

5 NEUROBEHAVIOUR

Neurobehavioural studies encompass the effects of exposure to ELF electromagnetic fields on the nervous system and its responses at different levels of organization. These include the direct stimulation of peripheral and central nerve tissue, perceptual effects resulting from sensory stimulation, and effects on central nervous system function. Effects on the latter can be assessed both electrophysiologically by recording the electrical activity of the brain, and by tests of cognition, assessment of mood, and other studies.

The nervous system also has a central role in the control of other body systems, particularly the cardiovascular system, through direct nervous control, and the endocrine system, through neural input into the pineal and pituitary glands. These glands in turn influence reproduction and development, and in a more general way, physiology and well-being.

The brain and nervous systems function by using electrical signals, and may therefore be considered particularly vulnerable to low frequency EMFs and the resultant induced electric fields and currents. Substantial numbers of laboratory experiments with volunteers and animals have investigated the possible consequences of exposure to weak EMFs on various aspects of nervous system function, including cognitive, behavioural and neuroendocrine responses. In addition, epidemiological studies have been carried out on the relationship between EMF exposure and both suicide and depression.

These studies have been reviewed by NRC (1997), NIEHS (1998), IARC (2002), ICNIRP (2003) and McKinlay et al. (2004). In particular, ICNIRP (2003) reviewed in detail some of the evidence summarized here.

In general, there are few effects for which the evidence is strong, and even the more robust field-induced responses seen in the laboratory studies tend to be small in magnitude, subtle and transitory in nature (Crasson et al., 1999; Sienkiewicz et al., 1993).

5.1 Electrophysiological considerations

An examination of the electrophysiological properties of the nervous system, particularly the central nervous system (CNS: brain and spinal cord) gives an indication of its likely susceptibility to the electric fields induced in the body by EMF exposure. Ion channels in cell membranes allow passage of particular ionic species across the cell membrane in response to the opening of a “gate” which is sensitive to the transmembrane voltage (Catterall, 1995; Hille & Anderson, 2001; Mathie, Kennard & Veale, 2003). It is well established that electric fields induced in the body either by direct contact with external electrodes, or by exposure to low frequency magnetic fields, will, if of sufficient magnitude, excite nerve tissue through their interaction with these voltage-gated ion channels. Sensitivity is therefore primarily to the transmembrane electric field and varies widely between different ion channels (Hille & Anderson, 2001; Mathie, Kennard & Veale, 2003; Saunders & Jefferys, 2002). Many voltage-gated ion channels are associated with electrical excitability and electrical signalling. Such electrically excit-

able cells not only comprise neurons, glial and muscle cells, but also endocrine cells of the anterior pituitary, adrenal medulla and pancreas, gametes and, with reservations, endothelial cells (Hille & Anderson, 2001).

All these cells generally express voltage-gated sodium and calcium channels. Both of these ion channels are involved in electrical signaling and calcium ions activate a number of crucial cellular processes including neurotransmitter release, excitation-contraction coupling in muscle cells and gene expression (Catterall, 2000; Hille & Anderson, 2001). Some ion channels, for example voltage-gated potassium and chloride ion channels, also exist in other, non-excitabile tissues such as those in the kidney and liver and show slow electric potential changes but their voltage sensitivity is likely to be lower (Begenisich & Melvin, 1998; Cahalan, Wulff & Chandy, 2001; Catterall, 2000; Jan & Jan, 1989; Nilius & Droogmans, 2001). Since voltage-gated ion channels in excitable cells are steeply sensitive to the transmembrane electric potential, electric field strength in tissue is a more relevant parameter to relate to electrically excitable cell thresholds than current density (Bailey et al., 1997; Blakemore & Trombley, 2003; Reilly, 2005; Shepard, Kavet & Renew, 2002). In fact, the relevant parameter in determining the transmembrane current and hence the excitability is the linear gradient in electric field (Tranchina & Nicholson, 1986), which in turn relates to geometric parameters of the neuron, including the degree of bending of the axon.

Peripheral nerves comprise neurons whose cell bodies are located within the CNS with extended processes (axons) that lie outside the CNS. They conduct action potentials (impulses) towards (sensory nerves) or from (motor nerves) the spinal cord and nerve stimulation shows an all-or-nothing threshold behaviour. Excitation results from a membrane depolarisation of between 10–20 mV, corresponding to an electric field in tissue of 5–25 V m⁻¹ (McKinlay et al., 2004). Pulsed magnetic fields, where the rate of change of field induces large localised electric fields, can directly stimulate peripheral nerves and nerve fibres located within the brain (see below).

Cells of the central nervous system are considered to be sensitive to electric fields induced in the body by exposure to ELF magnetic fields at levels that are below threshold for impulse initiation in nerve axons (Jefferys, 1995; Jefferys et al., 2003; Saunders, 2003; Saunders & Jefferys, 2002). Such weak electric field interactions have been shown in experimental studies mostly using isolated animal brain tissue to have physiological relevance. These interactions result from the extracellular voltage gradients generated by the synchronous activity of a number of neurons, or from those generated by applying pulsed or alternating currents directly through electrodes placed on either side of the tissue. Jefferys and colleagues (Jefferys, 1995; Jefferys et al., 2003) identified *in vitro* electric field thresholds of around 4–5 V m⁻¹. Essentially, the extracellular gradient alters the potential difference across the neuronal membrane with opposite polarities at either end of the neuron; a time-constant of a few tens (15–60) of milliseconds results from the capacitance of the neuronal membrane (Jefferys et al., 2003) and indicates a limited frequency response. Similar arguments concerning the limited frequency

response of weak electric field effects due to the long time-constants (25 ms) arising from cell membrane capacitance have been given by Reilly (2002) regarding phosphene data.

