6 AUDITORY, VESTIBULAR AND OCULAR FUNCTION

Sensory organs include extremely specialized and finely organized cellular and tissue structures, in direct connection with the CNS. These traits imply that ocular and auditory organs are quite sensitive to external physical agents such as radiofrequency fields, as already depicted in the WHO report (1993). With the broad spread of mobile phones in the last decades, the eye and the ear are subjected to RF emissions including new frequencies and modulation patterns.

6.1 Auditory function and vestibular function

Intense pulsed RF fields can be perceived as sound. When short duration, high-level RF pulses interact with the head, the subsequent small and fast increase in temperature causes the induction of a thermo-elastic wave that, via the temporal bone, is conveyed to the cochlea. Hair cells identify this signal as a normal acoustic stimulus, perceived as a 'buzz, clicking, hiss, or knocking' sound. This is the so-called 'microwave hearing' effect, described in animal and human subjects (Elder & Chou, 2003; Lin & Wang, 2007; Seaman & Lebovitz, 1987). Due to its physical position, the hearing system could be involved in interactions with RF EMF emitted by cellular phones (Parazzini et al., 2007c). The fact that the cochlear sensory structure, and mainly the hair cells, are particularly sensitive to various exogenous agents (Hatzopoulos et al., 1999; Henley & Rybak, 1995; Wu, Sha & Schacht, 2002), should be carefully considered.

6.1.1 Epidemiological studies

The WHO Environmental Health Criteria document on electromagnetic fields from 1993 did not report any epidemiological studies on potential effects of radiofrequency fields on auditory or vestibular function. Since then, a few studies have been published, most of them investigating tinnitus. The search identified 14 epidemiological studies related to auditory function. One of the studies was written in Russian language and could not be evaluated, while of the 13 remaining studies, six did not provide enough information to fully assess the quality and are therefore only briefly described, and three were excluded as they did not fulfil the quality criteria.

A cross-sectional study of the prevalence of self-reported symptoms, including tinnitus, among university students in Rafsanjan, Iran, was conducted by Mortazavi and colleagues (Mortazavi, Ahmadi & Shariati, 2007). Participants were recruited from two universities in the spring 2005, and 518 participated (75%). Questionnaires included questions about mobile phone use, use of cordless phones, and cathode ray tube (CRT) video display units, as well as potential confounding factors. Students with at least 30 s of mobile phone use per day on average over the last three months were considered exposed, in total 30%. The same definition was used for cordless phone use; 36% reported being users of cordless phones. For CRT, the definition of exposed was average use at least one minute per day over the last three months, which was reported by 56%. The prevalence of tinnitus was 9.9% of all participants, and no significant differences in the prevalence of tinnitus were found between exposed and unexposed students for any of the exposure sources studied. [No odds ratios were reported and information in tables does not allow calculations of risk estimates. It is unclear if potential confounding was appropriately evaluated. The cross-sectional design does not allow assessment of whether the investigated exposures preceded tinnitus development.]

A hospital based case-control study of mobile phone use and acute and chronic tinnitus was conducted by Hutter and colleagues (Hutter et al., 2010) at the Ear-Nose-Throat department of the Medical University of Vienna, Austria. Patients aged 16 to 80 years were recruited consecutively as they visited the clinic from November 2003 to November 2004. Patients were excluded if they had diseases of the middle ear, post middle ear surgery status, retrocochlear disease, severe psychiatric and systemic diseases, medication with drugs that can influence tinnitus, or an underlying disease such as hypertension, noise-induced hearing loss. Controls were outpatients at the same clinic (e.g. phoniatric patients without speech disorders and without myognathic problems, acute laryngitis, patients about to have a tonsillectomy, acute pharyngitis), and were matched to cases on age, sex and ethnic group. Participation rates were 96% among cases and 93% among controls. In total, 100 cases and 100 controls were interviewed. About half of the cases had chronic tinnitus (i.e. that had lasted more than 3 months). Mobile phone use was assessed using a paper version of the Interphone questionnaire. Exposure was assessed up to the date of first occurrence of tinnitus and the corresponding date for matched controls. Unexposed was defined as never use of a mobile phone (for intensity of use) and never use or use <1 year for duration of use. Categorization of the exposure was made according to the median level among controls. In some, but not all analyses, the categorization was based on the distribution among controls with ipsilateral phone use. Having ever used a mobile phone was associated with an odds ratio of 1.86 (95% CI 0.74–4.65). Results for

ipsilateral and contralateral use were of the same magnitude, although both were lower than the overall result; OR=1.37 (95% CI 0.73–2.57) for ipsilateral and 1.31 (95% CI 0.65–2.44) for contralateral use, respectively. This pattern was seen for all exposure indices except for years of mobile phone use. The overall OR for >4 years of mobile phone use was 1.26 (95% CI 0.63–2.50), for ipsilateral use the OR was 1.95 (95% CI 1.00–3.80), while the corresponding result for contralateral use was 0.91 (95% CI 0.39–2.09). [The exposure definition had no lower limit for the amount of mobile phone use required to be classified as exposed. Retrospective reports of mobile phone use are prone to potential reporting errors, and for conditions that affect hearing ability, reporting side of the head where the phone was held prior to disease onset is especially problematic. It is unclear if the same exclusion criteria were applied to both cases and controls. No information was available on exposure to loud music in portable players, which might be related to both mobile phone use and to risk of tinnitus.]

In a cohort study performed in 2008–2009 in Switzerland by Röösli and coworkers (Frei et al., 2012; Röösli, Mohler & Frei, 2010), 1375 participants returned a baseline questionnaire (37% of contacted). One year later, 1122 participants (82% of baseline responders) answered a follow-up questionnaire with regard to changes in perceived health, measured through questionnaire-based scales and also including questions about tinnitus, as well as updated information about far-field and near-field RF exposure. Exposure to RF fields was calculated based on a validated method including information on RF transmitters and base stations, building characteristics of homes and amount of time the subject spent indoors, as well as use of mobile and cordless phones. Exposure to RF fields was also estimated as self-reported mobile and cordless phone use and operator recorded mobile phone use. In addition, participants were asked to rate if their personal exposure situation was lower, the same, or higher than the average Swiss population. The study found no association between any of the RF exposure estimates and tinnitus. [The statistical power of the study is limited due to the low number of new cases with tinnitus with only one year of follow-up].

A study of mobile phone use and hearing loss in children was conducted based on data from the Danish National Birth Cohort (Sudan et al., 2013), including 52 680 children born between 1996 and 2002. The data are part of a cohort of 91 661 women enrolled during pregnancy, although the analyses of hearing loss are based on cross-sectional data collected when the child was 7 years old. The child's mobile phone use was assessed through one question in a web-based questionnaire: "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". The outcome, permanent hearing loss, was also self-reported in the same questionnaire: "Does your child have permanent hearing loss?"; 1.6% reported hearing loss at age 7 years. In an earlier interview when the child was 18 months, mothers were asked about the child's reduced hearing, at which time 2.7% reported reduced hearing. However, only 6% of the children with reduced hearing at age 18 month were also reported to have permanent hearing loss at age 7 years. Analyses were made using three different methods; logistic regression, marginal structural models (MSM), and a combination of logistic regression and MSM. Adjustment was made for maternal factors during pregnancy (mobile phone use, alcohol use, smoking, fever), socioeconomic status, breast feeding, ear infection by age 18 months, sex, gestational age, and reduced hearing at 18 months. In total, 36% of the 7-year old children reported to use mobile phones, but less than 1% used them more than one hour per week. In the analyses of hearing loss, mobile phone use was dichotomized. All three types of statistical methods gave similar results, a slightly increased risk of hearing loss among children who had used a mobile phone, with borderline statistical significance (e.g. the OR with the traditional logistic regression model was 1.21; 95% CI 0.99–1.46) . [Very crude exposure assessment; the exposed group may include a large proportion of children who have used a mobile phone only occasionally, as may the unexposed group because of the large difference between unexposed and lowest exposed answer alternative ("no, never" and <1 h/week (the highest was >1 h/week), with no answer alternative in between). Hearing loss in the child as self-reported by parents may also be subject to considerable misclassification, which may not be random. The cross-sectional design does not allow determination of the temporality of the association, thus it is unknown if the hearing loss was already present when the child started to use a mobile phone. Analyses were not adjusted for potential co-morbidity which may be related to [perceived] hearing loss, and may cause parents to provide their child with a mobile phone for easy contact, e.g. recurring inner ear infections until age 7, severe asthma. Control of potential confounding from loud noise exposure, e.g. through portable music players, was not made.]

Studies with insufficient information for assessment of inclusion criteria

Six studies below recruited subjects in a way that does not allow calculation of participation proportions or assessment of potential selection bias. They are briefly described, but results are not included in the table, and they are given no or little weight in the overall assessment.

Oktay and colleagues (Oktay et al., 2004) performed a cross-sectional study in Turkey of people working in a 1062 kHz medium wave broadcasting station and living in employee residential houses near the station. All employees at one media broadcasting station volunteered to participate in the study. Persons with ear diseases (n=5) were excluded from the study, leaving 28 men in the exposed group for further testing. A control group of 28 men were age-matched to the exposed group, but information about how they were selected, participation proportion, or type of workplaces is not given, and prevalent ear diseases in the control group is not reported. RF-E fields in the exposed workplace were on average 4.04 V/m, and power density 0.063 W/m^2. The average noise level in the broadcasting station was 70 dB. In the exposed homes the E-field was between 0.48 and 2.86 V/m and the power density 0.001–0.023 W/m^2. For the unexposed group, workplace and home measurements were not reported separately; the E-field was reported to vary between 0.74 and 2.00 V/m, and the power density between 0.0000 and 0.011 W/m^2. Noise levels at the workplaces of the control group were not reported. Brainstem Evoked Response Audiometer (BERA) and Pure Tone Audiometry (PTA) were used to measure hearing functions of participants. BERA records brainstem responses to clicks in the ear, and PTA measures the hearing threshold. No difference between the exposed and unexposed group in BERA recordings were found, whereas hearing thresholds at 4000 Hz and 8000 Hz were significantly higher in the exposed group. [It is not possible to assess if the control group is comparable to the exposed group with regard to other risk factors that might affect hearing, as no information is given about the control group. Confounding from loud noise may be an explanation for the observed finding, given an average noise level of 70 dB in the exposed group and the fact that noise exposure typically causes hearing damage in the frequency range between 4000 and 8000 Hz. These limitations make the study uninformative.]

A cross-sectional study of mobile phone use and problems with hearing and vision (discussed in the next section) was conducted in Saudi Arabia by Meo and colleagues (2005). The study included 873 volunteers (498 males and 348 females, 27 unknown sex) from the College of Medicine, King Saud University and from different areas of Riyadh. The age range was 18–46 years. [No information was provided on how participants were recruited, or participation rate.] Through a structured questionnaire, either as self-completed or through interviews, information was collected about general physical characteristics [age, sex], medical history, and amount and duration of mobile phone use. Chi-square test was used to assess differences in the distribution of hearing complaints according to amount of mobile phone use. Hearing complaints were measured as impaired hearing, ear ache and/or warmth on the ear, and was reported by 34.6% of participants, with no significant association with average total daily duration of mobile phone calls. [It is unclear if persons were randomly selected, or if a source population was defined. No control of confounding was made.]

Kerekhanjanarong and colleagues (Kerekhanjanarong et al., 2005) conducted a cross-sectional study at the Department of otolaryngology, King Chulalongkorn Memorial Hospital in Bangkok, Thailand. Participants underwent hearing evaluations between August 2001 and April 2003 (audiometry, tympanometry, otoacoustic emission, and auditory brain stem response). In total 112 persons were included [no information was provided about selection procedures or participation rate], and all were mobile phone users. The 14 persons who used the mobile phone on both sides were excluded from analysis, and for the remaining 98 subjects results of the hearing tests for the ear where the mobile phone was held ("dominant ear") was compared to results for the other ear ("non-dominant ear"). Results were presented as mean, SD and range. Analyses included 31 males and 67 females, mean age was 30.5 ± 9.5 years. Participants used a mobile phone on average 26.3 ±30.9 min per day, range 3–180 min, 57 on the right side, 41 on the left. No significant differences were found between the dominant and non-dominant ear. The 8 persons who used a mobile phone more than 60 min had a "worse" hearing threshold on the dominant side, but no statistics were presented, as the number of subjects was too small. [The cross-sectional design is particularly problematic in this study as hearing problems may affect choice of ear for mobile phone use. No control of confounding was made. Participant selection was not described, and the source population not defined.]

Oktay and Dasdag (2006) conducted a cross-sectional study on mobile phone use and hearing function. They recruited male study participants into three groups; 20 who had used a mobile phone approximately 2 h/day during 4 years, 20 who had used it 10–20 min per day during 4 years, and 20 who had never used a mobile phone. Hearing function was estimated through brainstem evoked response audiometric (BERA) and pure tone audiometric (PTA) measurements, and participants answered questions about various symptoms such as headache, difficulties concentrating, discomfort, warmth behind/around ear. No differences between groups were found for BERA measurements, while the group with heaviest users had higher detection thresholds than either moderate or non-users. The heaviest users also had a higher prevalence of symptoms than the other groups. [No information is provided on how subjects were selected, and it is impossible to assess whether the three groups are comparable with regard to other factors that might affect the outcome. The

prevalence of symptoms among the heaviest users was very high (35–55% for the various symptoms), which indicates that they may not be representative.]

