7 NEUROENDOCRINE SYSTEM

7.1 Epidemiological studies

No epidemiological studies on effects on the neuroendocrine system were available at the time of the previous WHO Environmental Health Criteria document (WHO, 1993). Today, three types of non-reproductive hormonal endpoints in relation to RF exposure have been investigated in epidemiological studies:

- Melatonin;
- Thyroid hormones (thyroxine (T4) and triiodothyronine (T3));
- So called "stress hormones", i.e. corticosteroids (cortisol, aldosterone, and dehydroepiandrosterone, secreted by the cortex of the adrenal glands), and catecholamines (epinephrine and norepinephrine - alias adrenaline and noradrenaline - secreted by the adrenal medulla).

7.1.1 Melatonin

Four observational studies assessed the relationship between melatonin and exposure to RF fields either from mobile phones, or from radio- and TV transmitters among operators or in the residential setting. Two studies did not report sufficient information for assessment of inclusion criteria, and are therefore not included in the table. The main features and results of the remaining two studies are summarized in Table 7.1.1.

Taking advantage of the shut-down of a shortwave broadcast transmitter (6–22 MHz, amplitude modulated signal) in March 1998 (Altpeter et al., 2006), a pre-post comparison of melatonin levels (and sleep quality, reported in Section 5.1) was performed among residents in the community of Schwarzenburg (Switzerland), during two 4-day periods, preceding and following the permanent close down of broadcasts. Participants were a convenience sample (54 subjects, 21 males and 33 females, aged between 24 and 70 years) from two previous cross-sectional studies that included 446 subjects (199 males and 247 females), carried out in 1992–93 and 1996, where the aim was to study the association between health complaints (sleep disturbances and unspecific symptoms) and estimated levels of exposure to frequency-specific RF fields. The convenience sample had a similar distribution of age, sex, and socioeconomic status as the original samples, but tended to live closer to the transmitter. During the study periods, saliva samples were taken five times a day (before breakfast, noon, tea time, dinner time, and before bed). Melatonin levels in saliva were determined by radio-immuno-assay. Changes in the melatonin cycle were investigated. Prior to shut down the average of measured magnetic field exposure was 1.5 mA/m. Using the median as a cutoff, the study subjects were divided into two (low and high) exposure groups. The median levels of melatonin excretion, during the baseline period (transmitter in operation), were 9.5 pg/ml in the high exposure group and 12.5 pg/ml in the low exposure group; the median total excretion in the post shut-down period increased in the high exposure group (14.8 pg/ml), but not in the low exposure group (13.7 pg/ml). The acrophase (when the peak of the melatonin rythm occurs) was delayed in both groups (about 1 hour) after shut-down [likely due only to the concurrent passage from winter to summer time, when the clock was put forward by one hour]. Two kinds of statistical analyses were performed. The first, aimed at assessing the chronic effects of RF exposure on the outcome variables, was based on a linear median regression model with baseline melatonin excretion (log transformed) as the dependent variable, and exposure group, age and sex as explicative variables. Acute effects, instead, were assessed in a within-subject analysis (with every subject serving as his/her own control), by fitting a random effect models to the outcome measurements in the post shut-down period, taking into account the respective baseline value, and adjusting for age and sex. The results of the "chronic effect" analyses indicated that melatonin excretion decreased by a factor of 0.90 for every 1 mA/m increase in magnetic field exposure (95% CI 0.68–1.20), and the peak time of melatonin excretion was put backward by 4.4 min for every 1 mA/m increase in magnetic field exposure (95% CI -25.4 to 16.6). However, the findings from the "acute effect" analyses were less in support of an exposure-outcome association; although there was an overall tendency for melatonin excretion to increase after shutdown of the transmitter by a factor of 1.15 (95% CI: 0.97–1.36) per mA/m decrease in magnetic field exposure, the association was confined to poor sleepers (defined as sleep quality below the median for the group) and was not present among good sleepers. Moreover, peak time of melatonin excretion was not related to magnetic field exposure in either good or poor sleepers. [The authors indicated that blinding of the participants regarding their exposure status was not possible and that this may have affected the outcome measurements in a direct or indirect (psychological) way.]

Potential effects of RF exposure on melatonin secretion and estrogens were investigated in a cross-sectional study of women living near broadcasting transmitters in Denver, Colorado (Clark et al., 2007). The study is described in detail in Section 11.1.3.3. Temporal and spatial characteristics of residential RF exposure in this area had been previously assessed by combining repeated spot measurements with geographic information. The study area was delimited by an interstate road to the south, a park neighbourhood to the west and the natural

topography to the north and east. The radio and TV transmitters in the area were arranged in three groups of antenna towers located about 0.4 to 1.2 km apart, and the total output power was approximately 9 MW. A random sample of 280 male and female participants aged 8 years or older was recruited from 161 residences belonging to three strata with high (>40 mW/m2), medium (5–40 mW/m2) or low (<5 mW/m2) RF exposures (participation rate: 64% among eligible persons contacted). The mean age and mean residential exposure level did not differ between participants and non-participants. A total of 127 post-menarche women aged 12 to 81 years participated in the study. The mean values of RF power density in the homes varied from not detectable to 67 mW/m2 (mean: 8 ± 10 mW/m2). Each participant collected one overnight urine sample after the first study night and a second overnight sample after the last study night. The primary hypothesis was that RF exposure would lead to a decrease in the excretion of 6-hydroxymelatonin sulfate (6-OHMS) and an increase in the estrogen metabolite estrone-3-glucuronide. Information on demographic characteristics, medical and reproductive history as well as on numerous lifestyle factors was gathered by self-administered questionnaires. Women reporting consumption of melatonin supplements (n=4), current intake of birth control pills (n=16), breastfeeding (n=4) or hormone replacement therapy (n=20) were excluded. The final analyses comprised 83 women, of whom 56 were premenopausal (median age: 43 years) and 27 postmenopausal (median age: 59 years). Subjects were grouped into RF exposure quartiles and adjusted mean metabolite concentrations in the upper and lower quartiles were compared using the least significant differences statistic. There were no exposure effects on 6-OHMS excretion among premenopausal women after adjustment for education, miscarriages and smoking, and also not among postmenopausal women after adjustment for month of participation and eye colour. [Main strengths of this study are the extensive exposure assessment and the comprehensive dataset. Limitations are the cross-sectional design, uncertainties about the coverage of the underlying population and the small numbers of participants in the subgroup analyses limiting the possibility to adequately control for confounding factors.]

Studies with uncertainties related to inclusion criteria

Burch and colleagues conducted a cross-sectional study in the US of mobile phone use during working hours and melatonin excretion profiles (Burch et al., 2002), based on repeated individual measurements. Participants were two separate populations of male electrical workers (aged between 18 and 60 years) from nine regional electric utilities (149 in study 1 and 77 subjects in study 2). Data collection was conducted January–September 1997 for study 1, and April–June 1998 for study 2) [no details were provided concerning the selection/approach procedures, or participation rates]. Descriptive data and findings were analysed and reported separately for the two groups. The mean age of subjects in study 1 was 44 (SD ± 9) years with 91% Caucasian non-Hispanic ancestry, and in study 2 mean age was 41 (± 8) years, and 88% Caucasian non-Hispanic ancestry. Both groups had similar proportions of aggregated job categories. Melatonin secretion was assessed by radioimmunoassay of 6-hydroxymelatonin sulfate (6-OHMS) in total overnight (first void) and post-work urine samples collected on 3 consecutive workdays by each participant. Three outcome variables were used in the analyses: total overnight 6-OHMS (µg), nocturnal 6-OHMS standardized on creatinine concentration (ng/mg creatinine), and post-work 6-OHMS (ng/mg creatinine). The self-reported amount of time spent using a mobile phone at work on each day of participation (minutes/day) was used as exposure variable. Information concerning potential confounding factors, including personal traits (e.g. age, height, weight, race, socio-economic status), occupational (e.g. years of work experience, physical activity, work with chemicals, work with electrical tools/equipment), lifestyle (e.g. tobacco, alcohol, caffeine and vitamin consumption, exercise, use of electrical appliances) and medical factors (e.g. consumption of melatonin, antidepressants, tranquillizers, steroid hormones, anti-inflammatory agents, disease history, health status), was collected by self-administered questionnaire at the end of the three-day participation period. Statistical analyses were performed with the SAS Proc Mixed procedure for repeated measures on log-transformed 6-OHMS values. Findings differed by group. No difference in overnight or post-work 6-OHMS excretion across categories of mobile phone call time were observed among workers in group 1 (the larger group), whereas in group 2 a decreased urinary concentration of nocturnal 6-OHMS was observed in mobile phone users with call time >25 min/day compared to non-users. The observed decrease was entirely confined to the third participation day. Only 3 workers in study 1 and 5 workers in study 2 had used a mobile phone >25 min/day. Alternative cut-points at 20 min or 30 min/day did not affect the results. Post-work 6-OHMS excretion was not associated with amount of mobile phone use. [The study is limited by the cross-sectional design and lack of information about the enrolment procedures and participation rates. First, assessment of exposure to mobile phone-related RF fields was based on self-report and non-exhaustive (no information was sought on off work mobile phone use). Second, the upper category of mobile phone use included few observations in both studies, and it is unclear why this specific cutoff was chosen. Third, it is worth noting that there seems to be group differences in overnight excretion of 6-OHMS among subjects in the comparison categories of mobile phone use (0 min/day), with study 2 non-users showing higher average 6-OHMS urinary concentrations (18.9 ng/g creatinine) than study 1 non-users (15 ng/g creatinine). Fourth, the

decreased overnight 6-OHMS excretion observed among "heavy" mobile phone users in study 2 was restricted to samples collected on the third participation day, which, given the non-experimental setting, may well be a chance finding. It is also unclear why the two studies were not combined, especially considering the small number of participants in study 2.]