The CNS *in vivo* is likely to be more sensitive to induced low frequency electric fields and currents than are *in vitro* preparations (Saunders & Jefferys, 2002). Spontaneous activity is higher, and interacting groups or networks of nerve cells exposed to weak electrical signals would be expected, on theoretical grounds, to show increased sensitivity through improved signal-to-noise ratios compared with the response of individual cells (Adair, 2001; Stering, 1998; Valberg, Kavet & Rafferty, 1997). Much of normal cognitive function of the brain depends on the collective activity of very large numbers of neurons; neural networks are thought to have complex non-linear dynamics that can be very sensitive to small voltages applied diffusely across the elements of the network (Adair, 2001; ICNIRP, 2003; Jefferys et al., 2003). Gluckman et al. (2001) placed the detection limit for network modulation in hippocampal slices by electric fields at around 100 mV m^{-1} . Recent experimental work by Francis, Gluckman & Schiff (2003) confirms a neural network threshold of around 140 mV m^{-1} , which the authors found was lower than single neuron thresholds, based on a limited number of measurements. A lower limit on neural network sensitivity to physiologically weak induced electric fields has elsewhere been considered on theoretical grounds to be around 1 mV m^{-1} (Adair, Astumian & Weaver, 1998; Veyret, 2003). The time-course of the opening of the fastest voltage-gated ion channels can be less than 1 ms (Hille & Anderson, 2001), suggesting that effects at frequencies up to a few kilohertz should not be ruled out. Accommodation to a slowly changing stimulus resulting from slow inactivation of the sodium channels will raise thresholds at frequencies less than around 10 Hz.

Other electrically excitable tissues with the potential to show network behaviour include glial cells located within the CNS (e.g. Pappas et al., 1994), and the autonomic and enteric nervous systems (see Sukkar, El-Munshid & Ardawi, 2000), which comprise interconnected non-myelinated nerve cells and are distributed throughout the body and gut, respectively. These systems are involved in regulating the visceral or “housekeeping” functions of the body; for example, the autonomic nervous system is involved in the maintenance of blood pressure. Muscle cells also show electrical excitability; only cardiac muscle tissue has electrically interconnected cells. However, Cooper, Garry & Kohl et al. (2003), in a review of cardiac ion channel activity, conclude that weak internal electric fields much below the excitation threshold are unlikely to have any significant effect on cardiac physiology. EMF effects on the heart could theoretically result from indirect effects mediated via the autonomic nervous system and CNS (Sienkiewicz, 2003). Effects on the endocrine system could potentially also be mediated this way, although the evidence from volunteer experiments indicates that acute ELF magnetic field exposure up to $20 \mu\text{T}$ does not influence the circadian variation in circulating levels of the hormone melatonin (Warman et al., 2003b), nor other plasma hormone levels (ICNIRP, 2003).

5.2 Volunteer studies

An electric charge is induced on the surface of a human (or other living organism) exposed to a low frequency electric field that alternates in amplitude with the frequency of the applied field. The alternation of the surface charge with time induces an electric field and therefore current flow within the body; in addition, exposure to a low frequency magnetic field induces circulating eddy currents and associated electric fields. If of sufficient magnitude, these induced electric fields and currents can interact with electrically excitable nerve and muscle tissue. Generally, however, the surface charge effects of exposure to low frequency electric fields become prohibitive long before the internal electric fields become large enough to elicit a response in the tissue.

5.2.1 Surface electric charge

The surface electric charge can be perceived directly through the induced vibration of body hair and tingling sensations in areas of the body, particularly the arms, in contact with clothing, and indirectly through spark discharges between a person and a conducting object within the field. In several studies carried out in the 1970's and 1980's (summarized by Reilly, 1998a; 1999), the threshold for direct perception has shown wide individual variation; 10% of the exposed subjects had detection thresholds of around 2–5 kV m⁻¹ at 60 Hz, whereas 50% could detect fields of 7–20 kV m⁻¹. These effects were considered annoying by 5% of the test subjects exposed under laboratory conditions above electric field strengths of about 15–20 kV m⁻¹. In addition to showing a wide variation in individual sensitivity, these responses also vary with environmental conditions, particularly humidity; the studies referred to above, however, included both wet and dry exposure conditions.

It has been estimated that spark discharges would be painful to 7% of subjects who are well-insulated and who touch a grounded object within a 5 kV m⁻¹ field (Reilly, 1998a; Reilly, 1999) whereas they would be painful to about 50% in a 10 kV m⁻¹ field. Unpleasant spark discharges can also occur when a grounded person touches a large conductive object such as a large vehicle that is “well-insulated” from ground and is situated within a strong electric field. Here, the threshold field strength required to induce such an effect varies inversely with the size of the conductive object. In both cases, the presence in the well-insulated person or object of a conductive pathway to ground would tend to mitigate the intensity of any effect (Reilly, 1998a; Reilly, 1999), as would the impedance to earth of the grounded object or person.

People can perceive electric currents directly applied to the body through touching, for example, a conductive loop in which current is induced by exposure to environmental electromagnetic fields. Thresholds for directly applied currents have also been characterised. At 50 to 60 Hz, the male median threshold for perception was between 0.36 mA (finger contact) and 1.1 mA (grip contact), while pain occurred at 1.8 mA (finger contact).

Median thresholds for women were generally found to be two thirds of the male thresholds, while children were assumed to have median thresholds half of male threshold values (WHO, 1993). There is also a wide variety in the individual's ability to detect currents, there is, for example, about one order of magnitude difference in the perception threshold at the 0.5 percentile and the 99.5 percentile at 50/60 Hz (Kornberg & Sagan, 1979). Generally, the ability to detect fields or currents decreases with increasing frequency. This has been characterised for the perception of currents; the threshold is increasing by about two orders of magnitude at higher frequencies: 0.36 mA at 50/60 Hz, 4 mA at 10 kHz and 40 mA at 100 kHz (WHO, 1993).

A series of extensive studies on 50 Hz population thresholds in more than 1000 people from all ages have recently been carried out by Leitgeb and colleagues. Leitgeb & Schröttner (2002) examined perception thresholds in 700 people aged between 16 and 60 years, approximately half of them women. This study was recently extended to include 240 children aged 9–16 years, and about 20 people aged 61 years or more (Leitgeb, Schroettner & Cech, 2005). In both studies, electric current was applied to the forearm using pre-gelled electrodes, and considerable care was taken to rule out subjective bias.

A summary of the studies on perception of electric currents directly applied to the body is given in Table 33.