A cross-sectional study of mobile phone use and prevalence of problems with hearing, tinnitus, or balance was conducted by Davidson & Lutman (2007). Study participants were recruited among postgraduate students at 16 departments of the University of Southampton, UK. Exclusion criteria were age over 30 years, any ear operation, or ear disease within the last 12 months. Electronic questionnaires were returned by 160 students, of whom 43 were excluded according to the exclusion criteria. Participation proportions could not be calculated as the number of students who initially received the questionnaire was unknown. A small survey was performed to assess the representativity of the participants by interviewing most postgraduate students present in the University cafeteria on a weekday lunchtime. About the same proportion of students in the small survey had never used a mobile phone (1.9%) as in the full study (1.7%). Hearing, tinnitus and balance were measured through validated questionnaires, were answers were given in five categories characterizing the degree of annoyance/severity of the outcome. The mean outcome scores were compared between exposed and unexposed groups. Mobile phone use was measured as time since first use, number of times per day, and total amount of time per day, with no distinction between calls and text messages. No significant differences between exposure groups were found for any of the measured outcomes. [No adjustment was made for any potential confounders. Participants may not be representative for all eligible students. No rationale for choice of exposure categories is given. The cross-sectional design does not allow assessment of whether the investigated exposures preceded the investigated outcomes.]

Kahn and colleagues conducted a cross-sectional study of adverse effects of excessive mobile phone use among second year medical students at King Saud University, Riyadh, Saudi Arabia (Khan, 2008). Questionnaires were distributed to 330 students [not specified how they were selected], and was returned by 286 (86.6%), 211 men and 75 women. All participants were mobile phone users. The questionnaire asked about various perceived symptoms, including also hearing problems, but also about the awareness of the health problems caused by mobile phones. The authors' goal was to "contribute to increasing social awareness of the health problems associated with the use of these devices" [mobile phones]. Hearing problems were reported by 14% who used a mobile phone <30 min/day, 33% among users for 30-60 min/day, 45% among users for 60-90 min/day, and 15% among those who used a mobile phone ≥90 min/day. No control of confounding was made. [Selection procedure is insufficiently described. Responses may have been affected by the predetermined message in the questionnaire that mobile phone use causes health effects.]

Table 6.1.1. Epidemiological studies of hearing

Outcome	Country Time period	Study population Design	Exposure	No. exp cases	Odds ratio (95% CI)	Comments	Reference
Tinnitus	Iran 2005	518 university students Cross-sectional study, all apparently healthy students at two universities	Mobile phone use >30s/day Cordless phone use >30s/day CRT VDU use >1min/day	Not given	Not reported No significant differences for any of the exposure sources	Probably no adjustment for confounding	Mortazavi et al. (2007)
Tinnitus	Austria 2003–2004	100 cases, 100 controls Hospital based case-control study	Mobile phone use Ever/never 1-3 years ≥4 years <160 cum. h ≥160 cum. h <4000 no. calls ≥4000 no. calls	 84 18 49 29 55 32 52	 1.86 (0.74–4.65) 0.76 (0.35–1.68) 1.26 (0.63–2.50) 1.60 (0.61–4.22) 2.25 (0.82–6.16) 1.93 (0.72–5.20) 1.80 (0.69–4.72)		Hutter et al. (2010)
Tinnitus	Switzerland 2008–2009	1122 persons Population based cohort study	Mobile phone use Environmental RF		Only reported in figure, no associations		Röösli et al. (2010) Frei et al. (2012)

Hearing loss	Denmark 2003–2009	52 680 children born 1996-2002 Cross-sectional	Mobile phone use			Results here are for traditional logistic regression – other models gave similar results Hearing loss self-reported by parents	Sudan et al. (2013)
			No, never	490	1.0		
			Yes, but less than 1 hour/week + yes, more than 1 hour/week	338	1.21 (0.99–1.46)		

194

195 *Excluded study*

196 Landgrebe et al. (2009)

197 ### *6.1.2 Volunteer studies*

198 WHO (1993) reported about human volunteer studies that had explored auditory perception of RF
199 pulses. This auditory effect, often called "microwave hearing" was noted to depend on the total energy of each
200 individual pulse. The mechanism of this hearing phenomenon is explained in Chapter 3.5. No volunteer studies
201 reported in WHO (1993) were concerned with other effects on the auditory system or with effects on the
202 vestibular or ocular functions.

203 The literature search for newer volunteer studies on effects of RF exposure on the auditory, vestibular
204 and ocular functions resulted in 24 relevant papers. Of these, 12 papers, representing 11 studies, were excluded
205 because exposure conditions were not blinded to the participants or the study did not include two or more
206 exposure levels (whereof one could be a sham) under otherwise similar conditions; these studies are listed at the
207 end of this section. Therefore, 12 studies are included in the review. Two of the identified studies (Colletti et al.,
208 2011; Stefanics et al., 2007) had uncertainties releted to the includion criteria and are not included in the table
209 but are briefly discussed at the end of the section. All studies reviewed here explored possible effects of mobile
210 phone signals on the auditory system. In addition, one study also tested effects on the vestibular system.

211 The interest over the last decade in effects on the hearing function is due to the close proximity
212 between the mobile phone during a call and the hearing sensory organ, the cochlea. In addition to testing hearing
213 thresholds by pure tone audiometry, the functioning of the outer hair cells of the cochlea and auditory brainstem
214 responses have been assessed. The outer hair cells are crucial for normal hearing. These sensory cells move in
215 response to sound stimulation and thereby amplify the waves propagating in the cochlea. The motions of the
216 outer hair cells also produce sound, so called otoacoustic emissions, which can be recorded in the ear canal. The
217 otoacoustic emissions reflect the functional state of the outer hair cells and have been used to assess effects of
218 RF exposure on hearing. Two types of methods are applied: distortion product otoacoustic emissions that are
219 produced by stimulating the hair cells simultaneously with two nearby frequencies and transient evoked
220 otoacoustic emissions that are responses to acoustic stimuli of very short duration, e.g. clicks. During sound
221 stimulation, responses of cochlear hair cells cause potentials to be elicited in the acoustic nerve and nuclei. These
222 potentials are recorded as auditory brainstem responses and their amplitudes and time delays provide information
223 about cochlear and higher order auditory sensitivity and functions.

224 Table 6.1.2 by the end of this section summarizes the results of each study and provide information
225 about their methods. Similar information is included in the following text, with the exceptions that the use of
226 double-blind design, meaning that neither participant or researcher was aware of the exposure conditions, is
227 usually not reported in the text. Comments about particularly small samples sizes are made since the smallest
228 samples are attached with highest uncertainties provided other study details are similar. Exposure was controlled
229 in all studies that are included in the analysis. If SAR was provided, it is specified in both tables and text.
230 Otherwise, output power along with other details of exposure setup is provided.

231 *Studies with healthy adult volunteers*

232 In a single blind study Janssen et al. (2005) investigated whether GSM-like 900 MHz signals may
233 interfere with the mobility of outer hair cells by recording distortion product otoacoustic emissions. The signal
234 was emitted by a monopole antenna positioned 5 cm from the ear. The intervals between the pulses of the signal
235 were about 24 ms, six times longer than that applied for the GSM 900 MHz signals. The peak output power of
236 the pulses was 20 W [10 times higher than the maximum peak power of GSM 900 MHz phones] and the mean

output power was 0.465 W resulting in a SAR of 0.1 W/kg [averaging mass not specified]. Twenty eight volunteers participated in 12 tests with different combinations of sound frequencies and levels. Each test lasted for 24 minutes and consisted of eight alternating 3-minute periods of RF and sham exposures. The tests started with real exposure for 14 participants and with sham exposure for the other 14 participants. The tests were "broken up into multiple sessions". Since the pulses would interfere with the recorded otoacoustic signals, the otoacoustic emissions were recorded during in the intervals between the pulses. When comparing sham and RF exposures, there was no statistically significant difference in the otoacoustic emission levels for any of the 12 acoustic stimulus conditions. When splitting the analyses between genders, one of the 12 stimulus conditions exhibited a difference between the RF and sham exposures ($p < 0.05$, exact value not provided) for females. When data from all tests and participants were included, the mean differences between sham and RF exposure was close to zero (0.0049 dB sound pressure level), and the individual test results were almost symmetrically distributed between -2.5614 and 2.0767 dB sound pressure level. [These results, together with the fact that no corrections were made for multiple testing suggest that the single statistically significant finding is most likely due to chance.]

As parts of two consecutive European projects, volunteer studies were performed in various laboratories to test the effects on the auditory function of mobile phone signals combined with a speech signal at 60 dB(A) to mimic real exposure conditions (Paglialonga et al., 2007; Parazzini et al., 2005; Parazzini et al., 2007a; Parazzini et al., 2009; Parazzini et al., 2010; Uloziene et al., 2005). The respective reported SARs were measured approximately at the location of the cochlea. In all laboratories the studies were performed double blind with sham and RF exposure sessions on separate days. The order of exposures was designed to be counterbalanced, which was not always completely achieved due to an odd number of participants. To analyse potential effects of exposures, shifts in the endpoints from before to immediately after exposure were used as parameters. While the basic criterion for significance was set to 0.05, Bonferroni adjustment to the criterion was applied for multiple comparisons when any test resulted in $p < 0.05$.

In the first European project (Paglialonga et al., 2007; Parazzini et al., 2005; Parazzini et al., 2007a; Uloziene et al., 2005), half of the participants 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 (Paglialonga et al., 2007; Parazzini et al., 2005; Parazzini et al., 2007a; Uloziene et al., 2005). 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. Uloziene et al. (2005) recorded hearing thresholds by pure tone audiometry and transient evoked otoacoustic emissions in 30 volunteers. No evidence for any effect of the EMF exposures was found. To ensure high sensitivity, Parazzini et al. (2005) explored potential effects on primary distortion and reflection mechanisms involved in producing distortion product otoacoustic emissions. Effects of time of exposure, exposure condition and interaction between these were analysed. The shift in distortion product amplitude from before to after exposure was statistically significant for the interaction term ($p = 0.036$) for one of the three acoustic stimulus conditions applied. After correction for multiple testing, the result was not statistically significant. None of the other four endpoints exhibited any statistically significant result. Because of the low number of participants, only six for each of the two RF exposure conditions, the probability to reveal an effect, if any existed, was low. Parazzini et al. (2007a) made a pooled analysis with data from several participating centres, which included in total 134 volunteers. Pure tone hearing thresholds, distortion product otoacoustic emissions, transient evoked otoacoustic emissions and auditory brain stem responses were assessed with a varying number of participants (20–118) for the different endpoints. The probability to detect a 1 dB difference was calculated to be 80% with the maximum number of participants. For pure tone audiometry at one of the frequencies (500 Hz), the shift in hearing threshold differed between RF and sham exposure (about 2.5 dB,[1] $p = 0.008$). When analysing the two exposure frequencies separately, statistical significance only remained for the 900 MHz exposure ($p= 0.007$). Shift in distortion product levels differed between sham and RF exposure for two out of 12 tested acoustic stimulus conditions, with about 2.2 dB ($p = 0.023$) and 1.2 dB ($p = 0.015$), respectively. After separate analyses for the two exposure frequencies a significant difference ($p = 0.024$) remained for one of the acoustic stimulus conditions and only for the GSM 1800 MHz exposure. No effect of exposure was observed for transient evoked otoacoustic emissions. Auditory brain stem responses were recorded using condensation, rarefaction and alternating polarity stimuli in the form of broadband bursts at two different

[1] The dB-values provided for the studies in the European projects (Parazzini et al., 2007a; Parazzini et al., 2009; Parazzini et al., 2010) were read from diagrams in the publication.

repetition rates. Analysing wave V amplitudes and latencies shifts from before to after exposure, no statistically significant effect of exposure was obtained. To test the ability of the auditory nerve to sustain high response rates, wave V amplitudes in response to the lowest and highest stimuli rates (33.1 and 74.1 clicks per second, respectively) were compared. A statistically significant difference between RF exposure at 900 MHz and sham ($p = 0.045$) was obtained when applying the condensation polarity. However, no finding in this study was statistically significant after correction for multiple comparisons. Paglialonga et al. (2007a) tested possible effects on the temporal and spectral features of transient evoked otoacoustic emission fine structure. Based on data from 27 volunteers, no indication of any effect of the exposures was observed.

In the second European project (Parazzini et al., 2009; Parazzini et al., 2010) the participants were exposed for 20 minutes to signals from a UMTS mobile phone. Parazzini et al. (2009) reported a multicentre study with 74–134 volunteers participating in the different auditory tests: pure tone audiometry, distortion product otoacoustic emissions and contralateral suppression of transient evoked otoacoustic emission. As in the previous project, the mobile phone was positioned against the ear that was tested for hearing functions and sham exposure was obtained by connecting a load to the phone so that the RF signals were dissipated to the load instead of transmitted to the antenna. The hearing threshold at 500 Hz and the average threshold for 2–8 kHz increased more after UMTS than sham exposure, about 1.2 dB ($p = 0.02$) at 500 Hz and 0.6 dB ($p = 0.03$) in the high frequency range. These results were not statistically significant when applying an adjusted criteria for significance due to multiple comparisons ($p < 0.004$). No effect of exposure was indicated for any other endpoint. Although the UMTS phone was operated at full power, the SAR at the position of cochlea was fairly low (0.069 W/kg). Parazzini et al. (2010) conducted a similar study but with 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 by a patch antenna positioned against the test ear. The number of participants varied between 25 and 57 in the various auditory tests. When comparing sham and UMTS exposure, the difference in shift of distortion product otoacoustic emission level was about 1.4 dB ($p = 0.045$) for one of the acoustic test conditions, which was not statistically significant after correction for multiple testing with significance criterion $p < 0.001$. No indication of any effect of exposure was observed for the other endpoints.