In a cross-sectional study in Bulgaria, Vangelova and co-workers studied 36 male operators working fast-rotating extended shifts (Vangelova & Israel, 2005). Participants were included from three groups with different exposure: 12 broadcasting station operators (BC) (mean age 49.7 ± 5.6 years), 12 TV station operators (TV) (mean age 47.1 ± 8.0 years), and 12 satellite station operators (SAT) (mean age 49.5 ± 7.7 years). The latter served as reference group [no information is provided about procedure for selection of participants or participation rates]. The working conditions, including also psychosocial factors, were similar in the three groups. The main psychosomatic complaints (more prevalent among TV operators) were mental and physical exhaustion, fatigue, pain in the chest, and musculoskeletal disorders. The mean time-weighted-average (TWA) exposure for broadcasting station operators was 3.10 μW/cm^2, for TV operators 1.89 μW/cm^2, and for satellite station operators 1.60 μW/cm^2. Urine samples were collected at 4-h intervals (at 09:00, 13:00, 17:00, 21:00, 01:00, 05:00, and 09:00 of the next day). Determinations of 6-OHMS and cortisol were based on RIA, while epinephrine and norepinephrine (alias adrenaline and noradrenaline) were measured by spectrofluorimetry. Oral temperature (sublingual) was measured 7 times by a digital thermometer, concurrently with each void. Two sets of statistical analyses were carried out. First, tests of between subjects effects (SPSS) were used to assess variations of hormone levels (6-OHMS, cortisol, adrenaline, noradrenaline) and oral temperature (OT) by time-of-day (6 time-specific samples) and by RF exposure (three different two-groups comparisons: BC vs SAT, TV vs SAT, and BC vs TV). Second, one-way ANOVA and correlation analyses were used to assess the relationship between RF exposure group (BC vs SAT, and TV vs SAT) on 24-h excretion of 6-OHMS, cortisol, and catecholamines. No information is provided on if and how non-detects were treated, and whether (log)-transformed outcome variables were used in the statistical analyses. The 24-h excretion of 6-OHMS did not differ by RF exposure group (ca 35–38 μmol/24h). On the contrary, relatively higher urine concentrations of cortisol (161 ± 87 nmol/24h) and noradrenaline (174 ± 71 nmol/24h) were observed among BC operators compared to SAT operators (cortisol = 89 ± 45 nmol/24h; noradrenaline = 117 ± 41 nmol/24h). The authors also report statistical significant correlations between RF exposure levels (in term of both TWA_{mean} and TWA_{max}) and 24-h excretions of cortisol (with r varying between 0.343 and 0.389, all $p<0.05$); these findings are of uncertain interpretation, because the RF exposure level was apparently estimated on a group basis, not at the individual level. [The study is limited by the cross-sectional design, and lack of information about recruitment procedures and participation rates. In addition, numbers of participants were small in each group.]

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Table 7.1.1. Epidemiological studies of melatonin

Outcome	Country Time period Age	Study population Design	RF exposure source /assessment/variables	Results	Comments	Reference
Melatonin	Switzerland 1998 24–70 years	Cross-over study in residential setting. 54 subjects (21 men, 33 women) followed for 1 week, before and after shut-down of a local radio-transmitter	Short-wave AM radio-transmitter (6-22 MHz; maximum power twice 150 kW) with transmission beam changing direction every 2 h ca) Calculated 24-h average magnetic field level (mA/m) for each subject's home Study population divided into high and low exposure group, based on before shut-down calculated levels (means: 2.6 vs 0.4 mA/m)	Melatonin excretion at baseline (transmitter in operation): High exposure group: median = 9.5 pg/ml Low exposure group: 12.5 pg/ml. The estimated decrease in melatonin excretion for 1 mA/m increase in exposure was 10% (95% CI -32% to 20%). The estimated forward shift in peak time excretion for unit increase in exposure was 4.4 min (95% CI -25.4 to 16.6). Median total excretion in post shut-down period increased in the high exposure group (14.8 pg/ml), but not in the low exposure group (13.7 pg/ml). The acrophase was delayed (about 1 hour) in both exposure groups after shut-down.	Possible self-selection of participants living closest to the transmitter. Blinding of study subjects to exposure was not possible. The acrophase shift in both group was likely due only to the concurrent change from winter to summer time. Effect on melatonin was restricted to poor sleepers and not observable in good sleepers.	Altpeter et al. (2006)
6-OHMS	USA 2002–2003 age range: 12–81 years	Cross-sectional study in residential setting; 87 women living close to broadcasting transmitters. Overall participation rate: 64%	15 radio and TV broadcasting transmitters, 55–687 MHz, ~9 MW of total output power Indoor spot measurements (broadband) Quartiles of house average RF power density with means: 0.04, 0.2, 0.4 and 1.4 μW/cm²	No associations between RF exposure (upper vs lower quartile) and mean urinary levels of 6-OHMS in either premenopausal (n=56) or postmenopausal (n=27) women.	Analyses were adjusted for education, miscarriages, smoking, month of participation and eye colour.	Clarke et al. (2007)

Abbreviations: 6-OHMS: 6-hydroxymelatonin sulfate; AM: amplitude modulation; CI: confidence interval

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149 ### *7.1.2 Corticosteroids, catecholamines and thyroid hormones*

150 Five studies were identified where effects of RF exposure on corticosteroids, catecholamines and
151 thyroid hormones were investigated, but none of them provided sufficient information to determine the
152 representativeness of participants. The studies are described below, but are not tabulated.

153 A small cross-sectional study from Turkey (Daşdağ et al., 1999) included 43 telecommunication
154 operators (aged 20 to 59 years), occupationally exposed to RF fields, along with a comparison group of 20
155 volunteers with "similar distribution by age, sex, type of work and working period (8 h/day)". The RF exposed
156 group included technicians from three different transmitter stations: 10 were employed at a TV station (202 to
157 781 MHz, 60 to 450 kW), 15 at a radio-broadcasting station (1 to 100 MHz, 30 to 300 kW), and 18 at a radio-
158 link station (420 MHz to 6 GHz, 1.5 to 200 W). Field strength measurements resulted in values between 65 and
159 85 dB μV. One blood sample per subject was collected during working hours, and plasma concentrations of
160 cortisol, dehydroepiandrosterone (DHEA), thyroid stimulating hormone (TSH), thyroid hormones (T3, T4, free-
161 T4), [and reproductive hormones – discussed in Chapter 11], were determined by radio-immuno-assay. Average
162 hormone levels by group (each of the three exposed groups vs the unexposed) were compared by student's t test.

Statistically significant increased levels of TSH, T3, T4 (but not of free-T4) were observed in almost all exposed groups compared to the unexposed, whereas cortisol and DHEA levels were similar across groups. [Basic characteristics of the participants, including age and sex distribution, are not described, and the comparability of participants across groups cannot be assessed. No information is available about the time of day when blood samples were taken, no detail is provided about the chemical determination method, and the measurement units of the hormonal levels are not reported. Exposure assessment was not individual-based, and the measured levels by group are extremely low. No potential confounders were taken into account.]

The relationship between occupational exposure to RF fields and stress hormones was the subject of a Bulgarian study (Vangelova, Israel & Mihaylov, 2002), which included 12 operators at a satellite TV station (mean age 42.6 ± 4.7 years), and a RF-unexposed group of 12 power facility workers (mean age 41.4 ± 5.9 years) [details concerning subjects' recruitment and participation rates are not provided]. Both the exposed and control workers were engaged in fast-rotating shifts. The estimated RF exposure among SAT station operators was around 19.2 $\mu W/cm^2/h$ at 300 MHz. Excretion rates (nmol/h) and total levels (nmol/24 hours) of 11-oxycorticosteroids (11-OCS), epinephrine, and norepinephrine were determined in repeated individual samples of urine, collected at three hour intervals during a 24-h work shift, by fluorophotometric methods. The parameters of diurnal excretion rhythms were calculated by single cosinor analysis. One-way analysis of variance (ANOVA) was used to compare 24-h hormonal excretion rates between the exposed and unexposed groups. Total excretion of 11-OCS was higher in SAT workers (98 $\pm$ 26 nmol/24 h) than among control workers (78 $\pm$ 17 nmol/24-h), while there were no differences between groups in total excretion of catecholamines (epinephrine ~40–45 nmol/24 h and norepinephrine ~165–187 nmol/24-h). The cosinor analysis revealed disorders in the circadian rhythms of 11-OCS and epinephrine (a higher amplitude/mesor ratio in both cases) among exposed workers compared to the control group. [The study is limited by the cross-sectional design, and small study size. Neither subject recruitment methods, nor response rates are reported. No confounding factors were accounted for in the analyses.]

The effect of mobile phone use on thyroid function was the purported aim of an Italian study, likely based on clinical data collected in the frame of an occupational health surveillance program (Bergamaschi et al., 2004). The study population consisted of 2598 workers from an unspecified industrial sector, 1355 of whom were males (aged on average 29 ± 6 years) and 1243 females (28 ± 6 years). [The study period, participant selection procedures and participation rates are not reported.] As to their distribution by job title, 68% were "operators" (involved in customer service activity via telephone and VDU, occasionally engaged in night shifts); 11% were "vendors" (involved in company marketing, usually dealing with customers via mobile phones and VDU); 21% were in charge of "network management" (i.e. technicians dealing with software and hardware management, occasionally involved in radio-base station control, eventually engaged in night shifts). Study subjects were also classified in categories of average monthly call time (including both private and business calls): 1913 (74%) subjects were included in the "normal" category (<19 hours per month), 493 (19%) in the intermediate (19-33 h/month), and 192 (7%) in the upper category (>33 h/month). The exposure assessment method was not specified, and the cutoff levels used to categorize amount of mobile phone use seem quite arbitrary. Each study subject underwent a general medical visit (apparently only one), ECG, spirometry, audiometry, and routine hematological analyses (including determination of TSH and free-T4 (methods unspecified, concentrations expressed in IU/L). Blood levels of TSH and free-T4 did not differ by job-title group. A higher prevalence of subjects with TSH levels below 0.4 IU/L was observed among subjects in the upper category of monthly call time (9.9%), compared to those in the intermediate (6.9%) and low (6%) categories. This finding is described in the text with reference to a graphical representation (indicated as Figure 1) that are not present in the published paper. Free-T4 blood concentrations, on the contrary, did not vary across categories of conversation time. [This study is regarded as uninformative. The reporting is insufficient for assessment of potential biases. No confounding factors were accounted for in the analyses (notably, information is lacking on prevalence of thyroid hormone replacement therapy in the study population).]