Table 33. 50 Hz electric current perception values (I_w) for different perception probabilities (p) for men, women and the general population ^a

p (%)	I_w (μA)			
	Men	Women	Children	Population
90	602	506	453	553
50	313	242	252	268
10	137	93	112	111
5	106	68	78	78
0.5	53	24	35	32

^a Source: Leitgeb & Schroettner, 2002; Leitgeb, Schroettner & Cech, 2005.

Leitgeb, Schroettner & Cech (2005) note that the median perception threshold for the population is 268 μA, almost 50% lower than the present limit of 500 μA recommended by the IEC (1994). They also note that whilst the median threshold for women is approximately two thirds of the male threshold values, children aged between 9 and 16 do not exhibit as a high a sensitivity as had been assumed.

An issue with perception levels is that they really depend on the site of application of the current (cheek and inner forearm being very sensitive)

and the area of application of the current (i.e. current density). The latter makes the comparison of current values difficult (Reilly, 1998a).

5.2.2 Nerve stimulation

Large, rapidly changing, pulsed magnetic fields used in various specialised medical applications such as magnetic resonance imaging (MRI) and transcranial magnetic stimulation (TMS) can induce electric fields large enough to stimulate nervous tissue in humans. Minimum, orientation-dependent stimulus thresholds for large diameter (20 μm) myelinated nerve axons have been estimated to be approximately 6 V m^{-1} at frequencies up to about 1–3 kHz (Reilly, 1998a; Reilly, 1999). In addition, accommodation to a slowly changing stimulus resulting from slow inactivation of sodium channels will raise thresholds at low frequencies. In MRI, nerve stimulation is an unwanted side effect of a procedure used to derive cross-sectional images of the body for clinical diagnosis (see Shellock, 2001). Threshold rates of change of the switched gradient magnetic fields used in MRI for perception, discomfort and pain resulting from peripheral nerve stimulation are extensively reviewed by Nyenhuis et al. (2001). Generally, median, minimum threshold rates of change of magnetic field (during periods of $< 1 \text{ ms}$) for perception were 15–25 $\mu\text{T s}^{-1}$ depending on orientation and showed considerable individual variation (Bourland, Nyenhuis & Schaefer, 1999). These values were somewhat lower than previously estimated by Reilly (1998a; 1999), possibly due to the constriction of eddy current flow by high impedance tissue such as bone (Nyenhuus et al., 2001). Thresholds rose as the pulse width of the current induced by the switched gradient field decreased; the median pulse width (the chronaxie) corresponding to a doubling of the minimum threshold (the rheobase) ranged between 360 and 380 μs but again showing considerable individual variation (Bourland, Nyenhuis & Schaefer, 1999). Numerical calculations of the electric field induced by pulses in the 84 subjects tested by Nyenhuis et al. (2001) have been used to estimate the median threshold for peripheral nerve stimulation at 60 Hz as 48 mT (Bailey & Nyenhuis, 2005). Furthermore, Nyenhuis et al. (2001) using data from measurements on human volunteers estimated a rheobase electric field of 2.2 V m^{-1} in tissue.

In TMS, parts of the brain are deliberately stimulated in order to produce a transient, functional impairment for use in the study of cognitive processes (see Reilly, 1998a; Ueno, 1999; Walsh, Ashbridge & Cowey, 1998). Furthermore, in TMS, brief, localised, suprathreshold stimuli are given, typically by discharging a capacitor through a coil situated over the surface of the head, in order to stimulate neurons in a small volume (a few cubic centimetres) of underlying cortical tissue (Reilly, 1998a). The induced current causes the neurons within that volume to depolarise synchronously, followed by a period of inhibition (Fitzpatrick & Rothman, 2000). When the pulsed field is applied to a part of the brain thought to be necessary for the performance of a cognitive task, the resulting depolarisation interferes with the ability to perform the task. In principle then, TMS provides cognitive neuroscientists with the capability to induce highly specific, temporally and

spatially precise interruptions in cognitive processing – sometimes known as “virtual lesions”. Reilly (1998a) noted induced electric field thresholds to be of the order of 20 V m^{-1} . However, Walsh & Cowey (1998) cited typical rates of change of magnetic field of 30 kT s^{-1} over a $100 \mu\text{s}$ period transiently inducing an electric field of 500 V m^{-1} in brain tissue.

People are likely to show variations in sensitivity to induced electric fields. In particular, epileptic syndromes are characterised by increased neuronal excitability and synchronicity (Engelborghs, D’Hooge & De Deyn, 2000); seizures arise from an excessively synchronous and sustained discharge of a group of neurons (Engelborghs, D’Hooge & De Deyn, 2000; Jefferys, 1994). TMS is widely used, apparently without adverse effects. However, repetitive TMS has been observed to trigger epileptic seizure in some susceptible subjects (Fitzpatrick & Rothman, 2000; Wassermann, 1998). These authors also reported short- to medium-term memory impairments and noted the possibility of long-term cognitive effects from altered synaptic activity or neurotransmitter balance. Contraindications for TMS use agreed at an international workshop on repetitive TMS safety (Wassermann, 1998) include epilepsy, a family history of seizure, the use of tricyclic antidepressants, neuroleptic agents and other drugs that lower seizure threshold. Serious heart disease and increased intracranial pressure have also been suggested as contraindications due to the potential complications that would be introduced by seizure.

5.2.3 Retinal function

The effects of exposure to weak low frequency magnetic fields on human retinal function are well established. Exposure of the head to magnetic flux densities above about 5 mT at 20 Hz , rising to about 15 mT at 50 Hz , will reliably induce faint flickering visual sensations called magnetic phosphenes (Attwell, 2003; Sienkiewicz, Saunders & Kowalczyk, 1991; Taki, Suzuki & Wake, 2003). It is generally agreed that these phosphenes result from the interaction of the induced electric current with electrically sensitive cells in the retina. Several lines of evidence suggest the production of phosphenes by a weak induced electric field does not involve the initial transduction of light into an electrical signal. Firstly, the amplification of the initial signal generated by the absorption of light takes place primarily through an intracellular “second-messenger cascade” of metabolic reactions prior to any change in ion channel conductivity (Hille & Anderson, 2001). Secondly, the phosphene threshold appears unaffected by “dark” adaptation to low light levels (Carpenter, 1972). In addition, phosphenes have been induced in a patient with retinitis pigmentosa, a degenerative illness primarily affecting the pigment epithelium and photoreceptors (Lövsund et al., 1980).