The aim of a study by Stefanics et al. (2008) was to investigate potential effects of UMTS mobile phone exposure on event-related brain potentials during an auditory task (see Section 5.2.2.1). They also measured hearing thresholds of the exposed ear by pure tone audiometry for frequencies in the range 250 Hz–8 kHz. This was done before the EEG recording that preceded the exposure and after the EEG recording that followed exposure. Thirty six healthy students were exposed for 20 minutes to UMTS signals at levels that were higher than caused by ordinary handset use (SAR_{1g} 30 mm from the surface: 0.39 W/kg). The signals were generated by an UMTS mobile phone connected to a patch antenna placed against the right ear. Real and sham exposure sessions were conducted one week apart in counterbalanced order. There was no evidence for any effect of exposure on hearing thresholds.

In a single blind study that was completed by 17 volunteers, Kwon et al. (2010) recorded auditory brainstem responses from the mid brain during 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 loudspeaker and the buzzer of the mobile phone were removed. Each participant was sham and RF exposed, first with the mobile phone placed against the right ear and then against the left ear, resulting in four exposure conditions. The order of RF and sham exposures was designed to be counterbalanced. Brainstem responses were recorded twice under baseline condition and during each of the four exposure conditions in a procedure lasting about 1 hour. Rarefaction clicks were used to elicite brainstem responses of the the exposed ear, while a masking white noise was delivered to the contralateral ear. In a few instances artefacts occurred due to interference by the mobile phone signals. Then the recording of the brainstem responses was interrupted until the phone had been repositioned to avoid the interference. Latency and interwave intervals of waves I, III and V, as well as amplitudes and relative amplitudes of waves I and V were assessed. These waves are electrical fields recorded with electrodes placed on the scalp and generated in response to the clicks at different levels along the auditory pathway. No difference between sham and RF exposure was observed for any of these parameters, suggesting that the applied exposure did not affect the transmission up to the level of the mid brain.

Studies including IEI-EMF volunteers

One study has been conducted to test effects on sensory functions of individuals with idiopathic environmental intolerance attributed to EMF (IEI-EMF). Bamiou et al. (2008) investigated whether continuous wave and GSM modulated RF signals affected the peripheral auditory and vestibular systems and whether nine individuals who reported symptoms after mobile phone exposure were more affected than 21 volunteers without

IEI-EMF. Both exposures were at 882 MHz. The signals were emitted by a generic mobile phone placed next to the side of the head, 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. Effects on the auditory and vestibular systems were tested on separate days, 2-4 weeks apart. Both ears were exposed separately to the RF and to the sham signals, each lasting 30 minutes and with the order of exposure conditions determined randomly. The sensory functions were recorded before the first exposure and immediately after each exposure. Analysis of the auditory function, assessed by the amplitude of transient evoked otoacoustic emission, indicated no effect of exposure in either group of volunteers. No statistical analysis was performed for the vestibulo-ocular reflex, recorded by video-oculography, due to the absence of clinically significant nystagmus. Minor nystagmus was observed in three participants, all controls, in two after sham exposure and in one after RF exposure. [Some uncertainty is attached to the results for the group of IEI-EMF volunteers due to the low number of participants, although the exposure used was consistent with that reported to cause symptoms. Furthermore, the authors provided no information about the testing room and the background levels of EMF, which would be of particular relevance for the IEI-EMF participants.]

Papers with uncertainties releted to the includion criteria

One study (Stefanics et al., 2007) was not included in the final analysis due to unsufficient statistical analysis, and another (Colletti et al., 2011) due to substantial uncertainties related to the exposure. Stefanics et al. (2007) exposed 15 volunteers to signals from a GSM 900 phone, fifteen other volunteers were sham exposed. For each of the two exposure conditions, the latencies of auditory brainstem responses recorded before and after exposure were compared. No significant changes from before to after sham or RF exposure were observed. However, some of the changes were in opposite directions for the sham and the RF exposures. [Even though each of the changes was not significant, the difference between them might have been. However, no statistical analysis was performed to compare the sham and the RF exposure conditions. Therefore, no conclusion can be drawn based on these results.]

Colletti et al. (2011) included patients with Ménière's disease. Seven patients were exposed for 5 minutes to signals from a mobile phone in "active call mode" during a surgical operation where the superficial tissues had been removed so that the cochlear nerve was directly exposed. A control group of five others was exposed with the mobile phone in stand-by mode. The mobile phone was held very close to the nerve (about 6 mm). A monopolar cotton-wick electrode was placed at the root entry zone of the nerve to record the compound action potential from the nerve cells. The latency increased and the amplitude decreased significantly during the exposure to the active call compared to the control condition. In addition, auditory brainstem responses were recorded without exhibiting any effect of exposure. [This study is difficult to interpret: there was no control of the output power of the mobile phone signals, and another substantial issue is the proximity of the metal electrode to the nerve. In the worst case, the electrode might have functioned as an antenna and caused relatively strong EMF fields in parts of the nerve.]

Table 6.1.2. Mobile phone handset related studies assessing effects on auditory and vestibular functions

Endpoint and Participants[a]	Exposure[b]	Response	Comment	Reference
Studies with healthy adults				
Distortion product otoacoustic emissions (DPOAE) recorded between RF/sham pulses 28 volunteers (16–30 years; 14 males, 14 females)	GSM-like signals emitted by monopole antenna 5 cm from the ear, 900 MHz, pulse duration 0.5763 ms, 24.204 ms between pulses SAR 0.1 W/kg 24 min with 8 alternating 3 min RF and sham exposures repeated 12 times with different acoustic test stimuli	No effect of exposure for males and females together. For females the DPOAE level differed between RF and sham exposure for one of 12 acoustic stimuli.	Single blind, counterbalanced, cross-over. No correction for multiple analyses.	Janssen et al. (2005)

Pure tone audiometry (PTA), transient evoked otoacoustic emission (TEOAE) recorded before and after exposure 30 volunteers (18–30 years; 18 males, 12 females)	GSM mobile phone against test ear 900 MHz (n=15): average output power 0.25 W 1800 MHz (n=15): average output power 0.125 W 10 min; concurrent speech signal	No effect of exposure.	Double blind, counterbalanced for each exposure frequency, cross-over. For subjective endpoints see Section 5.2.4.	Uloziene et al. (2005)
DPOAE recorded before and after exposure 12 volunteers (18–30 years)	GSM mobile phone against test ear 900 MHz (n=6): SAR_{1g} 0.41 W/kg in brain 30 mm from the surface 1800 MHz (n=6): SAR_{1g} 0.19 W/kg in brain 30 mm from the surface 10 min, concurrent speech signal	No effect of exposure.	Same project as Uloziene et al. (2005) Double blind, counterbalanced, cross-over. Small sample. Bonferroni correction for multiple comparisons (significance criterion not specified).	Parazzini et al. (2005)
PTA, TEOAE, DPOAE and auditory brainstem responses (ABR) recorded before and after exposure 118[c] volunteers (18–30 years)	GSM mobile phone against test ear 900 MHz (~ 50% of volunteers): SAR_{1g} 0.41 W/kg in brain 30 mm from the surface 1800 MHz (~ 50% of volunteers): SAR_{1g} 0.19 W/kg in brain 30 mm from the surface 10 min, concurrent speech signal	No effect of exposure.	Same project as Uloziene et al. (2005) Double blind, counterbalanced, cross-over. Bonferroni correction for multiple comparisons (significance criterion not specified).	Parazzini et al. (2007a)
TEOAE recorded before and after exposure 27 Volunteers (23–30 years; recruited:17 males, 12 females)	GSM mobile phone against test ear 900 MHz (~ 50% of volunteers): SAR_{1g} 0.41 W/kg 1800 MHz (~ 50% of volunteers): SAR_{1g} 0.19 W/kg in brain 30 mm from the surface 10 min, concurrent speech signal	No effect of exposure.	Same project as Uloziene et al. (2005) Double blind, cross-over.	Paglialonga et al. (2007)
PTA, DPOAE, and contralateral acoustic stimulation during TEOAE recorded before and after exposure 134[c] volunteers (18–30 years; 61 males, 73 females[c])	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. Bonferroni correction for multiple comparisons (significance criterion: $p < 0.004$). For auditory evoked potentials at the level of brain cortex see Section 5.2.1.	Parazzini et al. (2009)
PTA, DPOAE and contralateral acoustic stimulation during TEOAE, recorded before and after exposure 57[c] volunteers (18–30 years; recruited: 35 males, 38 females[c])	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. Bonferroni correction for multiple comparisons (significance criterion: $p < 0.001$). For auditory evoked potentials at the level of brain cortex see Section 5.2.1.	Parazzini et al. (2010)

PTA of exposed ear recorded 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 cognitive function see Section 5.2.1.; for event related potentials see Section 5.2.2.1.	Stefanics et al. (2008)
ABR recorded during exposure 17 volunteers (25.9 ± 4.3 years, 6 males, 11 females)	GSM mobile phone against one ear at the time, 902.4 MHz 1 h including baseline and sham SAR_{10g} 0.82 W/kg < 10 min on each side	No effect of exposure.	Single blind, nearly counterbalanced, cross-over. The phone was repositioned in a few cases to avoid EMF interference with recording equipment. For perception test see Section 5.2.4.	Kwon et al. (2010)
Studies including volunteers with IEI-EMF				
PTA, TEOAE and vestibulo-ocular reflex recorded before and after exposure 9 IEI-EMF volunteers (20–55 years; 6 males, 3 females) 21 healthy volunteers (20–55 years; 12 males, 9 females)	CW and GSM signals from generic mobile phone next to left and right side of head, 882 MHz SAR_{10g} 1.3 W/kg 30 min Auditory and vestibular functions and right and left sides exposures in different sessions	No effect of exposure.	Double blind, randomized, cross-over. Small sample of IEI-EMF volunteers. For detection test see Section 5.2.4.	Bamiou et al. (2008)

Abbreviations: ABR: auditory brainstem responses; DPOAE: Distortion product otoacoustic emissions; GSM: Global System For Mobile Communication; IEI-EMF: Idiopathic environmental intolerance attributed to EMF; PTA: Pure tone audiometry; TEOAE: transient evoked otoacoustic emission; UMTS: The Universal Mobile Telecommunications System

[a] The maximal number of volunteers participating in analyses is provided. Numbers of male and female participants are provided in the table if included in the paper.

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

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

Excluded studies

(Arai et al., 2003; Bak et al., 2003; Balachandran et al., 2012; de Sèze et al., 2001; Kellenyi et al., 1999; Monnery, Srouji & Bartlett, 2004; Mora et al., 2006; Oysu et al., 2005; Ozturan et al., 2002; Pau et al., 2005; Sievert, Eggert & Pau, 2005; Sievert et al., 2007)

6.1.3 Animal studies

The WHO (1993) report on effects of RF exposure addressed the subject of auditory function only from the point of view of auditory perception of pulsed RF, citing a few papers dealing with the verification of the energy density threshold for this endpoint. The vast majority of more recent studies on auditory effects are related to mobile communication devices. The WHO's 1993 Environmental Health Criteria (WHO, 1993) did not include any papers on animal studies of vestibular function. The current literature search covering 1990-2013 also did not find any studies dealing directly with the issue of effects of RF EMF exposure on vestibular function in animals.

Marino et al. (2000) performed an initial study on 10 week-old male rats, exposed at a frequency of 950 MHz CW (SAR values of 0.2 or 1 W/kg, for 3 days and 3 h per day, 8 exposed and 8 sham) or a frequency of 936 MHz (1 W/kg, 5 days, 3 h per day, 8 exposed and 8 sham). Distortion Product Otoacoustic Emissions, DPOAEs) were registered from both ears before exposure and immediately, 24 h and 48 h after exposure. The acoustic frequency range tested was 2000–6000 Hz, 70 dB sound pressure level (SPL) stimuli. Data obtained from both 950 and 936 MHz did not indicate any acoustic functional effects in terms of otoacoustic emissions due to exposure.

Four studies were performed in the framework of two projects funded by the European Commission (Aran et al., 2004; Galloni et al., 2005b; Galloni et al., 2009; Parazzini et al., 2007b). The first project (GUARD) dealt with effects of GSM cellular phones, while the second (EMF nEAR) focused on the effects of UMTS EMF exposure. These studies all used a localized exposure of one of the animals' ears, by means of a loop antenna as EMF source, as has been described in the section on exposure systems.

Aran et al. (2004) exposed guinea pigs (left ear, 8 animals per group) for 1 h per day, 5 days per week, for 2 months, to 900 MHz GSM modulated microwaves at SARs of 1, 2 and 4 W/kg respectively. DPOAEs from 0.5 to 8 kHz, 75 dB SPL stimulus intensity, were measured before exposure, at the end of the 2-month exposure period, and 2 months later. Afterwards, the same protocol was applied to 8 sham-exposed and 16 guinea pigs exposed at 4 W/kg, and auditory brain stem response (ABR) thresholds were monitored (stimuli of 4 ms, 1–24 kHz, 10–75 dB SPL). Repeated-measures ANOVA showed no difference in DPOAE amplitudes or in ABR thresholds between the exposed and non-exposed ears and between the sham-exposed and exposed groups. Acute effects were also investigated by measuring once, in all animals, ABR thresholds just before and just after the 1-h exposure: no statistically significant difference was observed.

A total of 58 male rats were utilized by Galloni et al. (2005a), with protocols including different exposure times (3 h per day, 5 days, or 2 h per day 5 days per week during 4 weeks), frequencies (923 or 936 MHz CW, or 900 or 960 MHz GSM), SARs (sham, 1 or 2 W/kg) and timing after the end of the exposure (1 day, 2 days, 3 days or 1 week) of DPOAEs test (in the range of 3000–7000 Hz, 35–70 dB SPL). No significant variation in any parameter due to exposure to any type of RF EMF exposure was observed.