Thyroid function in relation to mobile phone use was investigated in a cross-sectional study including 77 medical or nursing students (23 males and 54 females) from the University of Shiraz, Iran (Mortavazi et al., 2009), aged 19 to 29 years (mean age 23 ± 2.5 years). Study subjects were apparently randomly selected, but details concerning approach methods and participation rates are not provided. Pregnant women, subjects with thyroid disease, persons using drugs such as medicines interfering with thyroid function, oral contraceptives, oral anticonvulsants, as well as those with "other conditions known to affect thyroid function tests", were excluded (number unspecified). Average daily call time was used to classify study subjects in three groups: non-users (reference category, 21 persons); light users (5–20 minutes per day, 25 persons); heavy users (>120 min/day, 31 persons) [the choice of the cutoff points seems arbitrary, and the exposure variable itself seems curiously distributed, with no persons who used a mobile phone <5 minutes per day, and no one in the category between

20 minutes and 120 minutes. It seems likely that some non-random selection of participants was made, considering the even distribution of participants in three such diverse categories]. Based on questionnaire data concerning exposure to other RF sources and possible confounding factors (pattern of mobile phone use, residential proximity to base stations, medical history and life style), "every effort was made to make the three groups comparable in key characteristics" [confounding variables were not adjusted in the analyses, instead groups were made comparable, indicating a non-random selection of participants]. T3, T4 and TSH levels were determined by ELISA kits. No information is provided on blood sampling (e.g. time of day and setting). Statistical analyses were based on ANOVA (comparison across three groups), student's t test (heavy and light mobile phone users vs non users, one at a time), and regression analysis using average daily call time or length of mobile phone use in years as continuous exposure variables. Findings from the latter analyses showed no correlation between any thyroid function markers and either daily amount or duration of mobile phone use [although the actual numbers are not reported]. No difference in thyroid hormone levels across groups was detected by ANOVA. Increased levels of TSH were observed among mobile phone users compared to non-users (2.7 mIU/L ±1.75), although the increase was greater among light users (4.25 mIU/L ± 2.13) than among heavy users (3.75 mIU/L ± 2.05). [Limitations of this study are the cross-sectional design, lack of confounding control. In addition is unclear how participants were recruited, and participation rates are unknown. Many different analyses were performed, and study groups were small.]

A small study from Egypt investigated hormone profiles among mobile phone users and people living close to mobile phone base stations (Eskander, Estefan & Abd-Rabou, 2012). Two groups of mobile phone users (82 subjects in total) with different age ranges (14 to 22 years and 25 to 60 years, each n=41) were divided into three categories according to their daily call time (weak: <10 min/day, moderate: 30-60 min/day, strong: >60 min/day). Two other groups of volunteers, living at distances of 20–100 m or 100–500 m from a mobile phone base station (n=17 in each group) were enrolled. In addition, 20 subjects (10 per age group) living more than 500 m apart from a base station served as a control group. All participants were followed over 6 years and blood samples were collected after 1 year, 3 years and 6 years [it is not described if the blood sampling procedure was standardized as to time of day, day of week, and time of year]. The hormonal analyses included blood levels of adrenocorticotrophic hormone (ACTH), cortisol, total T3, T4, (as well as prolactin and reproductive hormones – discussed in Section 11.1). The paper does not state which statistical methods were used, but it appears as multiple cross-sectional analyses were made, instead of longitudinal follow-up of individual hormone levels. Many statistical tests resulted in several statistically significant, but inconsistent differences in hormone levels between groups, indicating that ACTH, cortisol, T3 and T4 levels were lower among mobile phone users and became lower over time. [This study is regarded as uninformative, since it does not meet basic methodological requirements for epidemiological studies. It is unclear how participants were recruited, and participation rates and loss to follow-up are unknown. The gender distribution, overall and by group, is also unknown. No confounding factors were accounted for in the analyses.]

7.2. Volunteer studies

Few studies have been conducted on the effects of radiofrequency (RF) electromagnetic fields (EMF) on the endocrine and neuroendocrine systems. The effects on the pineal and hypothalamo-pituitary adrenal glands were mostly studied. These glands secrete hormones that are released into the systemic circulation to distant target tissues and exert a profound influence on body metabolism and physiology. These hormones constitute good markers in the blood stream for the assessment of gland disruption.

The previous WHO EHC report on the effects of RF exposure issued in 1993 reported no studies on the endocrine and neuroendocrine system. The search strategy identified 13 relevant papers in this area of studies. Of these, five were excluded because they did not meet inclusion criteria for volunteer studies; exposure conditions were not blinded to the participants or the study did not include two or more exposure levels (whereof one could be a sham), under otherwise similar conditions; these studies are listed at the end of this section. Two studies had no evidence of exposure level control and thus had uncertainties in relation to the inclusion criteria. These are briefly reported in a separate section and not included in the table. This left six papers that fulfilled the inclusion criteria. The studies assessed the impact of exposure on melatonin, hormones of the hypothalamo-pituitary adrenal axis as well as other hormones. Each endpoint is considered separately below.

The table by the end of this section summarizes results and provide information about study details including study design. Similar and further details are included in the following text. Comments about particularly small samples sizes are made since the smallest samples are attached with highest uncertainties provided other study details are similar. Exposure was controlled in all studies that are included in the analysis as basis for the health risk assessment. If SAR was provided, it is specified in both the tables and text. Otherwise other exposure measures are provided.

7.2.1. Melatonin

Melatonin (or N-acetyl-5-methoxy-tryptamine) is an indoleamine compound derived from tryptophan, produced mainly in the pineal gland. Melatonin production is stimulated by darkness and inhibited by light. It displays a circadian rhythm characterized by a nocturnal peak and low concentrations during daylight hours into the bloodstream. Melatonin strongly influences circadian physiology and behaviour in vertebrates. It is also known for its antioxidant (Reiter et al., 2003; Reiter et al., 2013) (reviews) and oncostatic properties (Di Bella et al., 2013) (review), its association with some depressive disorders (Lanfumey, Mongeau & Hamon, 2013) (review) and with troubles of the circadian rhythmicity shown to generate neurobehavioral disturbances. Thus, studies of potential effects of RF EMF on melatonin are of interest. Melatonin can be assessed in blood, saliva or through its metabolite in urine, 6-sulphatoxymelatonin (aMT6s). Serum melatonin levels are about three times greater than levels obtained from saliva. Nonetheless, melatonin levels in saliva reflect those in serum at any time of the day and like serum melatonin levels increase at night.

7.2.1.1 Mobile phone handset related studies

Using signals from a GSM 900 mobile phone handset emitted by an antenna, Mann et al. (1998) exposed 22 male healthy volunteers during two successive nights (one night of exposure to GSM 900 MHz signal and one night sham) in which nocturnal profiles of some hormones were evaluated under polysomnographic control. These two experimental nights were preceded by and adaptation night, the order of exposure conditions was randomized and the study was performed single. The antenna was positioned behind the head at 40 cm from the vertex of the subject resulting in an average power density of 0.2 W/m^2 [SAR averaged over 10 g was 0.3 W/kg as reported from the same study by Wagner et al. (Wagner et al., 1998)]. Blood samples were taken every 20 minutes for nocturnal profile of melatonin and for other hormones. The results did not show any statistically significant effect of exposure on night-time serum melatonin.

Radon et al. (2001) exposed eight male healthy volunteers to a GSM 900 MHz mobile phone signal (SAR = 0.025 W/kg). They evaluated the effect on salivary melatonin of the RF signal transmitted by an antenna positioned 10 cm behind the head of each participant. The experimental protocol consisted of twenty 4-hour sessions in the experimental chamber, “with the sessions being at least 2 days apart after a day session and at least 3 days apart after a night session”. Half of the experiments (ten 4-hour sessions) were conducted with EMF exposure and the others with sham exposure in random order, and the sessions were evenly distributed between day and night. The study was performed double blind. The same time of day was used for all day and night sessions, respectively, and saliva was collected every 30 minutes during and after exposures. The results did not show any significant difference in salivary melatonin concentrations between the exposure and sham exposure conditions. [The weight of this study is limited due to its small sample size.]

Wood et al. (2006) exposed 55 adult male and female volunteers to a mobile phone GSM 895 MH signal before sleep to test whether the overnight melatonin secretion would be reduced. The mobile phone was fixed so that it rested against the right cheek of the participants. The 10 g maximum SAR was measured to be 0.67 W/kg. The participants were both exposed and sham exposed for 30 minutes in a random sequence on two successive Sunday nights. Urine was collected immediately after exposure before getting into bed and in the next morning upon waking. Melatonin was estimated from its main metabolite in urine: 6-sulphatoxymelatonin (aMT6s). Total aMT6s output during the night did not differ between the two exposure conditions. The pre- and post-bedtime results considered separately were also not significantly different, although the pre-bedtime value was lower for RF versus sham exposure. When normalized to creatinine concentrations, the pre-bedtime value of aMT6s was found to be significantly lower ($p = 0.037$) after RF exposure compared to sham exposure. According to the data reported in the paper, only four participants out of 55 had clearly shown a substantial decrease in pre-bedtime normalised aMT6s in the exposed condition. The authors reported that if the four individuals were excluded from the analysis, the results would not be significant ($p = 0.45$). [Due to the small number of participants showing a substantial decrease in their normalised aMT6s in the exposed condition, while the remaining data were close to normally distributed, it cannot be excluded that the observed effect was an artefact. [It should also be noted that even though the study was designed to be double blind, there is no information suggesting that measures were taken to control for acoustic cues from the transmitting phone or to prevent the participants from sensing the heat produced by phone when operating.]