There is good reason to view retinal circuitry as an appropriate model for induced electric field effects on CNS neuronal circuitry in general (Attwell, 2003). Firstly, the retina displays all the processes present in other CNS areas, such as graded voltage signalling and action potentials, and has a similar biochemistry. Secondly, in contrast to more subtle cognitive effects,

phosphenes represent a direct and reproducible perception of field interaction. A clear distinction can be made in this context between the detection of a normal visual stimulus and the abnormal induction of a visual signal by non-visual means (Saunders, 2003); the latter suggests the possibility of direct effects on cognitive processes elsewhere in the CNS.

Thresholds for electrically induced phosphenes have been estimated to be about 10–14 mA m⁻² at 20 Hz (Adrian, 1977; Carstensen, 1985). A similar value (10 mA m⁻² at 20 Hz), based on studies of magnetically induced phosphenes, has been derived by Wake et al. (1998). The equivalent electric field threshold can be estimated as around 100–140 mV m⁻¹ using a tissue conductivity for brain tissue of about 0.1 S m⁻¹ (Gabriel, Gabriel & Corthout, 1996). More recently, Reilly (2002) has calculated an approximate 20 Hz electric field threshold in the retina of 53 mV m⁻¹ for phosphene production. A similar value (60 mV m⁻¹) has been reported elsewhere (see Saunders, 2003). Subsequently, however, Taki et al. (2003) indicated that calculations of phosphene thresholds suggested that electrophosphene thresholds were around 100 mV m⁻¹, whereas magnetophosphene thresholds were around 10 mV m⁻¹ at 20 Hz.

More detailed calculation by Attwell (2003) based on neuroanatomical and physiological considerations, suggests that the phosphene electric field threshold in the extracellular fluid of the retina is in the range 10–60 mV m⁻¹ at 20 Hz. There is however, considerable uncertainty attached to these values. In addition, the extrapolation of values in the extracellular fluid to those appropriate for whole tissue, as used in most dosimetric models, is complex, depending critically on the extracellular volume and other factors. With regard to the frequency response, Reilly (2002) suggests that the narrow frequency response is the result of relatively long membrane time constants of around 25 ms. However, at present, the exact mechanism underlying phosphene induction is unknown. It is not clear whether the narrow frequency response is due to intrinsic physiological properties of the retinal neurons, as suggested by Reilly (2002) above and by Attwell (2003) considering active amplification process in the retinal neuron synaptic terminals, or is the result of central processing of the visual signal (Saunders, 2003; Saunders & Jefferys, 2002). This issue can only be resolved through further investigation.

5.2.4 Brain electrical activity

Since the first suggestion that occupational exposure to EMFs resulted in clinical changes in the electroencephalogram (EEG) was published in 1966 (Asanova & Rakov, 1966; 1972), various studies have investigated if exposure to magnetic fields can affect the electrical activity of the brain. Such methods can provide useful diagnostic information regarding the functional state of the brain, not only from recordings of the spontaneous activity at rest but also from recording the sensory functions and subsequent cognitive processes evoked in response to specific stimuli (evoked or event-related potentials, ERPs). Nevertheless, neurophysiological studies using magnetic fields need to be performed with much care and attention since

they can be prone to many potential sources of error and artefact (NIEHS, 1998). Changes in arousal and attention of volunteers, in particular, can substantially affect the outcome of these studies.

Various studies have investigated the effects of magnetic fields on brain activity by analysing the spectral power of the main frequency bands of the EEG (Bell et al., 1992; Bell et al., 1991; Bell, Marino & Chesson, 1994a; Bell, Marino & Chesson, 1994b; Gamberale et al., 1989; Heusser, Telschaft & Thoss, 1997; Lyskov et al., 1993b; Lyskov et al., 1993a; Marino, Bell & Chesson, 1996; Schienle et al., 1996; Silny, 1986). These studies have used a wide variety of experimental designs and exposure conditions, as well as healthy volunteers and patients with neurological conditions, and thus are difficult to compare and evaluate. Despite some scattered field-dependent changes, most notably in the alpha frequency band, and with intermittent exposure perhaps more effective than continuous exposure, these studies have produced inconsistent and sometimes contradictory results.

A difficulty with interpretation of the EEG in individuals at rest is that the intra-individual variability is very high. The variability of ERPs is much lower, resulting in better reproducibility, and other studies have investigated the effects of magnetic fields and combined electric and magnetic fields on these potentials within the EEG waveform. There are some differences between studies, but generally, the early components of the evoked response corresponding to sensory function do not appear affected by exposure (Graham & Cook, 1999; Lyskov et al., 1993b). In contrast, large and sustained changes on a later component of the waveform representing stimulus detection may be engendered by exposure at 60 mT (Silny, 1984; 1985; 1986), with lesser effects occurring using fields of 1.26 mT (Lyskov et al., 1993b), and nothing below 30 μ T (Graham & Cook, 1999). Finally, exposure during the performance of some discrimination and attention tasks may affect the late major components of the EEG which are believed to reflect cognitive processes involved with stimulus evaluation and decision making (Cook et al., 1992; Crasson et al., 1999; Graham et al., 1994), although Crasson and Legros (2005) were unable to replicate the effects they reported previously. There also is some evidence that task difficulty and field intermittency may be important experimental variables. However, all these subtle effects are not well defined, and some inconsistencies between studies require additional investigation and explanation.

A summary of studies on changes in brain electrical activity while awake is given in Table 34.