The same research team scheduled other trials on effects of GSM exposure on the auditory system of rats, after further developing both the exposure system set-up and the hearing test procedures. In Galloni et al. (2005b), a total of 48 rats were exposed or sham-exposed 2 h per day, 5 days per week for 4 weeks at a local SAR of 2 W/kg, at both 900 and 1800 MHz, GSM modulated. DPOAE tests (ranging between 3 and 21 kHz, 70/65 and 65/55 dB SPL stimuli) were carried out before, during (at the end of each week) and one week after the exposure. There were no statistically significant differences between the acoustic signals recorded from the ears of different exposure groups.

Parazzini et al. (2007b) evaluated possible combined effects of 900 MHz (CW) and gentamicin (GM), an ototoxic agent, on the cochlear functionality of rats as measured by DPOAEs. A population of 32 rats was divided into 4 groups: (1) treated with 150 mg/kg GM per day intramuscular for 15 days, (2) treated with GM + EMF exposure, (3) exposed to EMF only, (4) sham-exposed to EMF. Rats were exposed 2 h per day, 5 days per week for 4 weeks at a local SAR of 4 W/kg in the ear. DPOAEs tests in the acoustic range 3316–13250 Hz, stimuli of 70/65 and 65/55 dB SPL, were carried out before, during and after the combined exposure. No influence of EMF exposure, alone or in combination with GM, on the inner ear function, and no effects of the co-exposure to the ototoxic agent were found.

In Galloni et al. (2009) possible effects of UMTS emissions (1946 MHz) on the functionality of the cochlea outer hair cells in male rats are described. The local SAR was 10 W/kg, treatment time was 2 h per day, 5 days per week, for 4 weeks; 24 rats were exposed, and 24 were sham-exposed. As positive control group, 12 rats were administered with the antibiotic kanamycin, 250 mg/kg, by daily intramuscular injection for 21 days, starting at the same time as the real and sham exposures. DPOAEs (3–16 kHz, 65/55 and 60/50 dB SPL stimuli) recordings were performed before exposure, at the end of each week of exposure, and 1 week after the last exposure day. Notwithstanding the high local SAR level, far above the maximum level of 2 W/kg allowed for commercially available cell phones, no statistically significant effect of exposure to RF EMF at UMTS frequency was found. The DPOAE amplitudes were significantly decreased in kanamycin-treated rats; this effect started 4 weeks after the antibiotic injection and, as expected, was clearly marked at higher acoustic frequencies (Forge & Schacht, 2000).

Studies not included in the analysis

Kizilay et al. (2003) exposed newborn and adult male rats to 900 MHz GSM-modulated fields 1 h daily for 30 days. The maximum SAR of the used mobile phone as provided by the manufacturer was 0.95 W/kg, but no actual exposure level is given. DPOAEs ranging from 1 to 6.3 kHz, 36-75 dB SPL, were tested before and at the end of the 30-day exposure. The analysis of results in terms of the mean amplitudes did not reveal any statistically significant differences between exposure and non-exposure conditions. In addition, 30 days exposure of newborn rats did not cause any detectable alteration during cochlear development. [The exposure level is not provided. Only the maximum SAR of the phone and the distance between the animals and

the cell phone are provided, no measurements of the actual dose have been done. For the exposure system they refer to Burkhardt et al. (1997)]

Kayabasoglu et al. (2011) exposed newborn and adult rats for 6 hours per day, for 30 consecutive days, at 900 or 1800 MHz. Before and after the exposure period, DPOAEs at six frequencies between 1001 and 7996 Hz (stimuli of 65/55 dB SPL) were measured in each group and a signal-to-noise ratio was calculated. In both the newborn and adult rat groups, no significant difference was observed in the recordings before and after exposure. [No details are provided on the exposure setup and the exposure level. Only the maximum SAR levels provided by the manufacturers for the mobile phones used are given, not the actual exposure levels. It is not clear whether the unexposed controls were sham exposed or cage-controls.]

Budak et al. (2009a; b; 2009c) published three papers on infant and adult rabbits exposed in a shielded chamber to GSM-modulated 1800 MHz fields. In the first study (Budak et al., 2009a), male rabbits were whole-body exposed 15 min daily for 7 days as foetus between the 15th and 22nd day after conception, or after they reached 1-month of age after birth, or both. Exposure of foetuses resulted in increased DPOAEs amplitudes in the acoustic range 1.5–6 kHz, whereas exposure after birth decreased DPOAE amplitudes between 4 and 6 kHz. [The exposure level is not provided and it is not clear whether the unexposed controls were sham exposed or cage-controls.]

In the second study (Budak et al., 2009c),13 month-old pregnant and non-pregnant rabbits were included. They were exposed for 15 min daily for 7 days, or not exposed. In the exposed non-pregnant group DPOAEs levels at 1–4 kHz were lower if compared to non-exposed, non-pregnant animals, while no effects were found in pregnant rabbits. [No details are provided on the exposure setup and exposure level. It is not clear whether the unexposed controls were sham exposed or cage-controls.]

The third experiment (Budak et al., 2009b) used 1-month-old and 13-month-old female rabbits. They were whole-body exposed for 15 min daily for 7 days. The mean amplitude of DPOAEs of the adult exposed group was significantly lower than that if the controls, and, conversely, the mean amplitude of DPOAEs of young exposed animals was significantly higher. [The exposure level is not provided and it is not clear whether the unexposed controls were sham exposed or cage-controls.]

In Kaprana et al. (2011), rabbits were locally exposed to a 900 MHz field for 60 min by an in-ear antenna. During exposure and 24 h after, hearing thresholds, absolute wave latency and interwave latency on baseline ABR recordings were assessed. Effects were detectable only on the exposed ear, namely prolongation of interval latencies between waves I and V and between waves III and V after 30 minutes of exposure. [The exposure level is not provided, only the output power of the antenna.]

Seckin et al. (2014) evaluated possible effects of 900 and 1800 MH GSM fields on cochlear development in Wistar rats. Pregnant rats (two controls, three exposed at 900 MHz and three at 1800 MHz) were exposed 1 hour per day starting on the 12th day after conception until delivery; newborns (24 controls, 31 exposed with 900 MHz and 24 with 1800 MHz) were exposed again 1 hour per day for 21 days. Then DPOAE amplitudes were tested at 1–8 kHz, 80 dB SPL stimuli. Eight animals per group were selected for cochlear electron microscopy evaluation. A significant increase of 8-kHz DP levels in the 1800 MHz group compared to controls was reported, in the absence of any functional loss, as well as a higher level of apoptotic and necrotic cells in the middle segment of each cochlear turn after electron microscopy examination. [No dosimetry or SAR levels are included, only incident electric field values "measured weekly on the back of each newborn rat" during exposure are reported.]

Seaman and Beblo (1992) in a preliminary report and Seaman et al. (1994) evaluated possible modification of acoustic and tactile startle by microwave pulses expected to give rise to microwave hearing in rats. Male rats were exposed to 1.25 GHz, 0.9 and 7.82 μs pulses, resulting in a SAR averaged over the duration of the pulses of 15 or 86 kW/kg and an SA from 16–44.2 and 66.6–141.8 mJ/kg to 525.0–1055.7 mJ/kg. Medians of startle peak amplitude, response integral and latency were assessed. Different effects of exposure (inhibition or enhancement) were observed, depending on timing and intensity of the stimulus. [This study is weakened by the poor dosimetry. The authors reported that they performed thermometric measurement on a rat cadaver for the SAR assessment. However, it is difficult to extrapolate accurate dosimetric data from such measurements for two main reasons. First, a continuous wave signal at 1.25 GHz was used for the measurements while the experiments were carried out using microwave pulses of 0.8–1 μs that have a wide frequency content. Therefore a single frequency dosimetry is not enough to characterize the target. Second, the measurement points within the cadaver as well as all the whole measurement protocol were not specified, making the extrapolated data unreliable.]

Table 6.1.3. Animal studies on auditory function.

Endpoint, animals, number per group, age at start	Exposure: source, schedule, level, freely moving or restrained, coexposure	Response	Comments	References
Distortion Product Otoacoustic Emissions (DPOAE) Rat: Sprague Dawley (n=8) 10 weeks	Horn antenna, 936 and 950 MHz, CW 3 or 5 days SAR 0.2 or 1 W/kg in the cochlea region Restrained	No effects.	Exposure inside a shielded chamber. Gas anaesthesia during DPOAEs sessions.	Marino et al. (2000)
DPOAE and ABR Guinea pigs (n= 8) Age not provided	Loop antenna, 900 MHz GSM 1 h/d, 5 d/weeks, 2 months SAR 1, 2 and 4 W/kg in the cochlea region Restrained	No effects.	Also Organ of Corti's explants exposed in vitro to 1 W/kg, no effects.	Aran et al. (2004)
DPOAE Rat: Sprague Dawley (n=8) 8 weeks	Horn or loop antenna, 923 or 936 MHz CW 900 or 960 MHz GSM 2 or 3 h/d, 5 d, 1 or 4 weeks SAR 1 or 2 W/kg in the cochlea region Restrained	No effects.	Gas anaesthesia during DPOAEs sessions.	Galloni et al. (2005a)
DPOAE Rat: Sprague Dawley, (n=16) 10 weeks	Loop antenna, 900 or 1800 MHz GSM 2 h/d, 5 d/week, 4 weeks SAR 2 W/kg in the cochlea region Restrained	No effects.	Small changes in DPOAE level with time, not related to exposure.	Galloni et al. (2005b)
DPOAE Rat: Sprague Dawley (n=8) 10 weeks	Loop antenna, 900 MHz CW 2 h/d, 5 d/week, 4 weeks SAR 4 W/kg in the cochlea region Restrained Co-exposed to gentamicin (GM) 150 mg/kg, in the positive controls and RF+GM group	No effects.	No effects of co-exposure, confirmed ototoxic effect of GM in the positive control.	Parazzini et al. (2007b)
DPOAE Rat: Sprague Dawley (n=12 or 24) 10 weeks	Loop antenna, 1946 MHz, UMTS SAR 10 W/kg in the cochlea region 2 h/d, 5 d/weeks, 4 weeks Restrained Positive control: kanamycin (KM) 250 mg/kg	No effects.	Confirmed ototoxic effect of KM in the positive control.	Galloni et al. (2009)

6.1.4 In vitro studies

In the previous WHO report (WHO, 1993) no *in vitro* studies on auditory, vestibular and ocular functions were reported. The present literature search identified 20 relevant papers on this topic. Eleven of them were in a language that could not be understood. One paper was obtained from other sources. That left ten papers to be extracted. Among the relevant publications, three were excluded because they did not meet the inclusion criteria for in vitro studies, and references are listed at the end of this section. Three papers did not completely comply with the quality criteria for inclusion due to methodological issues, therefore they are only presented in the text. The four included studies are described below and summarized in Table 6.1.4 (auditory function) and in Table 6.2.4 (ocular function). No study related to vestibular function was identified. Unless specifically mentioned, papers did not report on blinding of the investigators to the exposure conditions.

In a study carried out by Aran and co-workers the effect of RF EMF on the ears of guinea pigs were investigated in vivo and in vitro **(**Aran et al., 2004). The results on in vivo experiments are reported in Section 6.3.1. Concerning the in vitro experiments, the two organs of Corti (OCs) of 15 newborn rats were isolated and placed in culture. For each animal, one OC was exposed for 24–48 h to a 900 MHz GSM signal (SAR = 1 W/kg), and the other was sham-exposed, following a blind procedure. After 2–3 days of culture, all OCs were observed under light microscopy. The auditory hair cell population and pattern of organization were completely normal at this stage of development. [In this paper, also reported Section 5.4.2 (Brain physiology and function), positive controls have not been included in the study design.]

Huang et al. (2008) exposed a mouse auditory hair cell line (HEI-OC1) to 1763 MHz CDMA-modulated RF EMF (SAR = 20 W/kg) and evaluated several biological endpoints. In three independent experiments, no changes in single and double DNA strand breaks were observed after 6, 24 and 48 h (see Section 12.3.1). Protein expression level of HSP27, HSP70 and HSP90 or phosphorylation status of ERK, JNK and p38 also were unaffected following 15–120 min RF exposure (see Sections 12.3.2 and 12.3.3). Furthermore, no alterations in cell cycle distribution were observed after 24 and 48 h RF exposure (see Section 12.3.6). [In this study heating of Jurkat cells to 43 ± 0.2 °C for 30 min was included as a positive control, whereby positive findings were detected.]

Table 6.1.4. In vitro studies assessing effects of RF EMF exposure on auditory function

Cell type Number of independent experiments	Biological endpoint	Exposure conditions	Results	Comment	Reference
Organs of Corti n=15	Auditory hair cells morphology	900 MHz, GSM Average SAR 1 W/kg 24–48 h	No effect.	See also 5.4.2.	Aran et al. (2004)
HEI-OC1 Mouse auditory hair cells n=3	DNA strand breaks, protein expression, ERK, JNK, p38 phosphorylation, Cell cycle	1763 MHz, CDMA SAR 20 W/kg 15 min–48 h	No effect.	No information on blinding of staff.	Huang et al. (2008)

"No effect" means no statistically significant effect.

Abbreviations*:* CDMA: code division multiple access; GSM: Global System for Mobile Communication; SAR: specific absorption rate.

6.2 Ocular function

The lens of the eye is potentially sensitive to RF exposure, because it lacks a blood supply and so has a reduced ability to dissipate heat compared with other tissues. In addition, the fibres that make up the bulk of the lens have only a limited capacity for repair and tend to accumulate the effects of minor insults. Cellular debris resulting from any cytotoxic insult to the lens tends either to be carried to the posterior subcapsular region due to the mechanical forces of epithelial cell proliferation and fibre formation, or is trapped in situ in the lens matrix.