Papers with uncertainties related to inclusion criteria

Two single blind studies have been published that report no information about exposure levels or about control of the levels. In order to evaluate the possible effect of RF mobile phone exposure on 6-

sulphatoxymelatonin (aMT6s), Bortkiewicz et al. (2002) exposed nine volunteers to a mobile phone GSM 900 MHz signal. Each participant was examined twice: on an exposure day and a control day (sham). Exposure lasted one hour starting from 19:00. Urine sampling was performed immediately before exposure (19:00), before bedtime (00:00) and in the next morning (07:00). The study showed that mean aMT6s levels did not differ significantly between the RF and sham conditions for any of the respective time points.

Jarupat et al. (2003) exposed eight female participants to a 1960 MHz mobile phone signal to test effects on salivary melatonin. Thirty minutes of exposure were performed each hour from 19:00 to 01:00. In this study saliva was collected at the beginning of and one hour after the series of exposures. Results showed that salivary melatonin levels were significantly reduced after exposure at 02:00. [In addition to uncertainties concerning exposure in both of these studies, no information was provided about randomization or counterbalance of order of about measures to ensure blinding as the phones were kept in the normal use position. Both studies had small sample sizes.]

7.2.2. Hypothalamo-pituitary adrenal and other hormones

7.2.2.1 Mobile phone handset related studies

Very few studies have been conducted on this topic. In the same study where serum melatonin was measured (see paragraph on melatonin above), Mann et al. (1998) also measured growth hormone, luteinizing hormone and cortisol during night-time exposure. As for melatonin, no significant effect was found for growth hormone and luteinizing hormone in response to signals from a GSM 900 exposure with a SAR_{10g} of 0.3 W/kg (Wagner et al., 1998). Also for cortisol no overall effect of exposure was observed, but there was an indication of interaction between exposure and time ($p = 0.033$), meaning that the time patterns of cortisol serum concentration differed between the GSM and sham conditions. By comparing the respective 1-hour segment of the two conditions, slightly higher cortisol levels were observed during the first hour ($p = 0.017$) and last hour of exposure ($p = 0.046$). Similarly, Radon et al. (2001) did not find any effect on salivary cortisol of an GSM-like signal transmitted by an antenna ($SAR_{10g} = 0.025$ W/kg) positioned 10 cm behind the head of the participants. In this study the participants underwent both day-time and night-time exposures. [The small sample should be noted. (The same study was reported by Radon et al. (2001) for melatonin, see above)].

In a single blind crossover study aiming to investigate the EMF exposure effect on vasoconstrictor activity, Braune et al. (2002) exposed 40 female and male volunteers to a signal from a GSM 900 MHz mobile phone. The phone was mounted in the typical phoning position and maximal 10 g SAR was measured to be 0.5 W/kg. The sound generated by the phone was masked by applying an external similar sound and sensing of heat from the phone was avoided by using an insulating material. Exposure lasted 55 minutes including 20 minutes in supine rest, 10 minutes of exposure in the 70° upright tilt position and then another 20 minutes of exposure in supine rest. Between the two sessions there was 15-minute break in supine position. Blood was collected first after an initial resting phase immediately before exposure and subsequently every 10 minutes. Adrenaline and noradrenaline (also known as epinephrine and norepinephrine), cortisol and endothelin serum levels were measured for each participant. Seven of the 40 included volunteers suffered from a presyncope during the 10-minute upright tilt during one of the two exposure conditions. These were excluded from the further analysis, but none of the parameters showed statistically significant differences between the excluded group and all participants. No data indicated that exposure to RF EMF emitted by mobile phones over a period of up to 50 minutes had any effect on the tested hormone levels.

In a large study, Barker et al. (2007) exposed 120 healthy volunteers to GSM and TETRA handset mobile signals. The aim of the study was to look for effects of those signals on blood pressure; in addition the authors investigated the effect on plasma catecholamines (adrenaline and noradrenaline) and heart rate variability as markers of sympathetic nervous system activity. Six different modes of transmission (modulated, carrier wave and sham both for GSM and TETRA signals) were used. All real exposures resulted in SAR_{10g} of 1.4 W/kg. All sessions were on separate days at least seven days apart. On each day, a 20-minute pre-exposure period was followed by 40 minutes of exposure. Blood was collected immediately before and after exposure. Analysis of covariance (ANCOVA) applied in this study did not show any significant differences in adrenaline and noradrenaline plasma concentrations between the various modes of transmission. [There was no information about carrier frequencies used in this study. (See Chapter 9.2.1 concerning results for heart rate variability.)]

379 *7.2.2.2 Mobile phone base station related studies*

380 Augner et al. (2010) investigated whether GSM 900 MHz base station signals from a real base station
381 mounted on the façade of the testing room may have an effect on the bodily defence system, with salivary alpha-
382 amylase and cortisol levels among the indicators. By applying different types of shielding, three different
383 exposure levels were obtained. The power density was measured during all exposure sessions and the average
384 values were calculated for each condition: high (2126.8 μW/m²), medium (153.6 μW/m²) and low (5.2 μW/m²).
385 Fifty-seven participants were randomly assigned to receive one of three exposure scenarios, each consisting of
386 five 50-minute exposure sessions separated from each other by 5-minute intervals. The scenarios were "HM"
387 (low exposure, high exposure, low, medium, low) with 22 volunteers, "MH" (low, medium, low, high, low) with
388 26 volunteers and "LL" (low, low, low, low, high), the control scenario with 9 volunteers. All scenarios were
389 conducted at the same time of day. : Saliva samples were taken after 10, 25, and 45 min in each session, and
390 analyses were performed by including age, gender, and degree of self-rated electromagnetic hypersensitivity as
391 covariates. Analysis of variance showed no difference between the three scenarios and no interaction between
392 scenario and session number (representing exposure time). The interaction term was expected to indicate
393 potential effects of exposure (Augner et al., 2010). The same analysis revealed an effect of order of the "low",
394 "medium" and "high" sessions. In a post hoc analysis where consecutive sessions were compared, the authors
395 found that cortisol increased significantly ($p = 0.002$) only in the LL scenario from session 4 to session 5 (from
396 "low" to "high" exposure). Despite the high number of participants included in the HM and MH scenarios, a
397 similar change from the "low" to the following "high" exposures was not observed. [The low number of
398 volunteers included in the LL scenario would make results from this scenario less reliable than from the others.]
399 In yet another analysis, the changes in serum concentrations from baseline to sessions 2–4 in the MH and HM
400 scenarios were compared to similar changes for the LL scenario with only low exposure levels in these sessions.
401 Here no effect on cortisol was revealed. Unlike cortisol, saliva alpha amylase increased significantly ($p = 0.037$)
402 when data from the HM and the MH scenarios were combined and compared to those from the low level
403 scenario. [This p-value is not much less than the significance level of 0.05, and taking into account that no
404 correction for multiple tests has been indicated, a random effect cannot be disregarded. The low number of
405 participants in the control scenario is a limiting factor also for this analysis. The general lack of compliance
406 between the different findings should be noted.]

Table 7.2.1 Studies accessing effects of RF EMF exposure on the endocrine and neuroendocrine system

Endpoint and Participants[a]	Exposure[b]	Response	Comment	Reference
Mobile phone handset related studies				
Nocturnal hormone profiles of serum melatonin, growth hormone (GH), cortisol and luteinizing hormone (LH) assessed during exposure 22 male volunteers (18-37 years)	GSM mobile phone signals emitted by circularly polarized antenna 40 cm from the vertex of the head, 900 MHz Power density 0.02 mW/cm^2 (0.2 W/m^2), SAR_{10g} 0.03 W/kg (Wagner et al., 1998) 8 h: 23:00–07:00	No effect of exposure on the GH, LH and melatonin hormones. Slight and transient increase in the cortisol in the first hour of exposure.	Single blind, randomized, cross-over. For sleep EEG see (Wagner et al., 1998) in Section 5.2.2.3.	(Mann et al., 1998)
Salivary melatonin and cortisol samples taken during and after exposure 8 male volunteers (20-30 years)	GSM mobile phone signal emitted by circular polarized antenna 10 cm behind head, 900 MHz SAR_{10g} 0.025 W/kg 4 h: 12:00–16:00 or 22:00–02:00; 10 times with RF and 10 with sham	No effect of exposure.	Double blind, randomized, counterbalanced, cross-over. Small group. For immune system see Section 10.2.	(Radon et al., 2001)
Urine 6-sulphatoxymelatonin (aMT6s) samples taken after exposure before and after bedtime 55 volunteers (18–60 years; 30 males, 25 females)	GSM mobile phone in test mode against right cheek, 895 MHz SAR_{10g} 0.67 W/kg 30 min, 1 h before bedtime	No effect on total melatonin output. When melatonin metabolite was normalized to creatinine concentrations, the pre-bedtime value was less for EMF compared to sham.	Double blind, randomized, almost counterbalanced, cross-over.	(Wood, Loughran & Stough, 2006)