Table 34. Brain electrical activity

Test a	Exposure	Response	Comments	Authors
During exposure to magnetic fields up to 10 Hz				
Standard EEG: C _{3,4} ; P _{3,4} ; O _{1,2} ; FFT at 10 Hz, no records during exposure 6 female and 4 male volunteers	10 Hz 100 μ T 10 min	Immediately after exposure the spectral power of the brain activity was lower than before exposure and 10 min afterwards, but only at the occipital electrodes was this difference significant.	Data for individual volunteers are not presented, and there is no information concerning the rate of responders.	Bell, Marino & Chesson, 1994b
Standard EEG: C _{3,4} ; P _{3,4} ; O _{1,2} ; FFT at 1.5 Hz or 10 Hz band 13 healthy subjects and 6 patients	5 or 10 Hz 20, 40 μ T 2 s on, 5 s off	In each person, the magnetic field altered the brain activity at the frequency of stimulation, but no systematic changes of brain activity.	The strength of the effect was proportional neither to frequency nor to field strength.	Bell, Marino & Chesson, 1994a
Standard EEG: C _{3,4} ; P _{3,4} ; O _{1,2} ; frequency spectrum analysis except for < 2.5 Hz and 9-11 Hz. 13 volunteers, 6 patients	1.5 or 10 Hz 80 μ T 2 s on, 5 s off	ICOS (intra-subject comparison of stimulus and non-stimulus state) was altered by ELF exposure in 58% of the subjects.		Marino, Bell & Chesson, 1996
Standard EEG, O _{1,2} spectral analysis of theta (3.5-7.5 Hz), alpha (7.5-12.5 Hz) and beta bands (12.5-25 Hz) 25 female and 36 male volunteers	3 Hz 100 μ T _{pp} 20 min one exposure and one control session	Significant changes in theta and beta frequency bands after exposure relative to controls, interpreted as slightly pronounced reduction of alertness during exposure.	Exposure and control sessions on different days, the two session days were not treated as a double blind study.	Heusser, Tollschaft & Thoss, 1997
During exposure to magnetic fields between 45 and 60 Hz				
Standard EEG 26 experienced power utility line men	50 Hz exposure during work-day average exposure 23 μ T one day live, one day sham	No changes in alpha EEG, nor evidence of EEG abnormalities.	Intervention study, not laboratory.	Gamberale et al., 1989

Table 34. Continued

<p>Standard EEG (10-20 system): C_{3,4}; P_{3,4}; O_{1,2}; FFT at 1-18.5 Hz in 0.5 Hz steps 3 female, 11 male volunteers</p>	<p>60 Hz 25 or 50 μT 2 s on, 8 s off, first 2 s used as control</p>	<p>No systematic effects for frequency bands and activity-power intensities. In 50 % of volunteers diminished EEG power was observed as a response to the field.</p>	<p>Bell et al., 1991</p>
<p>Standard EEG: C_{3,4}; P_{3,4}; O_{1,2}; FFT at 1-18.5 Hz in 0.5 Hz steps 10 healthy volunteers and 10 neu- rological patients</p>	<p>60 Hz B_{DC}: 78 μT, B_{AC}: 78 μT, sin- gle and combined 2 s on, 5 s off, first 2 s used as control</p>	<p>19 out of 20 persons responded to the fields: overall 35% to B_{DC}; 70% of the patients and 80% of the volun- teers to B_{AC}, response to B_{AC} was not different from the responses to the combination B_{AC}+ B_{DC}. Field- induced increase and decrease of brain activity, no systematic changes were observed for the hemispheres or activity loci.</p>	<p>Bell et al., 1992</p>
<p>Standard EEG spectral analysis 6 female and 8 male volunteers</p>	<p>45 Hz 1.26 mT 1s on, 1s off cycle over 15 min, one exposure and one control session</p>	<p>Significant increase of the power val- ues of alpha and beta bands after exposure, no changes in delta- and theta-bands.</p>	<p>Lyskov et al., 1993a</p>
<p>Standard EEG spectral analysis. before and after exposure 11 female and 9 male volunteers</p>	<p>45 Hz 1.26 mT 10 persons: 1 h continuous field, 10 persons: 1s on/off intermittent field for 1 h One exposure and one con- trol session</p>	<p>Several statistically significant changes: increase of alpha activity during intermittent exposure and decrease of delta activity. Increase of beta waves in frontal but not in occip- ital derivations.</p>	<p>Lyskov et al., 1993b</p>

Table 34. Continued

During exposure to magnetic fields at higher frequencies	
Standard EEG, F _{3,4} , P _{3,4} , O _{1,2} , tradi- tional frequency bands 0.1 - 30 Hz, psychological parameters and questionnaires 26 female and 26 male volunteers	Spherics simulation: 10 kHz 500 µs duration, random intervals between 50 and 150 ms 38 A m ⁻¹ peak value electric field shielded exposure 10 min and control session Significant reduction of the power only in the alpha frequency band (8- 13 Hz) in parietal and occipital deri- vations, when analysing sub-groups only in 10 - 10.75 Hz. P / O record- ings show significant reductions in the voltage power. Factors such as physical con- dition and neurotics were con- sidered as mediators of spherics effectiveness.
Evoked potentials after exposure to EMF	
Visual evoked potentials 100 subjects	5 - 50 Hz pulsed magnetic field up to 100 mT Phase reversal of components of the visual evoked potential at 60 mT. Sily, 1984; 1985; 1986
Auditory evoked potentials 6 female and 8 male volunteers	45 Hz 1.26 mT 1s on, 1 s off, 15 min one exposure and one control session N100 components were shorter, amplitudes were reduced. Lyskov et al., 1993a
Auditory evoked potentials 11 female and 9 male volunteers	45 Hz 1.26 mT 10 persons: 1 h continuous field 10 persons: 1 h 1 s on/off intermittent field one exposure and one control session Not affected. Lyskov et al., 1993b