6.2.1 Epidemiological studies

Potential ocular effects from exposure to RF fields have been studied in a few epidemiological studies. The WHO Environmental Health Criteria from 1993 (WHO, 1993) describes two occupational studies reporting general eye irritation and complaints among plastic sealers. Around 10 occupational studies of cataracts or other effects on the lens were discussed, where most of them found no ocular effects, including some large studies of military personnel, while two studies report lens changes, and one a higher incidence of cataracts among exposed. For cases with confirmed cataracts, exposure had exceeded 1 kW/m^2. The new search identified three epidemiological studies published since 1992, all focused on potential ocular effects associated with mobile phone use. None of the studies provided enough information to fully assess the quality and they are therefore only briefly described and not tabulated. They are given little or no weight in the overall assessment.

Balik and co-workers conducted a cross-sectional study in Elazig, Turkey (Balik et al., 2005), in which 695 (502 males, 193 females) persons agreed to participate, randomly selected "from different ages,

educations, earnings, locations and occupations" [participation rates are not described, and it is unclear how randomization could be performed in such detailed population strata]. Approximately 80% were mobile phone users (n=549). Analyses were made using ANOVA, with statistical significance at $p<0.05$. Information about ocular symptoms (blurring of vision, redness on the eyes, vision disturbance, secretion of the eyes, inflammation in the eyes, lacrimation of the eyes), was collected through a questionnaire. Persons who reported they had ocular symptoms prior to start of mobile phone use were included in the analyses as exposed to mobile phone use, with a prevalence of different symptoms varying from around 30% to slightly less than 50%. A higher prevalence of blurring of vision ($p=0.000$), secretion of the eyes ($p=0.031$), or inflammation in the eyes ($p=0.034$) was found among mobile phone users, but did not vary according to years of use. The prevalence of lacrimation of the eyes was higher among persons who had used a mobile phone during 2 years, while users with longer duration had lower prevalence, with an overall p-value of 0.031. No significant differences were found for vision disturbance or inflammation in the eyes. [The cross-sectional design is a limitation, which is illustrated by the large proportion of symptoms reported to have occurred prior to start of mobile phone use. Lack of information about participation rates prevents assessment of potential selection bias. The age distribution of the study population is not reported, and no confounding control was made.]

A cross-sectional study of mobile phone use and problems with hearing and vision (also described in in the previous section on auditory function) was conducted in Saudi Arabia by Meo and Al-Drees (2005). The study included 873 volunteers (498 males and 348 females, 27 unknown sex) from the College of Medicine, King Saud University and from different areas of Riyadh. The age range was 18–46 years. No information was provided on how participants were recruited, or participation rate. Through a structured questionnaire, either as self-completed or through interviews, information was collected about general physical characteristics [age, sex?], medical history, and amount and duration of mobile phone use. Chi-square test was used to assess differences in the distribution of vision complaints according to amount of mobile phone use. Vision complaints were measured as decreased vision and/or blurred vision, and were reported by 5.04% of participants, with no significant association with average total daily duration of mobile phone calls ($p= 0.373$). [It is unclear if persons were randomly selected, or if a source population was defined. No control of confounding was made.]

Kucer conducted a cross-sectional study of ocular symptoms among mobile phone users in Turkey (Kucer, 2008). The study included 229 students at the Kocaeli Vocational School of Health Service, 79% women and 21% men. All participants were mobile phone users. No information was provided about procedures for recruitment of participants or participation rate, nor age distribution. Questionnaires were distributed asking for information about ocular symptoms in the same categories as Balik et al. (2005) described above. Analyses using Chi-square with Yates correction compared prevalence of symptoms among mobile phone users with <2 years of mobile phone use to those with >2 years with significance at $p<0.05$ [it is unclear to which category 2 years belongs]. The prevalence of blurring of vision was 6.6% among women and 6.3% among men [substantially lower than in the study by Balik et al. (2005)], and was higher among mobile phone users with >2 years duration of use (27.2%) compared to <2 years (8.8%) [some of the reported prevalences must be erroneous, gender specific results indicate that 15 persons in total reported blurring of vision, while the corresponding number of persons according to categories of mobile phone use would be 54 persons]. No other significant differences were found. [The cross-sectional design, uncertainties regarding subject selection and participation, no confounding control, and possibly erroneous analysis makes the study uninformative.]

6.2.2 Animal studies

Studies have been carried out on the effects of exposure to RF radiation on the lens of the eye and other tissues including the retina. Many of the early studies carried out in the 1960s and 1970s used rabbits, later studies tended to use primates because of the greater similarity of their facial and ocular structures to those of humans. These studies have been reviewed by WHO (1993) and are briefly summarized below, along with a discussion of the evidence from more recent papers.

6.2.2.1 Effects on the lens

Briefly, as noted by WHO (1993), cataract is a well-established thermal effect of RF exposure in anaesthetised rabbits (e.g. Carpenter, 1979; Guy et al., 1975; Kramar et al., 1978; Kramar et al., 1975). High lens temperatures induced by exposure of the head to microwaves have been shown to induce cataracts in the lenses of anaesthetised rabbits (Guy et al., 1975; Kramar et al., 1978); threshold temperatures for prolonged (100–200 min) exposure lie between 41 and 43°C; corresponding local SARs are in the range 100–140 W/kg. These high local SARs and temperatures resulted from protracted (>140 min) localised exposure of the eye to RF radiation of 1–10 GHz at power densities greater than 1.5 kW/m^2; whole body exposure at such levels however is limited

by thermal stress (Elder, 2003). The few experiments which have investigated the effect of chronic whole-body exposure of conscious rabbits to lower power densities (up to 100 W/m^2) reported a lack of effect on the lens. Cataracts were not observed in rabbits after exposure to 2.45 GHz RF fields at 100 W/m^2 (whole-body SAR of 1.5 W/kg) for up to 17 weeks (Ferri & Hagan, 1976). Nor was any change found in the eyes of rabbits exposed for ~6 months to 2.45 GHz where the maximal SAR in the head was 17 W/kg (Guy et al., 1980). Chou et al. (1982; 1983) also reported that low level pulsed or CW 2.45 GHz RF exposures for 3 months at SARs of 0.55 and 5.5 W/kg in the head did not cause cataracts.

These early studies also found primates to be less susceptible to cataract induction than rabbits (WHO, 1993). Opacities have not been induced in the eyes of anaesthetised rhesus monkeys after repeated acute localized exposures of up to 5 kW/m^2, well above threshold levels for anaesthetised rabbits (McAfee et al., 1979; McAfee et al., 1983). In addition, McAfee and colleagues exposed conscious monkeys to 2.45 GHz CW for up to 12 h over a 4 month period or to 9.3 GHz RF radiation (pulsed or CW) for up to 15 h over a 34 month period at SARs in the head of up to 40 W/kg. Eye examinations carried out 1–4 years after exposure revealed no effects on the lens. The lower susceptibility of primates to cataract induction is thought to result from structural differences in the eyes and skull of the two species, resulting in lower power absorption and heating of the thinner primate lens. WHO (1993) concluded that with respect to effects on the lens, it depends on the conditions of exposure if and what type of opacity is formed. The depth of penetration of the RF fields, and hence the frequency, is an important factor. Below 1.5 GHz, the dimensions of the orbit-eye combination are too small to result in local field concentration. Above about 10 GHz, penetration decreases and power absorption becomes increasingly restricted to the superficial tissue.

In a study aimed at replicating the study of Kues et al. (1985) that observed damage of RF exposure to the cornea (see section 6.3.3.2), Kamimura et al. (1994) exposed the eyes of 5 conscious cynomolgus monkeys for 4 h to CW 2.45 GHz radiation at a level (430 W/m^2, corresponding to a local SAR of ~11.3 W/kg) that exceeded the levels that resulted in corneal damage in the Kues study. Kamimura et al. did not find any damage to the lens, but they note that the use of anaesthesia by Kues et al. may have compromised heat dissipation in the eye, increasing the susceptibility to RF heating.

Kues et al. (1999) exposed one of the eyes of two juvenile rhesus monkeys and of five rabbits to 60 GHz, while the other eye served as control. The animals were exposed either once during 8 h, or repeatedly during 5 days for 4 h per day. The exposure level was 100 W/m^2 at the cornea. No changes were observed in the lenses of both rabbits and rhesus monkeys following these treatments.

Saito et al. (1998) exposed the eyes of nine conscious Japanese White rabbits for ~2.5–4 h to 2.45 GHz at an SAR to the eye of 26.5 W/kg, with the contralateral eye serving as a control, and reported acute thermal damage in the lens (fibrinogenesis in the anterior chamber) and other structures of the exposed eye (transient oedema of the cornea and of the conjunctival tissue surrounding it, and contraction and congestion of the pupil) . This damage resolved in about a week. In contrast to studies with anaesthetised rabbits, using higher local SARs, the authors did not observe cataracts.

Studies with both conscious and anaesthetised Dutch rabbits have been carried out by Kojima et al. (2004) who investigated the way in which anaesthesia reduces the capacity of the eye to dissipate heat. They assessed the effects of localized exposure of rabbit eyes for 2x60 min with 1 h interval to 2.45 GHz RF at a local SAR to the eye of 108 W/kg (n=3-4). The RF-induced changes, which disappeared within a week, included corneal oedema, inflammation of the iris and increased light-scattering from the anterior cortex of the lens. These effects were much more marked in the anaesthetized rabbits than in those not anaesthetised, reflecting the greater temperature increases (of up to 9 °C) measured in the posterior (vitreous) chamber and to a lesser extent in the anterior (aqueous) chamber of the eyes of the anaesthetised rabbits. Increased heating of the posterior region of the lens, particularly in anaesthetised rabbits due to reductions in blood flow, was confirmed in dosimetric and thermal modelling studies by Hirata et al. (2006).

Studies not included in the analysis

Hässig et al. performed two observational studies on cows. In the first study (Hässig et al., 2009) 253 calves, 83 to 370 days old (mean 146 days), originating from 229 different farms, were randomly selected at different abattoirs in Switzerland immediately after slaughter. For each animal, they calculated the exposure as the maximum possible exposure from the nearest base station to the farm within 2 km, or from all the base stations within a distance of 10 km from the farm. Using a factorial ANOVA they observed no significant association between the field strength in the 3rd trimester of pregnancy and the occurrence of cataracts in the calf

(OR=1.19, 95% CI: 0.86–1.65). Corrections were made for the presence of several infectious agents known to cause cataract in cows. [Since actual exposure levels are not provided, this study cannot be readily interpreted. The authors also assessed several parameters indicative of oxidative stress (superoxide dismutase, catalase, glutathione peroxidase) in the aqueous humour of the eyes, but the reporting on these measurements was unclear and incomplete.]

In the second study, Hässig et al. (2012) assessed nuclear cataracts in the progeny of cows from a single farm in Switzerland that spent their pregnancy in areas with continuous exposure from a nearby 1800 MHz base station. The maximum measured field strength was 0.17 V/m in the stable and 0.5 V/m in the yard. The authors calculated an increased incidence of severe nuclear cataracts (OR=3.51, 95% CI: 1.36–9.46) over the period of May 2004 through June 2009 when compared to the average incidence of cataract in Swiss calves. The base station started operating in 1999 and was decommissioned in the middle of 2006. Although according to the owner of the farm the number of cataracts increased some 12 months after the start of operation of the base stations and declined some 12 months after its decommission, no attempt was made to compare periods of exposure and non-exposure. The authors do note that hereditary effects may have played a role, since 55% of the calves with cataract had a mother with cataract. [Since no correction for this was made in the calculation, the analysis is not meaningful.]

Ye et al. (2001) locally exposed one of the eyes 10 New Zealand white rabbits for 3 h to 2.54 GHz at either 50 or 100 W/m^2, with the contralateral eye serving as control. They removed the eyes directly after treatment and made a single cell suspension of the lens epithelial cells, but the method for this is not described. They observed an increased number of apopototic cells relative to the control eyes after 50 W/m^2 ($p<0.01$) and increased numbers of necrotic cells after 100 W/m^2 ($p<0.05$). [The numbers of apoptotic and necrotic cells in the control eyes for the two groups differed considerably, indicating that the method of cell harvesting was not stable. It cannot be ruled out that the procedure for cell harvesting augments and/or stabilizes sub-lethal damage in the cells that might have been repaired if the cells would have remained in situ. So it is not possible to draw any conclusions from this study on possible harmful effects of the RF EMF on the lens.]

Inalöz et al. (1997) placed cages with 7 Wistar rats per group in front of a working microwave oven for 15 or 30 min daily for 1 month. They did not observe pathological damage to the lens, only small histological aberrations. [No information is provided how the SAR values, 3.9 W/kg for the 15 min exposures and 1.9 W/kg for the 30 min ones, were calculated. These values seem very high in view of the maximum allowed leakage of 10 W/m^2 at 5 cm from the oven, with which the used device was stated to comply. Because of this lack of proper dosimetric information this study cannot be used in the overall analysis.]

Balci et al. (2007) placed 900 MHz GSM phones over cages each housing 10 Wistar rats. The phones, on standby, were called intermittently (four times a day for 10 min) over a 4 week period. There was no RF dosimetry. The authors reported increased levels of malondialdehyde, an oxidation product of fatty acids, in the lens tissue of the exposed group ($p<0.05$). They suggested that this indicates that mobile phone radiation leads to oxidative stress. [The absence of proper dosimetry renders the results uninterpretable. The experimental protocol was only briefly described, leading to the supposition that uncontrolled factors may account for the effects seen.]