Serum levels of cortisol, epinephrine, norepinephrine and endothelin samples taken after the initial resting phase and subsequently every 10 min 33 volunteers (20-34 years; 20 males and 20 females before 7 excluded)	GSM mobile phone in test mode against right ear, 900 MHz SAR_{10g} 0.50 W/kg 50 min in the afternoon	No effect of exposure.	Single blind, randomized counterbalanced, cross-over. Results from 7 volunteers excluded due to occurrence of presyncope during upright tilt. For cardiovascular system see Section 9.2.1	(Braune et al., 2002
Plasma catecholamine (adrenaline and noradrenaline) samples taken before and after exposure 120 volunteers (18-65 years; 43 males, 77 women)	Generic mobile phone handset against left ear, 4 mobile phone like signals: GSM modulated wave, GSM carrier wave, TETRA modulated wave and TETRA carrier wave [no information about frequencies] SAR_{10g} 1.4 W/kg 40 min	No effect of exposure.	Double blind, randomized, counterbalanced, cross-over. Large group. For cardiovascular system see Section 9.2.1.	(Barker et al., 2007)
Mobile phone base station related studies				
Salivary cortisol and alpha amylase samples taken before and during exposure 57 volunteers (18–67 years; 22 males, 35 females)	GSM 900 MHz base station on the building, shielding to reduce exposure L = 5.2 μW/m^2 M = 153.6 μW/m^2 H = 2126.8 μW/m^2 5 sessions of 50 min each between 09:00 and 13:30 ScenarioHM: L+H+L+M+L (n=22) Scenario MH:L+M+L+H+L (n=26) Scenario LL:L+L+L+L+H (n=9)	No overall effect of scenario and no effect on scenario – session interaction. Increase in alpha amylase from baseline to sessions 2–4 for combined data from HM and MH scenarios compared to LL scenario. No such effect for cortisol. Increase in cortisol from L level to H level in LL scenario. No other changes between consecutive sessions. .	Double blind, randomized, between groups. Small control group. A scenario – session interaction would indicate an effect of exposure. Not specified corrections for multiple comparisons. For immune system see Section 10.2; for subjective endpoints see (Augner et al., 2009) in Section 5.2.4.	(Augner et al., 2010

Abbreviations: EEG: electroencephalogram; GH: growth hormone; GSM: Global System For Mobile Communication; LH: luteinizing hormone; TETRA: Terrestrial Trunked Radio.

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

Excluded papers

(de Sèze, Fabbro-Peray & Miro, 1998; de Sèze et al., 1999; de Sèze et al., 2001; Djeridane, Touitou & de Sèze, 2008; Mollerlokken et al., 2012)

7.3 Animal studies

Most early studies reviewed by WHO (1993) described thermally-mediated responses of the endocrine system to RF exposure. Briefly, endocrine responses to acute RF (often CW 2.45 GHz) exposure are generally consistent with the acute responses to non-specific stressors such as heat. Several papers report that plasma corticosterone or cortisol levels are significantly enhanced in rodents (Lotz & Michaelson, 1978; Lu et al., 1980; 1981) and primates (Lotz & Podgorski, 1982) by exposures resulting in about a 1°C rise in body temperature; corresponding whole-body SARs were of the order of 4 W/kg. The response seems to be mediated by the release of adrenocorticotropic hormone by the hypothalamus via the anterior pituitary gland, and is modulated in amplitude by the circadian rhythm of cortisol or corticosterone levels. The hypothalamus also controls the secretion of growth hormone and thyroxin; stressful stimuli such as significantly elevated body temperatures are known to depress circulating plasma levels of both hormones in rodents (Michaelson et al., 1975). However, no effects on growth hormone and thyroxin have been seen in primates (Lotz & Podgorski, 1982).

7.3.1 Melatonin

The studies of endocrine effects that have been published since 1992 mostly focus on exposure associated with the use of mobile telephony. Several studies have examined possible effects on circulating melatonin, a hormone produced by the pineal gland in a distinct daily or circadian rhythm which is governed by day length, the disturbance of which has been implicated in breast and other cancers (e.g. Stevens, 1987).

Stärk et al. (1997) investigated salivary melatonin levels in pregnant, lactating cows that were continuously exposed by RF EMF from a nearby short-wave (3-30 MHz) radiotransmitter. Five cows from a farm located at 500 m from the transmitter were compared with an equal number of cows from a farm at 4 kilometers distance. Saliva was collected every two hours during the night (i.e. 7 times per night) during 10 consecutive nights. The average field strengths during the nights were 1.59 mA/m and 0.076 mA/m, respectively. No differences in melatonin levels between the two groups were observed during the first two nights. From the 3rd to the 5th day the transmitters were switched off for 3 days and the melatonin levels did not change. In the first night after the transmitters were switched on again, the levels in the exposed group were significantly higher by 3.89 pg/ml (95% CI 2.04-7.41 pg/ml). [This conclusion is based on data with a considerable variation, and the smoothed curves shown in the paper do not seem to follow the experimental datapoints very well. Moreover, on average about 20% of the samples could not be used because insufficient saliva was collected. Also, on the 4th day after switching the transmitters on again, there also seems to be an increase in the exposed group, but this is not mentioned in the paper. Since no numerical data are given it is not possible to ascertain whether this is significant or not. Also, a decrease rather than an increase in melatonin levels would be expected. In any case, as the authors also stress, this study concerns only a small number of animals and should be considered a preliminary investigation. It thus has limited value.]

Vollrath et al. (1997) studied the serum melatonin levels and other markers of melatonin synthesis in Sprague Dawley and Dark Agouti rats and in Djungarian hamsters that were exposed to 900 MHz GSM or CW fields for up to 6 h. Whole-body SARs were estimated as ranging from 0.06 to 0.36 W/kg in the rats and 0.04 W/kg in the hamsters. No effects of exposure were seen on any of the endpoints examined. [Interpretation is limited by a number of difficulties: the study comprised 26 experiments which were described and assessed individually; the first 12 experiments were dismissed by the authors because the results were affected by differences in sampling times in exposed and sham-exposed animals due to the sequential nature of the sham and exposure treatments. In addition, the sample numbers in all the individual experiments were small with 4–6 animals per group, limiting the statistical power to detect differences.]

In three studies primarily aimed at studying the effects of exposure to RF EMF with whole-body SARs up to 0.8 W/kg on carcinogenesis (see section 12.2.2), Imaida et al. (1998a; 1998b; 2001) also assessed the serum melatonin levels. In the first two studies, investigating the development of liver tumours induced by diethylnitrosamine using groups of 48 Fisher 344 rats, exposing them to either 929 or 1439 MHz TDMA signals for 1.5 h per day, 5 days per week, melatonin levels were increased at termination of the exposure after 6 weeks ($p<0.001$). In the third study, skin tumours were induced in CD-1 mice (n=30 or 48) by 7,12-dimethybenz[a]anthracene (DMBA). Exposure to a 1490 MHz TDMA signal for 5 h per day, 5 days per week during 19 weeks at a whole-body SAR of <0.084 W/kg had no effect on the serum melatonin level. [These studies are also discussed in Section 12.2.2 (Cancer).]

Heikkinen et al. (2003) also investigated skin tumour induction in mice, but in this case by UV radiation. Two types of mice were used, a tumour-prone transgenic strain (K2) and its wildtype, that were both exposed to two types of mobile phone signals, used in the USA (849 MHz DAMPS) and Europe (902 MHz GSM), respectively, for 1.5 h per day, 5 days per week and 52 weeks at a whole-body SAR of 0.5 W/kg. Group size of the exposed animals was 22–27 and of the controls 8–26. At 7–8 weeks after the start of exposure nocturnal urinary excretion of 6-sulfatoxymelatonin, a waste product of melatonin metabolism, was measured. No differences were observed between the exposed and sham-exposed and cage-control groups. [This study is also discussed in Section 12.2.2 (Cancer).]

Bakos et al. (2003) examined the daily urinary excretion of 6-sulfatoxymelatonin in male Wistar rats exposed or sham exposed to either 900 MHz or 1800 MHz GSM RF radiation for a 2-h period between 8.00 am and noon for 14 days. The exposure level for 900 MHz was 100 $\mu W/cm^2$, corresponding to a whole-body SAR of 0.009–0.012 W/kg, and for 1800 MHz it was 20 $\mu W/cm^2$, corresponding to a whole-body SAR of 0.022–0.045 W/kg. Three independent experiments with 6 animals were performed with each frequency and the results were pooled. The authors found no effect of exposure on daily 6-sulfatoxymelatonin excretion.

Hata et al. (2005) measured serum and pineal melatonin levels in Sprague Dawley rats that were on a reversed day/night schedule and were exposed or sham exposed to RF radiation from a Japanese Personal Digital Cellular (PDC) mobile phone system operating at 1.439 GHz. Treatment (exposure with an SAR in the brain of 7.5 W/kg or sham exposure) was for 4 h on one day, beginning at the onset of the 12 h dark period. Serum and pineal melatonin were assessed 3 and 6 h after the cessation of exposure. Exposed, sham-exposed and cage-control groups consisted of 64 animals, while a positive control group of 16 animals was exposed to light. No effects of RF exposure on melatonin levels were observed, but in the positive control the serum and pineal melatonin levels were reduced ($p<0.001$).

In a cancer study described in section 12.2.2, Shirai et al. (Shirai et al., 2005) exposed the heads of Fisher 344 rats, that were born from mothers that were treated with n-ethylnitrosourea (ENU) to induce brain cancer, to a 1439 MHz TDMA signal for 90 min per day, 5 days per week for 104 weeks. The SARs in the brain were 0.67 or 2.0 W/kg. Five rats per group of 100 were used to collect blood for the determination of serum melatonin levels. No effect of the RF exposure on the melatonin level was observed.

Belyaev et al. (2006) exposed four Fisher 344 rats for 2 h to a 915 MHz mobile phone signal at a whole-body SAR of 0.4 W/kg and a similar group received sham treatment. Immediately after exposure the brains were removed and the activity of 8800 genes was measured using a microarray. They found an upregulation of various genes, including N-acetyltransferase-1 ($p<0.0025$), that is involved in melatonin production. [Since melatonin contrations were not measured, this does not provide any evidence of changes in the level of this hormone. This is an exploratory study and needs to be follow-up. It is also discussed in Sections 5.3.3 (Blood-brain barrier integrity) and 12.2.1 (Genotoxicity).]

Kesari, Kumar and Behari (2012) exposed or sham exposed groups of 6 Wistar rats for 2 h per day during 45 days to 2.54 GHz RF EMF at a whole-body SAR that was estimated at 0.14 W/kg. A decreased level of pineal melatonin was measured compared to sham exposure ($p<0.05$). The same research group also exposed rats (6 per group) to 10 GHz for 2 h daily and 45 days at a whole-body SAR of 0.014 W/kg (Kumar, Behari & Sisodia, 2012). This resulted in a decrease in the serum melatonin level compared to the sham-exposed group ($p<0.004$). [This study is also discussed in Section 11.3 (Fertility, reproduction and development).]

