm shown poor scoring agreement, but up to 20% of the population has little or no measureable alpha rhythm activity under normal circumstances.[7]

Standardization of exposure conditions and detailed reporting would facilitate replicating results in different laboratories. Variation in exposure is known to occur with differences in mobile phone models and technology. For instance, studies on brain activity and behaviour generally show no significant effects of UMTS signals as opposed to the older GSM models with pulsed modulation. Realistically, individuals are exposed to multiple concurrent electromagnetic field exposures over long periods of time. For example, batteries in mobile phones are a source of EMF. Yet for practical purposes, assessing changes in brain function after short-term exposure to one source of RF is the norm.

A disadvantage of laboratory studies on human volunteers is the low power to detect a significant effect.[2] In addition to small sample size, failure to correct for multiple comparisons would result in an increased likelihood of false positive results. This is more likely to occur when there are modest effect sizes and few significant findings among many comparisons. Randomization of subjects and double-blinding help to mitigate possible effects of confounding and bias on the effect estimates obtained. Many of the early studies using single blinding (only the subject was unaware of their exposure status) could not be replicated with a double-blind design.[3,5] Newer studies generally incorporate improvements in study design such as reduced interference from environmental exposure to EMF, adequate study power, and appropriate statistical analysis.

The use of mobile phones, smart phones, tablets and other RF devices is a common form of communication and entertainment for youth, and increasingly so for children. Because the brain is particularly vulnerable to environmental insults during fetal development, childhood and adolescence, there is a need for further studies to ascertain whether there are effects during their developmental stages. For instance, a recent questionnaire-based study on mobile phone use during pregnancy (n=530)[21] concluded that there was no adverse effect on mental or psychomotor development of maternal mobile phone use during pregnancy on the early neurodevelopment of offspring. The anomaly was one statistically significant association of a lower psychomotor score for children whose mothers made at least five mobile phone calls per day in comparison to non-users. Further investigation is warranted to determine potential cognitive effects in children as well as adolescents. According to the AGNIR[22] the few existing relevant studies do not support the hypothesis that children are more susceptible to the effects of RF; however, the evidence is insufficient, particularly due to the small sample sizes in studies so far.

11.4.1 Gaps in the literature

A number of study issues still remain to be addressed to confidently answer the question "Is there convincing evidence of non-cancerous effects on the brain from exposure to mobile phones":

- determining biological plausible mechanisms of effects on the brain from low exposures to RF in order to characterize what properties of RF may affect neurocognition
- ascertaining whether subtle effects in cognitive function or brain activity manifest as behavioural changes, symptoms, and disability
- improving exposure assessment by considering effects from realistic levels of different mobile phone technologies and evaluating longer-term exposures
- simulating more realistic SARs which take into account the more sensitive nature of brain function (as opposed to absorption in any tissue)
- generalizing isolated laboratory exposures to real life situations of multiple exposures to ambient sources of RF
- including studies of RF effects during growth and development stages, including pregnancy and childhood, and on other vulnerable populations.

11.5 Conclusion

On the basis of current tests of memory and attention, the cumulative evidence to date does not support exposure to RF as having adverse effects on cognitive performance. Where an effect on brain physiology was observed (usually of unknown significance for behaviour or health), there was no corresponding effect on associated neurobehavioral tests.

Detailed measurement of exposure as well as dose, through improvements in the phantom models, will allow for generalizability of findings. In the majority of the study examples given, the SAR was measured to demonstrate that the power of the RF exposures applied was similar to “real world” situations, being less than allowable limits. The technology of wireless communication systems is changing rapidly. The pulsed modulation of the second generation GSM systems appear to have greater effects on neurophysiologic changes than does the third generation UMTS and other developing continuous wave RF applications.

The more consistent findings of EEG changes (particularly alpha frequency spectral power) and the positive results of some of the newer neurophysiologic techniques such as measurement of increased brain glucose metabolism, suggest subtle effects on brain physiology that may be better characterized with new types of measurements and carefully designed replicable larger-scale studies.

Given the broad exposure of the population on a voluntary and involuntary basis to many sources of RF, confirmation of associated effects on neurophysiology and cognitive performance would have important implications for public health. Studies of the pathophysiology of RF need to evolve with improved methodology for determining both exposure (and dose) and effect.

11.6 References

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