Table 6.2.1. Animal studies on the lens

Endpoint, animals, number per group, age at start	Exposure: source, schedule, level, freely moving or restrained, coexposure	Response	Comment	Reference
Cataract Rabbit : Japanese White (n=9) 10–12 weeks	2.45 GHz 160–240 min Whole eye average SAR 26.5 W/kg Restrained, unanaesthetized	Severe acute thermal damage, resolved in 1 week; no cataract.	No statistics.	Saito, Saiga & Suzuki (1998)
Temperature, macroscopic damage Rabbit: Dutch (exposed: n=3–4; sham: n=6) 13–16 weeks Unexposed eye served as control	2.54 GHz 60 min, 1 h interval, 60 min Whole eye average SAR 108 W/kg Restrained, with/without anaesthesia	Temporary inflammation of anterior segment, lens changes. Temperature increase with anesthesia 2–9°C higher than without.		Kojima et al. (2004)

Slit-lamp biomicroscopy of lens Rabbit, age not provided (n=5) Juvenile Rhesus monkey (n=2)	60 GHz 8 h; 4h/d, 5 d 10 mW/cm^2 (100 W/m^2) Restrained, anaesthesia unknown	No changes in lens of rabbit and rhesus monkey.	Descriptive study, no quantitative data.	Kues et al. (1999)
Slit-lamp biomicroscopy of lens Rhesus monkey (n=5) 9–11 years	2.54 GHz 4 h 43 mW/cm^2 (430 W/m^2)	No changes in lens.	Replication of Kues et al. (1985)	Kamimura et al. (1994)

6.2.2.2 Effects on iris and cornea

On the basis of only very few studies, WHO (1993) concluded that exposure of the eyes of monkeys to pulsed or CW 2.54 GHz fields may lead to corneal damage and vascular leakage in the iris.

Kues et al. (1992), in a follow-up to their previous studies, further investigated vascular leakage of the iris and corneal endothelial damage in rhesus and cynomolgus monkeys. They exposed the eyes to pulsed 2.45 GHz fields for 4 h per day during 3 days, with an SAR averaged over the eye of 0.052–3.9 W/kg. In addition, the effect of the opthalmologic drugs timolol maleate (which is used by people with glaucoma to lower the intraocular pressure by reducing the production of aqueous humour) and pilocarpine was studied. Ocular damage in the anaesthetized animals was observed with SARs of 2.6 W/kg and higher ($p<0.001$), but treatment with the opthalmologic drugs lowered the threshold to an SAR of 0.26 W/kg ($p<0.001$). [The number of animals is not reported, only the number of eyes (2-9 per group). It is unclear whether internal controls (unexposed eyes) were used.]

In contrast to these studies, Kamimura et al. (1994), in a study already mentioned in section 6.3.3.1, reported that they were unable to induce corneal or retinal lesions in the eyes of conscious rhesus monkeys exposed for 4 h to CW 2.45 GHz radiation at a level (430 W/m^2, corresponding to a local SAR of ~11.3 W/kg) exceeding the levels that resulted in corneal damage in the Kues et al. (1985) study. The technique used for the identification of corneal lesions (specular microscopy) was the same as that used by Kues et al. (1985), although these authors used histological techniques to confirm damage to both the cornea and retina, in contrast to Kamimura et al. (1994). However, Kamimura and colleagues note that the use of anaesthesia by Kues et al. may have compromised heat dissipation in the eye (see above) increasing the susceptibility to RF heating.

Lu et al. (2010) performed a study aimed at replicating the studies by Kues et al. (1985; 1992). They exposed the eyes of 4 anaesthetized rhesus monkeys to a 2.8 GHz field, pulse modulated at 34 Hz, and studied the corneal endothelial cell density and corneal thickness. In a first experiment they exposed the eyes to RF only for 4 h per day, 3 days per week, during 3 weeks. In a second experiment, 3 or 7 RF exposures of 4 h were combined with the application of the opthalmologic drugs timolol maleate and xalatan. In both experiments the SAR in the cornea was 5.07 W/kg. Neither of these treatments resulted in any effect on the cornea.

Two studies have been published that investigated ocular effects of exposure to RF EMF in the higher GHz range. In a study already mentioned in section 6.3.3.1, Kues et al. (1999) exposed eyes of both juvenile rhesus monkeys and rabbits to 60 GHz. The animals were exposed either once during 8 h, or repeatedly during 5 days for 4 h per day. The exposure level was 100 W/m^2 at the cornea. No changes were observed in the cornea and iris of both rabbits and rhesus monkeys following these treatments.

Chalfin et al. (2002) exposed the eyes of rhesus monkeys to pulsed 35 or 94 GHz, using exposures of very high power densities of 20–40 kW/m^2 for up to 5.5 seconds or 80 kW/m^2 for 1 second. They observed no difference in effect between the various exposure schedules. The fluence, i.e. the energy delivered per unit area, was considered the relevant parameter, since the penetration of RF fields at such high frequencies is minimal. The thresholds for corneal lesions, defined as a 50% chance for a grade 2 lesion (the middle of a scale of 5), were 7.5 J/cm^2 (75 kJ/m^2) for the 35 GHz exposure and 5 J/cm^2 (50 kJ/m^2) for 94 GHz. No effect was observed on corneal cell density.

Chalfin et al. (2002) also note that the rabbit cornea is not a particularly good model for human corneal damage, since it has significant differences from that of the primates. For example, the rabbit corneal epithelium undergoes a greater degree of keratinization than that of humans (Prince, 1964). The average

thickness central in the cornea of the rabbit is 0.40 mm, while it is 0.50 mm in rhesus monkeys and 0.56 mm in humans. But the most important difference is, that the rabbit corneal endothelial cells can proliferate upon injury, and thus have the capability of repair; primates lack this.

Study not included in the analysis

In a study already reported in the previous section, Balci et al. (2007) placed 900 MHz GSM phones over cages each housing 10 Wistar rats. The phones, on standby, were called intermittently (four times a day for 10 min) over a 4 week period. There was no RF dosimetry. The authors reported increased levels of malondialdehyde, an oxidation product of fatty acids, and reduced levels of superoxide dismutase, a radical scavenger, in corneal tissue of the exposed group ($p<0.05$). They suggested that this indicates that mobile phone radiation leads to oxidative stress. [The absence of proper dosimetry renders the results uninterpretable. The experimental protocol was only briefly described, leading to the supposition that uncontrolled factors may account for the effects seen.]

Demirel et al. (2012) exposed groups of 8-9 Wistar rats to 1.9–2.2 GHz fields generated by a tri-band mobile phone situated under the cage. The phone was operated daily for 20 min in 'listening' and and 20 min in 'speaking' mode for 20 days, and in standby the rest of the time. The authors investigated parameters indicative for oxidative stress in homogenized eyes (excluding the lens) and blood, and did not find any effects of exposure. [The actual exposure of the animals is unknown and therefore these results cannot be interpreted.]

Table 6.2.2. Animal studies on iris and cornea

Endpoint, animals, number per group, age at start	Exposure: source, schedule, level, freely moving or restrained, coexposure	Response	Comment	Reference
Vascular leakage iris; macroscopic corneal endothelial damage Rhesus, Cynomolgus monkey (n=2–9 eyes) 4–18 year	2.45 GHz, pulsed 4 h/day, 3 days Eye SAR 0.052, 0.26, 1.3, 2.6, 3.9 W/kg with/without timolol maleate, pilocarpine Restrained, anaesthetized	Threshold for ocular damage 2.6 W/kg; with opthalmologic drug treatment lowered to 0.26 W/kg.	Number of animals not reported, only number of eyes; unclear whether internal controls (unexposed eyes) were used.	Kues et al. (1992)
Corneal endothelial cell density, corneal thickness Rhesus monkey (n=4) Adult	2.8 GHz, 34 Hz pulsed Exp. 1: 4 h/day, 3 days/week, 3 weeks Exp.2: Timolol maleate + xalatan + 3 or 7x 4 h Cornea SAR 5.07 W/kg Restrained, anaesthetized	No effect on corneal endothelial cell density, corneal thickness. Studies of Kues et al. not confirmed.	Replication of Kues et al. (1992; 1997).	Lu et al. (2010)
Slit-lamp biomicroscopy of cornea and iris; wide-field specular microscopy of corneal endothelium; iris angiography Rabbit, age not provided (n=5) Juvenile Rhesus monkey (n=2)	60 GHz 8 h; 4h/day, 5 days 10 mW/cm^2 (100 W/m^2) Restrained, anaesthesia unknown	No changes in eyes of rabbit and rhesus monkey.	Descriptive study, no quantitative data.	Kues et al. (1999)
Slit-lamp biomicroscopy of cornea and iris Rhesus monkey (n=5) 9–11 y	2.54 GHz 4 h 43 mW/cm^2 (430 W/m^2)	No changes in cornea and iris.	Replication of Kues et al. (1997)	Kamimura et al. (1994)

Corneal microscopy, cell density, thickness Rhesus monkey (n=5)	35 GHz, pulsed: 2 W/cm^2 (20 kW/m^2), 2–5.5 s 4 W/cm^2 (40 kW/m^2), 1 s 94 GHz, pulsed: 2 W/cm^2 (20 kW/m^2), 2–4 s 8 W/cm^2 (80 kW/m^2), 1 s Fluence range 0–11 J/cm^2 (0-110 kJ/m^2) Restrained, anesthetized	No difference between various exposure schedules, fluence considered as relevant parameter; threshold corneal lesion (50% chance grade 2 lesion) at 75 kJ/m^2 (35 GHz) or 50 kJ/m^2 (94 GHz); no effect on corneal cell density.	Study to obtain data in a range where there is hardly any, to support standard setting.	Chalfin et al. (2002)

757

758 *6.2.2.3 Effects on the retina and the whole eye*

759 In the WHO (1993) report no studies on the effect of RF EMF on the retina or the whole eye are
760 discussed. Only a few studies, performed in recent years, have been identified.

761 Lu et al. (2000) exposed or sham-exposed unanaesthetised rhesus monkeys to pulsed 1.25 GHz over a
762 3 week period at localised SARs averaged over the retina of 4.3, 8.4 or 20.2 W/kg. RF-induced changes in the
763 retina were examined using various measures of retinal integrity both before and after exposure, and complete
764 retinal histopathology following termination of the experiment. No significant changes were seen in the exposed
765 eyes compared to those pre- or sham-exposed either in the appearance of the retina or in the pattern of blood
766 vessels in the retina. The electroretinogram resulting from electrical fields generated by cone photoreceptors in
767 response to light flashes was enhanced in monkeys exposed at retinal SARs of 8.4 or 20.2 W/kg ($p<0.05$), but
768 not in those exposed at 4.3 W/kg. The authors suggest that this effect is likely to represent a transient
769 physiological change, since histopathologic examination did not reveal any pathological changes.

770 Two studies in rats investigated parameters indicative for oxidative stress in the retina or the whole
771 eye. Ozguner et al. (2006) exposed Sprague Dawley rats for 30 min per day during 60 days to a 900 MHz mobile
772 phone signal to the head, with an SAR of 4 W/kg. Separate groups of 10 rats were given the antioxidants
773 melatonin or caffeic acid phenethyl ester (CAPE) directly before each exposure. After the last exposure the
774 retinas were removed and the levels of oxidative stress parameters measured. In the group only exposed to RF
775 EMF the levels of malondialdehyde and nitrous oxide (NO) were increased (both $p<0.0001$), indicating
776 increased oxidative stress, and the levels of the antioxidants superoxide dismutase ($p<0.001$), catalase
777 ($p<0.0001$) and glutathione peroxidase ($p<0.0005$) were reduced. Administration of either melatonin or CAPE
778 prevented the increase in the levels of malondialdehyde and NO, with the exception of the NO level after CAPE
779 administration that also was reduced compared to that in the RF-only group, but still significantly higher than in
780 the sham controls ($p<0.01$). Melatonin and CAPE administration before RF exposure counteracted the decrease
781 in the levels of the three antioxidants, where melatonin even increased the level of superoxide dismutase
782 significantly above that of the sham controls ($p<0.001$).

783 Jelodar et al. (2013) exposed groups of 8 Sprague Dawley rats to a simulated mobile phone base
784 station signal for 4 h per day and 45 days at a power density similar to that measured at a distance of 17 m from a
785 base station antenna: 6.789 W/m^2, which can be calculated to correspond to a whole-body SAR of approximately
786 0.01 W/kg. One group received RF exposure only, and one group was administered vitamin C before each
787 exposure as an antioxidant. RF EMF exposure decreased superoxide dismutase, glutathione peroxidase and
788 catalase in the eye, and increased malondialdehyde (all $p<0.05$). This indicates an increased oxidative stress.
789 Treatment with vitamin C prevented the changes of the biomarkers for oxidative stress.

790 *Studies not included in the analysis*

791 Zareen, Khan and Minhas (2009) investigated the effect of exposure of unhatched chicken to a mobile
792 phone signal on the retina. Eggs were exposed by placing an 1800 MHz GSM phone within 16.5 cm from the
793 eggs. The phone was called for 2 x 15 min per day during either 10 or 15 days. In the animals exposed for 10
794 days, retinal epithelial pigmentation was lower than in controls ($p<0.001$), while after 15 days exposure it was
795 higher ($p<0.001$). In the 15-day group also the epithelial thickness was higher ($p<0.01$) while in the 10-day
796 group it was less then in the controls ($p<0.05$). [It is not clear what the exposure level was in this study, therefore
797 it cannot be interpreted. Moreover, the initial group size is stated to be 30 eggs, but in the analysis for epithelial
798 pigmentation group size varies from 22 to 29. No explanation or correction is given for the missing eggs.]