Qin et al. (2012) investigated the effect of the exposure of Sprague Dawley rats to an 1800 MHz signal 2 hours daily for 32 days at a whole-body SAR of 0.58 W/kg; the group size was 6 animals. They measured a decreased level of plasma melatonin compared to the sham-exposed group and a forward shift of the circadian rhythm of melatonin (both $p<0.05$). [They also measured a decrease in the level of testosterone, but their conclusion that melatonin regulates testosterone is unsubstantiated.]

As part of a series of experiments in which Sprague Dawley rats were exposed to two mobile telecommunication signals simultaneously, Jin et al. (2013) investigated the effects of such treatments on various hormones, including serum melatonin. Exposure of the 40 animals per group was to either a CDMA (Code Division Multiple Access, GSM-type) signal, or a combination of CDMA and WCDMA (Wideband Code Division Multiple Access, UMTS-like) signal. The whole-body SAR in both cases was 4 W/kg. The exposures lasted for up to 8 weeks, 45 min per day and 5 days per week, and had no effect on the serum melatonin level.

Studies not included in the analysis

Koyu et al. (2005b) looked at nocturnal serum melatonin levels in groups of 10 Sprague Dawley rats exposed or sham exposed either to 900 MHz or to 1800 MHz GSM RF radiation for 30 min per day, 5 days per week over a 4-week period. The peak SAR was 2 W/kg. There was no statistically significant effect on melatonin levels recorded in response to 900 MHz or to 1800 MHz GSM RF radiation. [The location of the peak SAR is not provided, nor the whole-body average SAR. Therefore this study cannot be interpreted.]

Kesari, Kumar and Behari (2011) exposed groups of 6 Wistar rats to a signal from a 900 MHz mobile phone operating at maximum power for 1 min followed by 15 seconds off time, for 2 hours per day for 45 days. The maximum SAR of the phone as provided by the manufacturer was 0.9 W/kg. They observed a decreased pineal melatonin level compared to the sham-exposed group ($p<0.05$). [Since no more information is provided than that the phone was located on top of the cage, the actual exposure is not known. Therefore this study cannot be interpreted due to the lack of proper dosimetric data.]

Table 7.3.1. Animal studies on serum or pineal melatonin levels

Animals, number per group, age at start	Exposure: source, schedule, level, freely moving or restrained	Response	Comment	Reference
Cow: Red Holstein (n=5) 3-4 years	3-30 MHz continuous, transmitter switched off for 3 d Exposed: 1.59 mA/m; control: 0.076 mA/m Free	No difference in salivary melatonin after continuous exposure, but higher in 1st night after re-exposure following 3-d switch off.	Small groups. Considerable variation in data. Temporary increase on 4th day after re-exposure not discussed.	Stärk et al. (1997)
Rat: Sprague Dawley, Dark Agouti; Djungarian hamster (n=4-6)	900 MHz, CW or GSM modulated 15 min - 6 h rat: WBA SAR 0.06-0.36 W/kg hamster: WBA SAR 0.04 W/kg Free	No effect on pineal melatonin synthesis in both types of animals.	26 individual experiments of which 12 dismissed. Small number of animals per group.	Vollrath et al. (1997)
Rat: Fischer 344, normal (n=48) 5 weeks + 1 week acclimatization Treated with diethylnitrosamine to initiate liver tumours	TDMA 929 MHz 1.5 h/d, 5 d/week, 6 weeks WBA SAR 0.58-0.8 W/kg Restrained	Increase in serum melatonin.	Also discussed in Section 12.2.2 (Cancer).	Imaida et al. (1998b)
Rat: Fischer 344, normal (n=48) 5 weeks +1 week acclimatization Treated with diethylnitrosamine to initiate liver tumours	TDMA 1439 MHz 1.5 h/d, 5 d/week, 6 weeks WBA SAR 0.453-0.68 W/kg Restrained	Increase in serum melatonin.	Also discussed in Section 12.2.2 (Cancer).	Imaida et al. (1998a)
Mouse: CD-1, normal (n=30, 48) 5 weeks Treated with DMBA to initiate skin tumours	TDMA 1490 MHz 1.5 h/d, 5 d/week, 19 weeks WBA SAR <0.084 W/kg Restrained	No effect on serum melatonin	Also discussed in Section 12.2.2 (Cancer).	Imaida et al. (2001)
Mouse: K2 (ODC transgenic) and wild-type (n=45-49; cage control: n=20) 12-15 weeks Treated with UV to initiate skin tumours	902 MHz GSM, 849 MHz DAMPS 1.5 h/d, 5 d/week, 52 weeks WBA SAR 0.5 W/kg Restrained	No effect on urinary 6-sulfatoxymelatonin at week 7 and 8.	Also discussed in Section 12.2.2 (Cancer).	Heikkinen et al. (2003)
Rat: Wistar (n=3 x 6) 10-14 weeks	900, 1800 GSM 2 h/d, 14 d WBA SAR: 900 MHz: 0.009-0.012 W/kg 1800 MHz: 0.022-0.045 W/kg Free	No effect on urinary 6-sulfatoxymelatonin.		Bakos et al. (2003)
Rat: Sprague Dawley (n=64) 8-10 weeks + 2 weeks acclimatization	1439 MHz TDMA mobile phone signal 4 h Brain SAR 7.5 W/kg; WBA SAR 1.9-2.0 W/kg Restrained	No effect on pineal, serum melatonin and pineal serotonin.	Positive control (exposure to light): reduction pineal and serum melatonin.	Hata et al. (2005)

Rat: Fischer 344, normal (n=100) Gestation d 18 Mothers treated with ENU	TDMA 1439 GHz 90 min/d, 5 d/week, 104 weeks Brain SAR 0.67, 2.0 W/kg Restrained	No effect on serum melatonin.	Tumour induction discussed in section 12.2.2.	Shirai et al. (2005)
Rat: Fischer 344 (n=4) 12 weeks	915 MHz mobile phone 2 h WBA SAR 0.4 W/kg Free	Upregulation of various genes, including N-acetyltransferase-1, involved in melatonin production.	Also discussed in Sections 5.3.3 (Blood-brain barrier integrity) and 12.2.1 (Genotoxicity).	Belyaev et al. (2006)
Rat: Wistar (n=6) 35 d	2.54 GHz 2 h/d, 45 d WBA SAR 0.14 W/kg Free	Decreased pineal melatonin.		Kesari, Kumar & Behari (2012)
Rat: Wistar (n=6) 70 d	10 GHz 2 h/d, 45 d WBA SAR 0.014 W/kg Restrained	Increased serum melatonin.	Also discussed in Section 11.3 (Fertility, reproduction and development).	Kumar, Behari & Sisodia . (2012)
Rat: Sprague Dawley (n=6) 4 weeks + 4 weeks acclimatization	1800 MHz 2 h/d, 32 d WBA SAR 0.58 W/kg Free	Decreased level of plasma melatonin .		Qin et al. (2012)
Rat: Sprague Dawley (male, female: n=20) 8 weeks	849 MHz CDMA ± 1950 MHz WCDMA 45 min/d, 5 d/week, 4 or 8 weeks WBA SAR 4 W/kg Free	No effect on serum melatonin.		Jin et al. (2013)

Abbreviations: CDMA: Code Division Multiple Access; CW: continuous wave; DAMPS: Digital Advanced Mobile Phone System; DMBA: 7,12-dimethybenz[a]anthracene; GSM: Global System For Mobile Communication; TDMA: Time Division Multiple Access; UV: ultraviolet; WBA SAR: whole-body SAR; WCDMA: Wideband Code Division Multiple Access

7.3.2 Other hormones

Hypothalamus-pituitary axis

Sinha (2008) and Sinha et al. (2008) described the effects of exposure to RF EMF in groups of 5 young and adult Charles Foster rats, respectively. A 2450 MHz signal, square modulated at 1 kHz, was applied for 2 h per day and 21 days, at a whole-body SAR of 0.036 W/kg. In the adult animals this induced a decrease in tri-iodothronine (T3) ($p<0.01$) and and an increase in thyroxin (T4) ($p<0.05$) relative to sham-exposed animals; the authors did not state the timing of this assay, but most likely it was at the end of the exposures, since blood was obtained by cardiac puncture. In the young animals blood was taken from the tail, and sequential measurements were made at 1, 6, 11, 16 and 21 days after start of treatment. A decrease in T3 compared to the sham-exposed group was measured at days 16 ($p<0.05$) and 21 ($p<0.01$) and an increase in T4 at day 21 ($p<0.05$), which corresponds to the observations in adult animals. In both groups no effects on TSH were observed. [These studies are also discussed in Section 5.3.1.2 (Non-spatial tasks and behaviour).]

Esmekaya, Seyhan & Ömerglu (2010) exposed Wistar rats to a 900 MHz mobile phone-like signal, 20 min per day for 21 days, at a whole-body SAR of 1.35 W/kg. They used groups of 10 animals and observed hypotrophy of the thyroid gland and a decreased thyroid hormone secretion. They also observed an increase in caspase-3 and caspase-9 activity in thyroid cells, indicating apoptosis (all $p<0.05$).

In the experiments described above for melatonin, where Jin et al. (2013) exposed rats to either CDMA or CDMA+WDCMA signals, no effect of these treatments were observed on T3, T4 and thyroid

stimulating hormone (TSH) levels. (TSH is released from the hypothalamus via the anterior pituitary gland and regulates thyroid activity.)