Table 34. Continued

<p>Auditory, visual and somatosensory evoked potentials before, during and after exposure 36 (male and female) subjects</p>	<p>60 Hz 14.1 or 28.3 μT 45 min</p>	<p>No effect except a reduced amplitude of the somatosensory evoked potential in the lower exposure group.</p>	<p>Double-blind, counterbalanced study. Graham & Cook, 1999</p>
<p>Event-related potentials after exposure to EMF</p>			
<p>Electrodes C_z, $P_{3,4}$ for event-related potentials (P300), following auditory or visual stimuli in the Oddball task during exposure 30 male volunteers</p>	<p>60 Hz 9 kV m^{-1}, 20 μT 18 exposed and sham-exposed over four 6-h sessions, 12 exposed in all sessions</p>	<p>Amplitude of the auditory P300 was increased. Visual ERPs were not affected.</p>	<p>Effects on auditory ERP components were greatest soon after activation of field and after switching off at the end of the session. Cook et al., 1992</p>
<p>Event-related brain potentials (N200-P300) following auditory stimuli in the Oddball task during exposure 54 male subjects</p>	<p>3 matched groups of 18 men each, two 6-h sessions, exposure or sham, 60 Hz: a) 6 kV m^{-1}, 10 μT b) 9 kV m^{-1}, 20 μT c) 12 kV m^{-1}, 30 μT</p>	<p>Significant increases of P300 latency in group b), but decrease during sham exposure.</p>	<p>N200-P300 component complex altered in all groups, order of exposure did not affect results. Double blind, counterbalanced study. Graham et al., 1994</p>
<p>Event-related potentials during performance of the Oddball task, the dichotic listening task and the CNV paradigm after exposure 21 male subjects</p>	<p>50 Hz 100 μT 30 min, continuous or intermittent head only</p>	<p>Differences in ERP amplitudes were seen during the dichotic listening task.</p>	<p>Some effects were inconsistent between trials. Double-blind studies. Crasson et al., 1999</p>
<p>Event-related potentials during performance of the Oddball task, the dichotic listening task and the CNV paradigm after exposure 18 male subjects</p>	<p>50 Hz 100 μT 30 min, continuous or intermittent head only</p>	<p>No effects in ERP amplitudes were seen during the dichotic listening task or in other measures of performance.</p>	<p>Replication and extension of above study by the same group. Crasson & Legros, 2005</p>

a C, F, O & P represent standard EEG recording electrode positions; FFT = Fast Fourier Transform.

5.2.5 Sleep

Sleep is a complex biological process controlled by the central nervous system and is necessary for general health and well-being. The possibility that EMFs may exert a detrimental effect on sleep has been examined in two studies. Using the EEG to assess sleep parameters, Åkerstedt et al. (1999) reported that continuous exposure of healthy volunteers to 50 Hz at 1 μ T at night caused disturbances in sleep. In this study, total sleep time, sleep efficiency, slow-wave sleep (stage III and IV), and slow-wave activity were significantly reduced by exposure, as was subjective depth of sleep. Graham & Cook (1999) reported that intermittent, but not continuous, exposure to 60 Hz, 28 μ T magnetic fields at night resulted in less total sleep time, reduced sleep efficiency, increased time in stage II sleep, decreased time in rapid eye movement (REM) sleep and increased latency to first REM period. Consistent with a pattern of poor and broken sleep, volunteers exposed to the intermittent field also reported sleeping less well and feeling less rested in the morning.

A comparison between these two studies is made difficult because of the differences in the exposure levels used, 1 μ T (Åkerstedt et al., 1999) vs. 28 μ T (Graham & Cook, 1999) and also of other differences in the design. As to the results, in the Åkerstedt study, results were apparently obtained by low-level continuous exposure, whereas the Graham study failed to elicit such results by continuous exposure, but did produce similar results with intermittent exposures. Further studies with similar designs are needed before any conclusions can be drawn.

A summary of studies on brain electrical activity during sleep is given in Table 35.

Table 35. Brain electrical activity during sleep

Test	Exposure	Response	Comments	Authors
Sleep EEGs, conventional recordings 8 female and 10 male healthy volunteers	50 Hz 1 μ T one night (23:00-07:00) with field on, one night with field off	Significantly reduced slow wave activity and slow wave sleep. Also tendency for reduced total sleep time, sleep efficiency, REM sleep (not statistically significant).	Absolute values were within the normal variability; the observed changes are far from clinical significance. Blind study, balanced design.	Åkerstedt et al., 1999
Sleep EEG, 3 nights (23:00-07:00), C ₂ , C ₄ , O ₂ 24 male volunteers	60 Hz 28.3 μ T, circularly polarised 8 sham-exposed controls, 7 subjects exposed to continuous fields, 9 to intermittent 1 h on, 1 h off, 15 s on/off cycle	Intermittent exposure to magnetic fields produced significant disturbances in nocturnal sleep EEGs in 6 of 9 persons: decreased sleep efficiency, altered sleep architecture, suppression of REM sleep, lower well-feeling of several subjects in the morning.	No effect was seen during continuous field exposure relative to sham-exposed controls. Double-blind, counter-balanced study.	Graham & Cook, 1999

5.2.6 Cognitive effects

Despite the potential importance of field-induced effects on attention, vigilance, memory and other information processing functions, relatively few studies have looked for evidence of changes in cognitive ability during or after exposure to low frequency EMFs. These have been reviewed by NIEHS (1998), Cook, Thomas & Prato (2002), Bailey (2001), Crasson (2003) and ICNIRP (2003). While few field-dependent changes have been observed, it is important to consider that this type of study may be particularly susceptible to various environmental and individual factors which may increase the variance of the experimental endpoint and decrease the power to detect a small effect. This may be particularly important, since any field-dependent effects are likely to be small with fields at environmental levels (Sienkiewicz et al., 1993; Whittington, Podd & Rapley, 1996).