Table 6.2.3. Animal studies on retina and whole eye				
Endpoint, animals, number per group, age at start	**Exposure: source, schedule, level, freely moving or restrained, coexposure)[b]**	**Response**	**Comment**	**Reference**
Monkeys				
Fundus photographs, angiography, electroretinograms, histopathology Rhesus monkey (n=17 monkeys; 3–10 eyes/group) 4.0–9.5 years	Radar: 1.25 GHz, pulsed at 0, 0.59, 1.18, 2.79 Hz 4 h/d, 3 d/week, 3 weeks Retina SAR 0, 4.3, 8.4, 20.2 W/kg Restrained, unanaesthetized	Small physiological changes (enhanced electroretinogram), no damage. Kues studies not confirmed, perhaps there effect of ketamine anaesthesia.	Replication of unpublished studies by Kues et al.	Lu et al. (2000)
Rodents				
Oxidative stress enzymes in retina Rat: Sprague Dawley (n=10) 8 weeks	900 MHz mobile phone 30 min/day, 60 days Head average SAR 4 W/kg with/without melatonin or caffeic acid phenethyl ester (CAPE) Restrained	Malondialdehyde, nitrous oxide increased, superoxide dismutase, catalase, glutathione peroxidase reduced. No or reduced effect of RF EMF in combination withmelatonin or CAPE.		Ozguner, Bardak & Comlekci (2006)
Oxidative stress enzymes in whole eye Rat: Sprague Dawley (n=8)	Signal generator simulating 900 MHz base station signal 4 h/day, 45 days 0.6789 mW/cm^2(6.789 W/m^2); whole body SAR about 0.01 W/kg With/without vitamin C Free	Decreased superoxide dismutase, glutathione peroxidase, catalase, increased malondialdehyde. No effect of RF EMF in combination with vitamin C.		Jelodar, Akbari & Nazifi, (2013)

6.2.3 In vitro studies

Lens epithelial cell cultures exposed to an intermittent (5 min on/10 min off cycles) 1800 MHz GSM signal (SAR = 1, 2, 3, 4 W/kg) for 2 hours were used by Yao et al. (2008a) to evaluate the induction of genotoxic effects and oxidative stress. Moreover, RF was also superposed with 2 μT magnetic noise (30–90 Hz magnetic fields in Helmholtz coils) for 2 hours. In three independent experiments, a significant increase in single strand breaks was observed at SARs of 3 and 4 W/kg ($p<0.001$), while no differences were detected on double strand breaks, as assessed by gamma-H2A histone family, member X (γ-H2AX) foci formation. As positive controls, the cells were treated with 4-nitroquinoline-1-oxide, an inducer of foci, which resulted in positive findings. Reactive oxygen species (ROS) also increased after exposure at 2, 3 and 4 W/kg ($p<0.05$), as assessed by applying cytofluorimetric techniques. When using superposed electromagnetic noise, no DNA damage and ROS formation were observed. [This study has been also described in sections 12.3.1 (Genotoxicity) and 12.3.5 (Oxidative stress).]

Ni et al. (2013) investigated the induction of oxidative stress in human lens epithelial B3 (HLE-B3) cells intermittently exposed (5 min on/10 min off cycles) to 1800 MHz RF EMF, GSM signal (average SAR = 2, 3 or 4 W/kg). The levels of ROS were measured with the 2',7'-dichlorofluorescein (DCFH-DA) assay in cells exposed for 0.5, 1 and 1.5 h. Lipid peroxidation was detected by a malondialdehyde (MDA, a member of a family of end products of lipid peroxidation) test in cells exposed for 6, 12 and 24 h. The mRNA expression of superoxide dismutases (SOD1, SOD2), catalase (CAT) and glutathione peroxidase (GPx1)genes and the expression of SOD1, SOD2, CAT and GPx1 proteins was measured by quantitative reverse transcriptase-polymerase chain reaction (qRT-PCR) and Western blot assays in the cells exposed for 1 h. For all the experimental conditions tested, in the RF exposed cultures ROS and MDA levels increased ($p<0.05$) and mRNA and protein expression significantly decreased ($p<0.05$) in comparison to sham-exposed cells; cell viability was also decreased ($p<0.05$). Three independent experiments for each exposure condition and endpoint were performed. Positive controls have not been included in the study design. [This study has also been described in Section 12.3.5 (Oxidative stress).]

Studies not included in the analysis

Li et al**.** (2007) exposed human lens epithelial cells (HLEC) to 1800 MHz GSM-modulated RF EMF for 2 h at SARs of 1–3.5 W/kg. Immediately after exposure, proteins were extracted and analyzed by 2D gel electrophoresis (3 independent experiments). The authors observed that four protein spots were up-regulated by more than 3-fold after exposure to 3.5 W/kg and 2-fold after exposure to 2.0 W/kg (no p-values reported). No proteins demonstrated altered expression after a 1 W/kg RF exposure. The authors used mass spectroscopy to identify these spots as stress-related proteins, namely HSP70 and ribonucleoporin K. However, differential expression of these proteins was not confirmed by Western blot analysis. [It is unclear whether differential expression was determined by fold-changes or statistical analysis. In this study, also reported in Section 12.3.3 (Gene and protein expression), positive controls have not been included.]

Lixia et al. (2006) also exposed human lens epithelial cells (HLEC) to 1800 MHz GSM-modulated RF EMF, at SARs of 1–3 W/kg for 2 h. Compared to sham-exposed cells, no differences were detected in cell proliferation rate, measured immediately and 1 and 4 days after exposure (see Section 12.3.6). DNA strand breaks and their repair were measured immediately after 2 h RF exposure and at incubation times of 30, 60, 120 and 240 min post-exposure, respectively. The comet assay revealed no differences in strand breaks at 1 and 2 W/kg, while a significant increase was observed at 3 W/kg immediately after exposure and after 30 min incubation ($p<0.05$). No effect of the RF exposure was observed on DNA repair rate (see Section 12.3.1). Increased HSP70 protein expression was detected at higher doses ($p<0.05$), but no corresponding change was observed in mRNA expression (see Section 12.3.3). [In this study, the number of independent experiments is not reported, although statistical analysis was performed.]

In a study by Yao and co-workers (Yao et al., 2004), cultured rabbit lens epithelial cells (RLEC) were exposed to continuous RF EMF at 2450 MHz and power densities of 1.0, 2.5, 5.0, 10.0 and 20 W/m^2 for up to 8 h. Cell cycle progression was not affected in cultures exposed to power densities lower than 5.0 W/m^2, while cultures exposed to 5.0, 10 and 20 W/m^2 were arrested in the G0/G1 phase of the cell cycle when compared to sham-exposed cultures ($p<0.01$) (see Section 12.3.6). Moreover, the expression of two genes involved in the cell cycle, P21WAF1 and P27Kip1, was evaluated using Western blot analysis. Increased expression of P27Kip1 protein was detected in cultures exposed to 20 W/m^2 for 4, 6 and 8 h. This latter finding was not confirmed by RT-PCR analysis (see Section 12.3.3). [The results of this study cannot be interpreted since no dosimetric evaluation was performed.]

Table 6.2.4. In vitro studies assessing effects of RF EMF exposure on ocular function

Cell type Number of independent experiments	Biological endpoint	Exposure conditions	Results	Comment	Reference
Lens epithelial cells n=3	Strand breaks, ɣ-H2AX foci ROS	1800 MHz, GSM Average SAR = 1, 2, 3, 4 W/kg 2 h (5 min on/10 min off cycles) Magnetic field noise superposition (2 µT, 30-90 Hz)	Increased single strand breaks at 3 and 4 W/kg. No effects on double strand breaks (ɣ-H2AX foci). Increased ROS production at 2, 3 and 4 W/kg. No increase in strand breaks and ROS with magnetic field noise.	For Genotoxicity and oxidative stress see Sections 12.3.1 and 12.3.5. No information on blinding of staff.	Yao et al. (2008a)

Human lens epithelial (HLE-B3) cells n=3	ROS (DCFH-DA assay) Lipid peroxidation (MDA test) Gene and protein expression of SOD1, SOD2, CAT and GPx1	1800 MHz, GSM Average SAR 2, 3, 4 W/kg 0.5, 1, 1.5 h (ROS) 6, 12, 24 h (lipid peroxidation) 1 h (gene and protein expression) (5 min on/10 min off cycles)	Increase of ROS and lipid peroxidation. Decrease of gene and protein expression.	Decreased cell viability. For oxidative stress see Section 12.3.5 No information on blinding of staff.	Ni et al. (2013)

"No effect" means no statistically significant effect.

Abbreviations: CAT: catalase; DCFH-DA: 2',7'-dichlorofluorescein; GSM: Global System for Mobile Communication; GPx: glutathione peroxidase; Gamma H2AX: H2A histone family, member X; MDA: malondialdehyde; ROS: reactive oxygen species; SAR: specific absorption rate; SOD: superoxide-dismutase

Excluded references

(Dovrat et al., 2005), (Zhou et al., 2008), (Yao et al., 2008b).

REFERENCES

Adair ER, Adams BW, Hartman SK (1992). Physiological interaction processes and radio-frequency energy absorption. Bioelectromagnetics, 13(6):497-512.

Arai N et al. (2003). Thirty minutes mobile phone use has no short-term adverse effects on central auditory pathways. Clin Neurophysiol, 114(8):1390-1394.

Aran JM et al. (2004). Effects of exposure of the ear to GSM microwaves: in vivo and in vitro experimental studies. Int J Audiol, 43(9):545-554.

Bak M et al. (2003). No effects of acute exposure to the electromagnetic field emitted by mobile phones on brainstem auditory potentials in young volunteers. Int J Occup Med Environ Health, 16(3):201-208.

Balachandran R et al. (2012). Effects of Bluetooth device electromagnetic field on hearing: pilot study. J Laryngol Otol, 126(4):345-348.

Balci M, Devrim E, Durak I (2007). Effects of mobile phones on oxidant/antioxidant balance in cornea and lens of rats. Curr Eye Res, 32(1):21-25.

Balik HH et al. (2005). Some ocular symptoms and sensations experienced by long term users of mobile phones. Pathol Biol (Paris), 53(2):88-91. Epub 2005/02/15.

Bamiou DE et al. (2008). Mobile telephone use effects an peripheral audiovestibular function: A case-control study. Bioelectromagnetics, 29(2):108-117.

Budak GG et al. (2009a). Effects of intrauterine and extrauterine exposure to GSM-like radiofrequency on distortion product otoacoustic emissions in infant male rabbits. Int J Pediatr Otorhinolaryngol, 73(3):391-399.

Budak GG et al. (2009b). Effects of GSM-like radiofrequency on distortion product otoacoustic emissions of rabbits: comparison of infants versus adults. Int J Pediatr Otorhinolaryngol, 73(8):1143-1147.

Budak GG et al. (2009c). Effects of GSM-like radiofrequency on distortion product otoacoustic emissions in pregnant adult rabbits. Clin Invest Med, 32(2):E112-E116.

Burkhardt M, Spinelli Y, Kuster N (1997). Exposure setup to test effects of wireless communications systems on the CNS. Health Phys, 73(5):770-778.

Carpenter RL (1979). Ocular effects of microwave radiation. Bull NY Acad Med, 55(11):1048-1057.

Chalfin S et al. (2002). Millimeter wave absorption in the nonhuman primate eye at 35 GHz and 94 GHz. Health Phys, 83(1):83-90.

885 Chou CK et al. (1982). Effects of continuous and pulsed chronic microwave exposure on rabbits. Radio Sci, 17(5S):185S-
886 193S.

887 Chou CK et al. (1983). Chronic exposure of rabbits to 0.5 and 5 mW/cm2 2450-MHz CW microwave radiation.
888 Bioelectromagnetics, 4(1):63-77.

889 Colletti V et al. (2011). Intraoperative observation of changes in cochlear nerve action potentials during exposure to
890 electromagnetic fields generated by mobile phones. Journal of Neurology Neurosurgery and Psychiatry, 82(7):766-771.

891 Davidson HC, Lutman ME (2007). Survey of mobile phone use and their chronic effects on the hearing of a student
892 population. Int J Audiol, 46(3):113-118. Epub 2007/03/17.

893 de Sèze R et al. (2001). Evaluation of the health impact of the radio-frequency fields from mobile telephones. Indoor Built
894 Environ, 10(5):284-290.

895 Demirel S et al. (2012). Effects of third generation mobile phone-emitted electromagnetic radiation on oxidative stress
896 parameters in eye tissue and blood of rats. Cutan Ocul Toxicol, 31(2):89-94.

897 Dovrat A et al. (2005). Localized effects of microwave radiation on the intact eye lens in culture conditions.
898 Bioelectromagnetics, 26(5):398-405.

899 Elder JA (2003). Ocular effects of radiofrequency energy. Bioelectromagnetics, Suppl. 6:S148-161.

900 Elder JA, Chou CK (2003). Auditory response to pulsed radiofrequency energy. Bioelectromagnetics, Suppl 6:S162-S173.

901 Ferri ES, Hagan GJ. Chronic, low-level exposure of rabbits to microwaves. In: Johnson CC, Shore ML, eds. Biological
902 effects of electromagnetic waves. Vol. 1. Rockville, MD, HEW, 1976:129-142 ((FDA) 77-8010).

903 Forge A, Schacht J (2000). Aminoglycoside antibiotics. Audiol Neurootol, 5(1):3-22.

904 Frei P et al. (2012). Cohort study on the effects of everyday life radio frequency electromagnetic field exposure on non-
905 specific symptoms and tinnitus. Environ Int, 38(1):29-36. Epub 2011/10/11.

906 Galloni P et al. (2005a). Effects of 900 MHz electromagnetic fields exposure on cochlear cells' functionality in rats:
907 Evaluation of distortion product otoacoustic emissions. Bioelectromagnetics.

908 Galloni P et al. (2005b). Electromagnetic fields from mobile phones do not affect the inner auditory system of Sprague-
909 Dawley rats. Radiat Res, 164(6):798-804.

910 Galloni P et al. (2009). No effects of UMTS exposure on the function of rat outer hair cells. Bioelectromagnetics, 30(5):385-
911 392.

912 Guy AW et al. (1975). Effect of 2450-MHz radiation on the rabbit eye. IEEE Trans Microw Theory Tech, 23(6):492-498.

913 Guy AW et al. (1980). Long-term 2450 MHz CW microwave irradiation of rabbits: Methodology and evaluation of ocular
914 and physiologic effects. J Microw Power, 15:37-44.