Li et al. (2008) exposed Wistar rats to pulsed 2450 MHz RF EMF for 3 h per day during 30 days in the presence of or without the glucocorticoid receptor antagonist RU468. The whole-body SAR was 0.2 W/kg. The SAR of the brain was reported as 0.7 W/kg. [It is difficult to conceive this as accurate, since the animals could move freely.] At the end of the exposure period, blood and tissue samples were collected from each of the 14 animals per group. An increased plasma corticosterone level was observed ($p<0.01$), which was further increased by administration of the glucocorticoid receptor antagonist every fifth day concurrent with the EMF exposures. They also observed a shift of the cellular distribution of glucocorticosterone receptors in brain cells from the cytosolic to the nuclear fraction. According to the authors this indicates an increase in the DNA binding of glucocorticoid receptor and, consequently, an increase in transcriptional efficacy. This effect was partly counteracted by administration of the glucocorticoid receptor antagonist. [This study is also discussed in Section 5.3.1.1 (Place learning and spatial memory).]

Nakamura et al. (1997; 2000a) performed a series of experiments on the effects of single, 90-min exposures to 2450 MHz RF EMF on hormone levels in female Wistar rats. In the first study (Nakamura et al., 1997), groups of 6 virgin and 6 pregnant animals were assayed; the animals were restrained during exposure and the whole-body SAR was 1.8–2.2 W/kg. The authors observed increased serum levels of corticosterone and adrenocorticotropic hormone (ACTH) in both virgin and pregnant rats ($p<0.05$). An increase in β-endorphin ($p<0.05$) was only found in pregnant rats. [This study is also discussed in Section 10.3 (Immune system and haematology).] In Nakamura et al. (2000a) virgin and pregnant animals (6 per group) were exposed at a whole-body SAR of 0.36–0.44 W/kg. In virgins, increased corticotropin releasing hormone (CRH) and β-endorphin levels were found in blood ($p<0.05$); administration of the CRH receptor antagonist α-helical CRH had no effect. Also in pregnant animals the CRH and β-endorphin levels in blood were increased ($p<0.05$), but exposure had no effect on the placental β-endorphin level. Administration of α-helical CRH decreased the β-endorphin level in both blood ($p<0.05$) and placenta ($p<0.01$). . [This study is also discussed in Section 9.3.2.2 (Studies investigating RF exposure at non-hyperthermic levels - Experiments with rodents: non-behavioural thermoregulation).]

Khirazova et al. (2012) exposed 10-12 week old rats to an 905 MHz RF field for 2 h at a whole-body SAR of 1.67 W/kg. Twenty minutes and 24 h after exposure plasma glucocorticoid levels were assessed. At 20 min after exposure they were decreased in females and increased in males, while at 24 h after exposure they were decreased in males (all $p<0.05$). [This study is also discussed in Section 5.3.1.2 (Non-spatial tasks and behaviour).]

Bouji (2012) exposed 6 week and 12 months old Sprague Dawley rats to a 900 MHz GSM signal for 15 minutes locally to the head at a SAR of 6 W/kg. In the young animals plasma corticosterone was increased after exposure, while in the older animals no effect was observed. [This study is also discussed in Section 5.3.1.2 (Non-spatial tasks and behaviour).]

Female reproductive hormones

In the experiments of Nakamura et al. (1997) on the effects of exposures to 2450 MHz RF EMF on hormone levels in female rats, exposure of restrained animals at a whole-body SAR of 1.8–2.2 W/kg decreased the level of oestradiol in both virgin and pregnant rats, and increased progesterone in pregnant rats ($p<0.05$) . [This study is also discussed in Section 10.3 (Immune system and haematology).]

Yamashita et al. (2010) exposed or sham exposed groups of 16 ovariectomized Sprague Dawley rats to a 1439 MHz TDMA mobile phone signal for 4 h per day and 3 days. The animals were restrained and exposure was directed at the brain. The brain SAR was 5.5–6.1 W/kg, while the whole body SAR was 0.88–0.99 W/kg. This treatment had no effect on the blood oestrogen level.

In the experiments described above with melatonin and thyroid hormones, where Jin et al. (2013) exposed rats to either CDMA or CDMA+WDCMA signals, no effect of these treatments were observed on serum oestrogen levels.

Male reproductive hormones

In a mouse study, Forgács et al. (2006) exposed free roaming animals (11–12 per group) for 2 weeks, 2 h daily during work days, to an 1800 MHz mobile phone signal resulting in a whole body SAR of 0.018–0.023 W/kg. They observed an increase in the testosterone level in the testes of the NMRI mice ($p<0.05$). [This study is also discussed in Section 10.3 (Immune system and haematology).]

Ribeiro et al. (2007) exposed Wistar rats to an 1800 MHz mobile phone signal 1 h daily for 11 weeks (n=8 per group). The power density in the cage of the free roaming animals was 0.04-1.4 mW/cm^2 (0.4-14 W/m^2). SAR levels were not provided. They observed no changes in the serum testosterone level. [This study is also discussed in Section 11.3 (Fertility, reproduction and development).]

As part of a series of experiments described earlier with the melatonin studies, in which animals were exposed to two mobile telecommunication signals simultaneously, no effect of these treatments on the serum testosterone level in male Sprague Dawley rats was observed after either 8 weeks (Jin et al., 2013) or 12 weeks of exposure (Lee et al., 2012). [This study is also discussed in Section 11.3 (Fertility, reproduction and development).]

In a study employing a higher frequency than the ones used in mobile telecommunication, Kumar, Behari and Sisodia (2013) exposed groups of 6 Wistar rats to 10 GHz for 2 h daily and 45 days at a whole-body SAR of 0.014 W/kg. They observed a decrease in the serum testosterone level ($p<0.0007$). [This study is also discussed in Section 11.3 (Fertility, reproduction and development).]

Other hormones

Braithwaite et al. (1991) performed an experiment in which chicken (11 per group) were exposed to either infrared radiation or 2.54 GHz RF EMF with a power density of 13 mW/cm^2 (130 W/m^2). The animals were kept in a cool environment (16 °C) and the exposure served to provide heat upon demand. The experiment ran for 20 days. The demand for heat from RF was less than that from IR, but neither type of exposure had any effect on the serum corticosterone level. [This study is also discussed in Section 10.3 (Immune system and haematology).]

In a study primarily aimed at carcinogenesis and more fully described in section 12.2.1.1, Chou et al. (1992) exposed groups of 100 Sprague Dawley rats for 25 months and 21.5 h per day to pulsed 2450 MHz fields, at whole-body SARs of 0.15–0.4 W/kg. This treatment had no effect on the serum corticosterone level. [This study is also discussed in section3 10.3 (Immune system and haematology) and 12.2.2 (Cancer).]

Stagg et al. (2001) exposed Fisher 344 rats (n=5) to the brain for 2 h to the 1.6 GHz Iridium signal used in satellite telephony. The SAR in the brain was 0.15, 1.6 or 5 W/kg. No effect on corticosterone level was observed. [Although p values were provided, the type of statistical analysis is not mentioned.]

In a cancer study described in section 12.2.2, Shirai et al. (2005) exposed the heads of Fisher 344 rats, that were born from mothers that were treated with n-ethylnitrosourea (ENU) to induce brain cancer, to a 1439 MHz TDMA signal for 90 min per day, 5 days per week for 104 weeks. The SARs in the brain were 0.67 or 2.0 W/kg. Five rats out of each group of 100 were used to collect blood for the determination of corticosterone and ACTH. No effect of the exposure on either hormone was observed. (Serum melatonin levels are discussed in section 7.2.1).

Daniels et al. (2009) exposed newborn Sprague Dawley rats for 3 h per day from day 2–14 after birth to an 850 MHz field at a power density of 60 $\mu W/m^2$. At an age of 62 days the animals were killed and the level of corticosterone in plasma was measured. No effect of exposure was observed. [This study is also discussed in sections 5.3.1.1 (Place learning and spatial memory) and 5.3.1.2 (Non-spatial tasks and behaviour).]

In a study using Wistar rats, Prochnow et al. (2011) exposed groups of 6 animals to the brain using a 2 GHz UMTS signal for 2 h, at brain SARs of 2 and 10 W/kg. No effect of either treatment was found on the serum ACTH level, but after exposure to the highest SAR level they found the blood corticosterone level to be decreased ($p<0.001$).

In the series of experiments in which Sprague Dawley rats were exposed to two mobile telecommunication signals simultaneously for 45 min per day, 5 days per week and up to 8 weeks, Jin et al. (2013) found no effect of the exposure on the serum ACTH level.

Lai et al. (1990) exposed or sham exposed groups of 8-12 Sprague Dawley rats to a pulsed 2450 MHz signal for 45 min at a whole-body SAR of 0.6 W/kg. They observed a decreased uptake of sodium-dependent high-affinity choline ($p<0.005$), which was counteracted by a corticotropin-releasing factor receptor antagonist. This indicates activation of corticotropin-releasing factor.

Studies not included in the analysis

Ozguner et al. (2005) exposed male rats (10 per group) for 30 min per day, 5 days per week and 4 weeks to a 900 MHz mobile phone signal. The animals were restrained in a tube and the antenna was placed directly below the tube. The output of the signal generator is provided as an "average power density 1 ± 04 mW/cm^2", but it is not clear what the actual exposure level of the animals (and in particular of the testes) was. The authors observed a decrease in the serum testosterone level ($p<0.05$), but this is difficult to interpret with the lack of exposure information.

Kesari and Behari (2012) exposed Wistar rats for 2 h per day during 45 days to a signal from a 900 MHz mobile phone. They observed a decrease in serum testosterone level ($p<0.003$). [This finding cannot be interpreted since the exposure level is not provided.]

Koyu et al. (2005a) investigated the effects in Sprague Dawley rats of exposure to 900 MHz CW RF radiation on circulating levels of TSH and serum T3 and T4 levels. The authors found that exposure during 30 min per day for 5 days a week during 4 weeks at a peak SAR of 2 W/kg significantly reduced TSH, T3 and T4 levels compared to sham exposed animals ($p<0.01$). [The location of the peak SAR is not provided, nor the whole-body average SAR. Therefore this study cannot be interpreted.]