The effects of acute exposure to magnetic fields on simple and choice reaction time have been investigated in several recent studies using a wide range of magnetic flux densities (20 μ T – 1.26 mT) and experimental conditions. Some studies did not find any field-dependent effects (Gamberale et al., 1989; Kurokawa et al., 2003b; Lyskov et al., 1993b; Lyskov et al., 1993a; Podd et al., 2002; Podd et al., 1995), although modest effects on speed (Crasson et al., 1999; Graham et al., 1994; Whittington, Podd & Rapley, 1996) and accuracy during task performance (Cook et al., 1992; Kazantzis, Podd & Whittington, 1998; Preece, Wesnes & Iwi, 1998) have been reported. However, Crasson & Legros (2005) were unable to replicate these observations. These data also suggest that effects may depend on the difficulty of the task (Kazantzis, Podd & Whittington, 1998; Whittington, Podd & Rapley, 1996) and that exposure may attenuate the usual improvement seen with practice in reaction time (Lyskov et al., 1993b; Lyskov et al., 1993a; Stollery, 1986)

A few studies have reported subtle field-dependent changes in other cognitive functions, including memory and attention. Using a battery of neuropsychological tests, Preece, Wesnes & Iwi (1998) found that exposure to a 50 Hz magnetic field at 0.6 mT decreased accuracy in the performance of numerical working memory task and decreased sensitivity of the performance in a word recognition task. Similarly Keetley et al. (2001) investigated the effects of exposure to 28 μ T, 50 Hz fields using a series of cognitive tests. A significant decrease in performance was seen with one working memory task (the trail-making test, part B) that involves visual-motor tracking and information processing within the prefrontal and parietal areas of the cortex. Podd et al. (2002) reported delayed deficits in the performance of a recognition memory task following exposure to a 50 Hz field at 100 μ T. Trimmel & Schweiger (1998) investigated the effects of acute exposure to 50 Hz magnetic fields at 1 mT. The fields were produced using a power transformer, and volunteers were exposed in the presence of a 45 dB sound pressure level noise. Compared with a no-field, no-noise condition and noise alone (generated using a tape recording) significant reductions in visual attention, perception and verbal memory performance were observed during

Table 36. Cognitive effects

Test	Exposure	Response	Comments	Authors
Reaction time, vigilance, memory and perception speed tested before and after each day 26 experienced power utility linemen.	50 Hz exposure during workday average exposure 23 μ T one day live, one day sham	No difference in performance between exposed and non-exposed days.	Intervention study, not laboratory.	Gamberale et al., 1989
Reaction time (RT) and target-deletion test (TDT) 6 female and 8 male volunteers	45 Hz 1.26 mT 1 s on, 1 s off cycle, 15 min one exposure and one control session	No significant differences for RT, TDT not affected.		Lyskov et al., 1993a
Reaction time (RT) 11 female and 9 male volunteers	45 Hz 1.26 mT 10 persons: 1 h continuous field 10 persons: 1 hour 1 s on/off intermittent field one exposure and one control session	RT not directly affected.	Learning to perform the RT test (decrease of RT in repeated trials) affected by exposure .	Lyskov et al., 1993b
Reaction time to light flashed at variable intervals during exposure 12 subjects (expt 1) and 24 subjects (expt 2), male and female	Experiment 1: 10.1 or 0.2 Hz 1.1 mT 300 s Experiment 2: 0.2 or 43 Hz 1.8 mT 300 s	No effects found.	Experiment 2 designed to test for possible parametric resonance theory. Double blind studies.	Podd et al., 1995
Reaction time, accuracy and memory recognition	60 Hz 100 μ T 1 s on, 1 s off for 11 min	Effect on memory, not on reaction time or accuracy.	Results different from previous studies (Whittington et al., 1996)	Podd et al., 2002

Table 36. Continued

Reaction time, accuracy, time perception and visual perception 12 male and 8 female subjects	50 Hz 22 μT circularly polarised with harmonics and repetitive transients up to 100 μT 55 min	No effects.	Kurokawa et al., 2003b
Reaction time (RT), attention, differential reinforcement of low response rate (DRL) 54 male volunteers	3 matched groups of 18 men each, two 6-h sessions, exposure or sham, 60 Hz: a) 6 kV m^{-1} , 10 μT b) 9 kV m^{-1} , 20 μT c) 12 kV m^{-1} , 30 μT	Slower reaction time in Odd-ball task and lower accuracy of DRL in group a) only.	Graham et al., 1994
A visual duration-discrimination task with 3 levels of difficulty 100 male and female subjects	50 Hz 100 μT intermittent 9 min	Decreased reaction time for the hardest level of performance.	Whittington, Podd & Rapley, 1996
Rey Auditory Verbal Learning test (with delayed recall) and Digit Span Task 21 male subjects.	50 Hz 100 μT continuous or intermittent 30 min head only	No effects (reported in discussion).	Crasson et al., 1999
Choice serial reaction time task, time estimation task, interval production task, vigilance task, digit span memory task and Wilkinson Addition task during exposure 54 male subjects	60 Hz 9 kV m^{-1} and 20 μT 2 x 3 h / day for 4 days	Fewer errors in choice reaction time task. No effects on reaction time, memory or vigilance.	Cook et al., 1992

Table 36. Continued

<p>A visual duration-discrimination task with 3 levels of difficulty. 40 male and 59 female subjects</p>	<p>50 Hz 100 μT intermittent 7.9 min</p>	<p>Improved accuracy for the hardest level of performance.</p>	<p>A relaxed significance level (0.3) was used. Double-blind, counter-balanced study.</p>	<p>Kazantzis, Podd & Whittington, 1998</p>
<p>Immediate word recall, reaction time, digit vigilance task, choice reaction time, spatial working memory, numeric working memory, delayed word recall and recognition and picture recognition during exposure. 16 (male and female) subjects</p>	<p>50 Hz or static magnetic fields at 0.6 mT applied to the head. Duration not specified. Current density in head estimated as 2–6 mA m⁻²</p>	<p>Reduced accuracy of word and number recall and performance of choice reaction time task.</p>	<p>Randomised blind cross-over design.</p>	<p>Preece, Wesnes & Iwi, 1998</p>
<p>Duration Discrimination Task and Stroop Colour Word test. 18 male subjects</p>	<p>50 Hz 100 μT continuous or intermittent 30 min head only</p>	<p>No effect on reaction time and performance accuracy.</p>	<p>Double blind with counter-balanced exposure order.</p>	<p>Crasson & Legros, 2005</p>
<p>Syntactic and semantic verbal reasoning tasks, 5-choice serial reaction time task, and visual search tasks during exposure. 76 male subjects</p>	<p>50 Hz current 500 μA directly applied to head and shoulders 5.5 h / day for 2 days</p>	<p>Increased latency in syntactic reasoning task.</p>	<p>Possible differences between groups. Double-blind procedures with cross over design.</p>	<p>Stollery, 1986; Stollery 1987</p>
<p>Rey Auditory Verbal Learning test; Digit Span Memory Task; Digit Symbol Substitution test; Speed of Comprehension Test and Trail Making Test. 30 subjects, both sexes</p>	<p>50 Hz 28 μT 50 min Test verbal and written tests administered 20 min from exposure onset</p>	<p>Most results indicated no effect, but data suggestive of detrimental effect on short-term learning and executive functioning.</p>	<p>Double-blind cross-over design.</p>	<p>Keetley et al., 2001</p>
<p>Visual discrimination, perception, verbal memory and mood and symptom checklist. 66 (male and female) subjects</p>	<p>50 Hz 1 mT 45dB noise compared to noise alone</p>	<p>Significant reduction in visual attention, perception and verbal memory performance.</p>	<p>Double blind studies.</p>	<p>Trimmel & Schweiger, 1998</p>