915 Hässig M et al. (2009). Prevalence of nuclear cataract in Swiss veal calves and its possible association with mobile telephone
916 antenna base stations. Schweiz Arch Tierheilkd, 151(10):471-478.

917 Hässig M, Jud F, Spiess B (2012). [Increased occurrence of nuclear cataract in the calf after erection of a mobile phone base
918 station]. Schweiz Arch Tierheilkd, 154(2):82-86.

919 Hatzopoulos S et al. (1999). Evaluation of cisplatin ototoxicity in a rat animal model. Ann N Y Acad Sci, 884:211-225.

920 Henley CM, Rybak LP (1995). Ototoxicity in developing mammals. Brain Res Brain Res Rev, 20(1):68-90.

921 Hirata A et al. (2006). Computational verification of anesthesia effect on temperature variations in rabbit eyes exposed to
922 2.45 GHz microwave energy. Bioelectromagnetics, 27(8):602-612.

923 Huang TQ et al. (2008). Characterization of biological effect of 1763 MHz radiofrequency exposure on auditory hair cells.
924 Int J Radiat Biol, 84(11):909-915.

Hutter HP et al. (2010). Tinnitus and mobile phone use. Occup Environ Med, 67(12):804-808. Epub 2010/06/25.

Inalöz SS et al. (1997). Acceptable radiation leakage of microwave ovens on pregnant and newborn rat brains. Clin Exp Obstet Gynecol, 24(4):215-219.

Janssen T et al. (2005). Investigation of potential effects of cellular phones on human auditory function by means of distortion product otoacoustic emissions. J Acoust Soc Am, 117(3 Pt 1):1241-1247. Epub 2005/04/06.

Jelodar G, Akbari A, Nazifi S (2013). The prophylactic effect of vitamin C on oxidative stress indexes in rat eyes following exposure to radiofrequency wave generated by a BTS antenna model. Int J Radiat Biol, 89(2):128-131.

Kamimura Y et al. (1994). Effect of 2.45 GHz microwave irradiation on monkey eyes. IEICE Trans Commun, E77-B:762-765.

Kaprana AE et al. (2011). Auditory brainstem response changes during exposure to GSM-900 radiation: an experimental study. Audiol Neurootol, 16(4):270-276.

Kayabasoglu G et al. (2011). Effect of chronic exposure to cellular telephone electromagnetic fields on hearing in rats. J Laryngol Otol, 125(4):348-353.

Kellenyi L et al. (1999). Effects of mobile GSM radiotelephone exposure on the auditory brainstem response (ABR). Neurobiology (Bp), 7(1):79-81.

Kerekhanjanarong V et al. (2005). The effect of mobile phone to audiologic system. J Med Assoc Thai, 88 Suppl 4:S231-234. Epub 2006/04/21.

Khan MM (2008). Adverse effects of excessive mobile phone use. Int J Occup Med Environ Health, 21(4):289-293.

Kizilay A et al. (2003). Effects of chronic exposure of electromagnetic fields from mobile phones on hearing in rats. Auris Nasus Larynx, 30(3):239-245.

Kojima M et al. (2004). Influence of anesthesia on ocular effects and temperature in rabbit eyes exposed to microwaves. Bioelectromagnetics, 25(3):228-233.

Kramar P et al. (1978). Acute microwave irradiation and cataract formation in rabbits and monkeys. J Microw Power, 13(3):239-249.

Kramar PO et al. (1975). The ocular effects of microwaves on hypothermic rabbits: a study of microwave cataractogenic mechanisms. Ann N Y Acad Sci, 247:155-165.

Kucer N (2008). Some ocular symptoms experienced by users of mobile phones. Electromagn Biol Med, 27(2):205-209.

Kues HA et al. (1985). Effects of 2.45-GHz microwaves on primate corneal endothelium. Bioelectromagnetics, 6(2):177-188.

Kues HA et al. (1992). Increased sensitivity of the non-human primate eye to microwave radiation following ophthalmic drug pretreatment. Bioelectromagnetics, 13(5):379-393.

Kues HA et al. (1999). Absence of ocular effects after either single or repeated exposure to 10 mW/cm(2) from a 60 GHz CW source. Bioelectromagnetics, 20(8):463-473.

Kwon MS et al. (2010). No effects of mobile phone electromagnetic field on auditory brainstem response. Bioelectromagnetics, 31(1):48-55. Epub 2009/07/18.

Landgrebe M et al. (2009). Association of tinnitus and electromagnetic hypersensitivity: hints for a shared pathophysiology? PLoS One, 4(3):e5026. Epub 2009/03/28.

Li HW et al. (2007). Proteomic analysis of human lens epithelial cells exposed to microwaves. Jpn J Ophthalmol, 51(6):412-416.

Lin JC, Wang Z (2007). Hearing of microwave pulses by humans and animals: effects, mechanism, and thresholds. Health Phys, 92(6):621-628.

Lixia S et al. (2006). Effects of 1.8 GHz radiofrequency field on DNA damage and expression of heat shock protein 70 in human lens epithelial cells. Mutat Res, 602(1-2):135-142.

967 Lu ST et al. (2000). Effects of high peak power microwaves on the retina of the rhesus monkey. Bioelectromagnetics,
968 21(6):439-454.

969 Lu ST et al. (2010). Absence of corneal endothelium injury in non-human primates treated with and without ophthalmologic
970 drugs and exposed to 2.8 GHz pulsed microwaves. Bioelectromagnetics, 31(4):324-333.

971 Marino C et al. (2000). Effects of microwaves (900 MHz) on the cochlear receptor: exposure systems and preliminary results.
972 Radiat Environ Biophys, 39(2):131-136.

973 McAfee RD et al. (1979). Absence of ocular pathology after repeated exposure of unanesthetized monkeys to 9.3-GHz
974 microwaves. J Microw Power, 14(1):41-44.

975 McAfee RD et al. (1983). Absence of deleterious effects of chronic microwave radiation on the eyes of rhesus monkeys.
976 Ophthalmology, 90(10):1243-1245.

977 Meo SA, Al-Drees AM (2005). Mobile phone related-hazards and subjective hearing and vision symptoms in the Saudi
978 population. Int J Occup Med Environ Health, 18(1):53-57. Epub 2005/08/02.

979 Monnery PM, Srouji EI, Bartlett J (2004). Is cochlear outer hair cell function affected by mobile telephone radiation? Clin
980 Otolaryngol Allied Sci, 29(6):747-749.

981 Mora R et al. (2006). A study of the effects of cellular telephone microwave radiation on the auditory system in healthy men.
982 Ear Nose Throat J, 85(3):160, 162-163.

983 Mortazavi SM, Ahmadi J, Shariati M (2007). Prevalence of subjective poor health symptoms associated with exposure to
984 electromagnetic fields among university students. Bioelectromagnetics, 28(4):326-330. Epub 2007/03/03.

985 Ni S et al. (2013). Study of oxidative stress in human lens epithelial cells exposed to 1.8 GHz radiofrequency fields. PLoS
986 One, 8(8):e72370.

987 Oktay MF et al. (2004). Occupational safety: effects of workplace radiofrequencies on hearing function. Arch Med Res,
988 35(6):517-521. Epub 2005/01/06.

989 Oktay MF, Dasdag S (2006). Effects of intensive and moderate cellular phone use on hearing function. Electromagn Biol
990 Med, 25(1):13-21. Epub 2006/04/06.

991 Oysu C et al. (2005). Effects of the acute exposure to the electromagnetic field of mobile phones on human auditory
992 brainstem responses. Eur Arch Otorhinolaryngol, 262(10):839-843.

993 Ozguner F, Bardak Y, Comlekci S (2006). Protective effects of melatonin and caffeic acid phenethyl ester against retinal
994 oxidative stress in long-term use of mobile phone: a comparative study. Mol Cell Biochem, 282(1-2):83-88.

995 Ozturan O et al. (2002). Effects of the electromagnetic field of mobile telephones on hearing. Acta Otolaryngol, 122(3):289-
996 293.

997 Paglialonga A et al. (2007). Effects of mobile phone exposure on time frequency fine structure of transiently evoked
998 otoacoustic emissions. J Acoust Soc Am, 122(4):2174-2182. Epub 2007/10/02.

999 Parazzini M et al. (2005). Influence on the mechanisms of generation of distortion product otoacoustic emissions of mobile
1000 phone exposure. Hear Res, 208(1-2):68-78. Epub 2005/08/02.

1001 Parazzini M et al. (2007a). Effects of GSM cellular phones on human hearing: The European project "GUARD". Radiation
1002 Research, 168(5):608-613.

1003 Parazzini M et al. (2007b). Possible combined effects of 900 MHz continuous-wave electromagnetic fields and gentamicin on
1004 the auditory system of rats. Radiat Res, 167(5):600-605.

1005 Parazzini M et al. (2007c). Modeling of the internal fields distribution in human inner hearing system exposed to 900 and
1006 1800 MHz. IEEE Trans Biomed Eng, 54(1):39-48.

1007 Parazzini M et al. (2009). Effects of UMTS cellular phones on human hearing: results of the European project EMFnEAR.
1008 Radiat Res, 172(2):244-251. Epub 2009/07/28.

1009 Parazzini M et al. (2010). Absence of short-term effects of UMTS exposure on the human auditory system. Radiat Res,
1010 173(1):91-97. Epub 2010/01/01.

1011 Pau HW et al. (2005). Can electromagnetic fields emitted by mobile phones stimulate the vestibular organ? Otolaryngol Head
1012 Neck Surg, 132(1):43-49.

1013 Prince JH. The rabbit in eye research. In: The cornea. Springfield, IL, Charles C. Thomas Publishers, 1964:86-139.

1014 Röösli M, Mohler E, Frei P (2010). Sense and sensibility in the context of radiofrequency electromagnetic field exposure.
1015 Comptes-Rendus Physique de l'Académie des Sciences, 11(9-10):576-584.

1016 Saito K, Saiga T, Suzuki K (1998). Reversible irritative effect of acute 2.45 GHz microwave exposure on rabbit eyes--a
1017 preliminary evaluation. J Toxicol Sci, 23(3):197-203.

1018 Seaman RL, Lebovitz RM (1987). Auditory unit responses to single-pulse and twin-pulse microwave stimuli. Hear Res,
1019 26(1):105-116.

1020 Seaman RL, Beblo DA (1992). Modification of acoustic startle by microwave pulses in the rat: a preliminary report.
1021 Bioelectromagnetics, 13(4):323-328.

1022 Seaman RL, Beblo DA, Raslear TG (1994). Modification of acoustic and tactile startle by single microwave pulses. Physiol
1023 Behav, 55(3):587-595.

1024 Seckin E et al. (2014). The effect of radiofrequency radiation generated by a Global System for Mobile Communications
1025 source on cochlear development in a rat model. J Laryngol Otol, 128(5):400-405.

1026 Sievert U, Eggert S, Pau HW (2005). Can mobile phone emissions affect auditory functions of cochlea or brain stem?
1027 Otolaryngol Head Neck Surg, 132(3):451-455.

1028 Sievert U et al. (2007). [Effects of electromagnetic fields emitted by cellular phone on auditory and vestibular labyrinth].
1029 Laryngorhinootologie, 86(4):264-270. Wirkung elektromagnetischer Felder des GSM-Mobilfunksystems auf auditives und
1030 vestibulares Labyrinth und Hirnstamm.

1031 Stefanics G et al. (2007). Short GSM mobile phone exposure does not alter human auditory brainstem response. BMC Public
1032 Health, 7:325. Epub 2007/11/14.

1033 Stefanics G et al. (2008). Effects of twenty-minute 3G mobile phone irradiation on event related potential components and
1034 early gamma synchronization in auditory oddball paradigm. Neuroscience, 157(2):453-462.

1035 Sudan M et al. (2013). Cell phone exposures and hearing loss in children in the Danish National Birth Cohort. Paediatr
1036 Perinat Epidemiol, 27(3):247-257. Epub 2013/04/12.

1037 Uloziene I et al. (2005). Assessment of potential effects of the electromagnetic fields of mobile phones on hearing. BMC
1038 Public Health, 5:39. Epub 2005/04/21.

1039 WHO - World Health Organization. *Electromagnetic fields (300 Hz to 300 GHz)*. Geneva, World Health Organization, 1993.

1040 Wu WJ, Sha SH, Schacht J (2002). Recent advances in understanding aminoglycoside ototoxicity and its prevention. Audiol
1041 Neurootol, 7(3):171-174.

1042 Yao K et al. (2004). Low power microwave radiation inhibits the proliferation of rabbit lens epithelial cells by upregulating
1043 P27Kip1 expression. Mol Vis, 10:138-143.

1044 Yao K et al. (2008a). Electromagnetic noise inhibits radiofrequency radiation-induced DNA damage and reactive oxygen
1045 species increase in human lens epithelial cells. Mol Vis, 14:964-969.

1046 Yao K et al. (2008b). Effect of superposed electromagnetic noise on DNA damage of lens epithelial cells induced by
1047 microwave radiation. Invest Ophthalmol Vis Sci, 49(5):2009-2015.

1048 Ye J et al. (2001). Low power density microwave radiation induced early changes in rabbit lens epithelial cells. Chin Med J
1049 (Engl), 114(12):1290-1294.

1050 Zareen N, Khan MY, Minhas LA (2009). Derangement of chick embryo retinal differentiation caused by radiofrequency
1051 electromagnetic fields. Congenit Anom (Kyoto), 49(1):15-19.

Zhou XR et al. (2008). The study of retinal ganglion cell apoptosis induced by different intensities of microwave irradiation. Ophthalmologica, 222(1):6-10.