Pellegrini et al. (1994) exposed Wistar rats of 3 or 21 months of age to a continuous 2450 MHz signal for 45 min (n=4–6). They investigated the effect of this treatment on the functional activity of the beta and alpha receptor agonists isoprenaline and noradrenaline on tissues from the heart and the aorta. While in young rats they observed no effect of the exposure, they claim to have found in aged rats a decreased effectiveness of isoprenaline in the heart and an increased effectiveness in the aorta. [The description of the functional tests is incomplete and therefore the study cannot be properly interpreted.]

Table 7.3.2. Animal studies on various hormones

Animals, number per group, age at start	Exposure: source, schedule, level, freely moving or restrained	Response	Comment	Reference
Hypothalamus-pituitary axis				
Rat: Charles Foster (n=5) 4-5 weeks	2450 MHz, square wave modulated at 1 kHz 2 h/day, 21 days WBA SAR 0.036 W/kg Free	Decreased T3 at d 16, 21, increased T4 at d 21, no effect on TSH.	Also discussed in Section 5.3.1.2 (Non-spatial tasks and behaviour).	Sinha (2008)
Rat: Charles Foster (n=5) 9-10 weeks	2450 MHz, square wave modulated 1 kHz 2 h/day, 21 days WBA SAR 0.036 W/kg Free	Decreased T3, increased T4, no effect on TSH.	Also discussed in Section 5.3.1.2 (Non-spatial tasks and behaviour).	Sinha et al. (2008)

Rat: Wistar (n=10) 2 months	900 MHz mobile phone-like signal 20 min/day, 21 days WBA SAR max 1.35 W/kg	Thyroid gland: hypotrophy, decreased thyroid hormone secretion, increase in caspase-3, caspase-9 (indicating apoptosis).	Average SAR could be less due to free roaming.	Esmekaya et al. (2010)
Rat: Sprague Dawley (male, female: n=20) 8 weeks	849 MHz CDMA ± 1950 MHz WCDMA 45 min/day, 5 days/weeks, 4 or 8 weeks WBA SAR 4 W/kg Free	No effect on TSH, T3, T4.		Jin et al. (2013)
Rat: Wistar (n=14) 3 months	Pulsed 2450 MHz ± glucocorticod receptor antagonist RU468 3 h/day, 30 days Brain SAR : 0.7 W/kg; WBA SAR: 0.2 W/kg Free	Increased plasma corticosterone, further increased by RU468; altered cellular distribution of glucocorticosterone receptor, partly counteracted by RU468.	Correctness brain SAR doubtful. Also discussed in Section 5.3.1.1 (Place learning and spatial memory).	Li et al. (2008)
Rat: Wistar (n=6) Age not provided; weight: 290±16.4 g (virgins); 296±18.5 g (pregnants)	2450 MHz 90 min WBA SAR 1.8-2.2 W/kg Restrained	Increased serum corticosterone and ACTH in virgin and pregnant rats, increased β-endorphin in pregnant rats.	Also discussed in Section 10.3 (Immune system and haematology).	Nakamura et al. (1997)
Rat: Wistar (n=6) Age not provided; weight: 268±5.6 g (virgins); 271±7.7 g (pregnants)	2450 MHz 90 min WBA SAR 0.36-0.44 W/kg Restrained	Virgins: increased blood corticotropin releasing hormone (CRH) & β-endorphin, no effect of CRH antagonist α-helical CRH; Pregnants: increased blood CRH & β-endorphin, no effect placental β-endorphin, α-helical CRH decreased blood & placental β-endorphin.	Also discussed in Section 9.3.2.2 (Studies investigating RF exposure at non-hyperthermic levels - Experiments with rodents: non-behavioural thermoregulation).	Nakamura et al. (2000a)
Rat (n=10) 10–12 weeks	905 MHz 2 h WBA SAR 1.67 W/kg Restrained	Plasma corticosteoid: 20 min after exposure decreased in females, increased in males; 24 h after exposure decreased in males.	Also discussed in 5.3.2.1 (Non-spatial tasks and behaviour).	Khirazova et al. (2012)
Rat: Sprague Dawley (n=6) 6 weeks, 12 months	900 MHz GSM 15 min Brain SAR 6 W/kg Restrained	Increased plasma corticosterone in young, not in old animals.	Also discussed in 5.3.2.1(Non-spatial tasks and behaviour).	Bouji et al. (2012)
Female reproductive hormones				
Rat: Wistar (n=6) Age not provided; weight: 290±16.4 g (virgins); 296±18.5 g (pregnants)	2450 MHz 90 min WBA SAR 1.8-2.2 W/kg Restrained	Decreased oestradiol in virgin and pregnant rats, increased progesterone in pregnant rats.	Also discussed in Section 10.3 (Immune system and haematology).	Nakamura et al. (1997)

Rat: Sprague Dawley (n=16) 12-13 weeks, ovariectomized at 8 weeks	1439 MHz TDMA mob phone 4 h/day, 3 days Brain SAR: 5.5-6.1 W/kg; WBA SAR: 0.88-0.99 W/kg Restrained	No effect on oestrogen.		Yamashita et al. (2010)
Rat: Sprague Dawley (n=20) 8 weeks	849 MHz CDMA ± 1950 MHz WCDMA 45 min/day, 5 days/weeks, 4 or 8 weeks WBA SAR 4 W/kg Free	No effect on oestrogen.		Jin et al. (2013)
Male reproductive hormones				
Mouse: NMRI (n=11-12) 9-10 weeks	1800 MHz GSM 2 h/day, 5 days/week, 2 weeks WBA SAR 0.018-0.023 W/kg Free	Increased testicular testosterone.	Also discussed in Section 10.3 (Immune system and haematology).	Forgács et al. (2006)
Rat: Wistar (n=8) 30 d	1800 MHz mobile phone 1 h/day, 11 weeks 0.04-1.4 mW/cm^2 (0.4-14 W/m^2) Free	No effect on serum testosterone.	Also discussed in Section 11.3 (Fertility, reproduction and development).	Ribeiro et al. (2007)
Rat: Sprague Dawley (n=20) 8 weeks	849 MHz CDMA ± 1950 MHz WCDMA 45 min/day, 5 days/weeks, 4 or 8 weeks WBA SAR 4 W/kg Free	No effect on testosterone.		Jin et al. (2013)
Rat: Sprague Dawley (control: n=5; exposed: n=20) 4 weeks	849 MHz CDMA & 1950 MHz WCDMA 45 min/day, 5 days/weeks, 12 weeks WBA SAR 4.0 W/kg Free	No effect on serum testosterone.	Also discussed in Section 11.3 (Fertility, reproduction and development).	Lee et al. (2012)
Rat: Wistar (n=6) 70 d	10 GHz 2 h/day, 45 days WBA SAR 0.014 W/kg Restrained	Decreased serum testosterone.	Also discussed in Section 11.3 (Fertility, reproduction and development).	Kumar et al. (2013)
Other hormones				
Chicken 1 week	2.45 GHz Upon demand, 20 days 13 mW/cm^2 (130 W/m^2) Free	No effect on serum corticosterone.	Also discussed in Section 10.3 (Immune system and haematology).	Braithwaite et al. (1991)
Rat: Sprague Dawley, normal (n=100) 3 weeks + 5 weeks acclimatization	2450 MHz, pulsed 21.5 h/day, 25 months WBA SAR 0.15-0.4 W/kg Free	No effect on serum corticosterone.	Also discussed in section3 10.3 (Immune system and haematology) and 12.2.2 (Cancer).	Chou et al. (1992)

Rat: Fischer 344 (n=5) 30-35 d + 3 weeks acclimatization	1.6 GHz Iridium 2 h Brain SAR 0.15, 1.6, 5 W/kg Restrained	No effect on corticosterone and ACTH.	Statistical analysis not clear.	Stagg et al. (2001)
Rat: Fischer 344, normal (n=100) Gestation d 18 Mothers treated with ENU	TDMA 1439 GHz 90 min/day, 5 days/week, 104 weeks Brain SAR 0.67, 2.0 W/kg Restrained	No effect on serum corticosterone and ACTH.	Melatonin discussed in section 07.2.1. Tumour induction discussed in section 12.2.2.	Shirai et al. (2005)
Rat: Sprague Dawley (n=6) 2 days	840 MHz 3 h/day, 12 days 60 μW/m^2 Free	No effect on plasma corticosterone.	Also discussed in sections 5.3.1.1 (Place learning and spatial memory) and 5.3.1.2. (Non-spatial tasks and behaviour).	Daniels et al. (2009)
Rat: Wistar (n=6) 12-15 weeks	2000 MHz UMTS 120 min Brain SAR 2, 10 W/kg Restrained	No effect on blood ACTH; blood corticosterone decreased after 10 W/kg.		Prochnow et al. (2011)
Rat: Sprague Dawley (male, female: n=20) 8 weeks	849 MHz CDMA ± 1950 MHz WCDMA 45 min/day, 5 days/weeks, 4 or 8 weeks WBA SAR 4 W/kg Free	No effect on ACTH.		Jin et al. (2013)
Rat: Sprague Dawley (n=8-12)	2450 MHz, pulsed 45 min WBA SAR 0.6 W/kg Free	Decreased sodium-dependent high-affinity choline uptake, counteracted by a corticotropin-releasing factor receptor antagonist, indicating activation of corticotropin-releasing factor .		Lai et al. (1990)

Abbreviations: ACTH: adrenocorticotropic hormone; CDMA: Code Division Multiple Access; CRH: corticotropin releasing hormone; GSM: Global System For Mobile Communication; TDMA: Time Division Multiple Access; TSH: thyroid stimulating hormone; T3: tri-iodothronine; T4: thyroxin; UMTS: Universal Mobile Telecommunications Signal; WBA SAR: whole-body SAR; WCDMA: Wideband Code Division Multiple Access

Excluded papers

(Nakamura et al., 2000b); (Nakamura et al., 2003)

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