field exposure. The presence of the noise during exposure, however, complicates interpretation of this study.

Generally, while electrophysiological considerations suggest that the central nervous system is potentially susceptible to induced electric fields; cognitive studies have not revealed any clear, unambiguous finding. There is a need for a harmonisation of methodological procedures used in different laboratories, and for dose-response relationships to be investigated. The studies on various cognitive effects from ELF field exposure are summarized in Table 36.

5.2.7 Hypersensitivity

It has been suggested that some individuals display increased sensitivity to levels of EMFs well below recommended restrictions on exposure. People self-reporting hypersensitivity may experience a wide range of severe and debilitating symptoms, including sleep disturbances, general fatigue, difficulty in concentrating, dizziness, and eyestrain. In extreme forms, everyday living may become problematical. A number of skin problems such as eczema and sensations of itching and burning have also been reported, especially on the face, and, although there may be no specific symptom profile (see Hillert et al., 2002), increased sensitivity to chemical and other factors often occurs (Levallois et al., 2002). The responses to EMFs are reported to occur at field strengths orders of magnitude below those required for conventional perception of the field (Silny, 1999). These data have been reviewed by Bergqvist & Vogel (1997) and more recently by Levallois (2002), ICNIRP (2003) and Rubin et al. (2005).

In contrast to anecdotal reports, the evidence from double-blind provocation studies (Andersson et al., 1996; Flodin, Seneby & Tegenfeldt, 2000; Lonne-Rahm et al., 2000; Lyskov, Sandström & Hansson Mild, 2001b; Swanbeck & Bleeker, 1989) indicate that neither healthy volunteers nor self-reporting hypersensitive individuals can reliably distinguish field exposure from sham-exposure. In addition, subjective symptoms and circulating levels of stress-related hormones and inflammatory mediators could not be related to field exposure. Similar results were reported in a survey of office workers (Arnetz, 1997). In studies reported by Keisu (1996) and by Toomingas (1996), the outcome of tests on an individual was used therapeutically in the medical handling of the patient. In none of these series was there any reproducible association between exposure and symptoms. Further test series have been performed in Sweden, the UK and in Germany, including an unsuccessful repetition of the Rea et al. (1991) study (see below), but these have not been published in a peer reviewed form. For a review, see Bergqvist & Vogel (1997). These results are consistent with the view that hypersensitivity to EMFs is a psychosomatic syndrome, suggested by Gothe, Odoni & Nilsson (1995).

Not all studies dismiss the possibility of EMF hypersensitivity, however. Two studies have reported weak positive field discrimination (Mueller, Krueger & Schierz, 2002; Rea et al., 1991) and another two studies

reported subtle differences in heart rate, visual evoked potentials, electroretinogram amplitudes and electrodermal activity between normal and hypersensitive volunteers (Lyskov, Sandström & Hansson Mild, 2001a; Sandström et al., 1997). The study by Rea et al. (1991) has, however, been criticised on several methodological grounds (ICNIRP, 2003): the selection of individuals, the exposure situation and whether the test was blind or not. There is some morphological evidence to suggest that the numbers and distribution of mast cells in the dermis of the skin on the face may be increased in individuals displaying hypersensitive reactions (Gangi & Johansson, 2000; Johansson et al., 1994; Johansson, Hilliges & Han, 1996). Increased responsiveness was attributed to changes in the expression of histamine and somatostatin and other inflammatory peptides. Similar effects in the dermis have also been reported following provocation tests to VDU-type fields in normal, healthy volunteers (Johansson et al., 2001).

EMF hypersensitivity was addressed by the World Health Organization (WHO) at a workshop held in Prague in October 2004 (WHO, 2005). It was proposed that this hypersensitivity, which has multiple recurrent symptoms and is associated with diverse environmental factors tolerated by the majority of people, should be termed “idiopathic environmental intolerance (IEI) with attribution to EMF”. The workshop concluded that IEI incorporates a number of disorders sharing similar nonspecific symptoms that adversely affect people and cause disruptions in their occupational, social, and personal functioning. These symptoms are not explained by any known medical, psychiatric or psychological disorder, and the term IEI has no medical diagnostic value. IEI individuals cannot detect EMF exposure any more accurately than non-IEI individuals, and well-controlled and conducted double-blind studies have consistently shown that their symptoms are not related to EMF exposure *per se*. A summary of hypersensitivity studies is given in Table 37.

5.2.8 Mood and alertness

The possible impact of EMFs on mood and arousal has also been assessed in double-blind studies in which volunteers completed mood checklists before and after exposure. No field-dependent effects have been reported using a range of field conditions (Cook et al., 1992; Crasson et al., 1999; Crasson & Legros, 2005; Graham et al., 1994). However, in contrast Stollery (1986) reported decreased arousal in one of two participating groups of subjects when mild (500 μ A) 50 Hz electric current was passed through the head, upper arms, and feet. This was done to simulate the internal electric fields generated by exposure to an external electric field strength of 36 kV m^{-1} . Also Stevens (2001) reported that exposure to a 20 Hz, 50 μ T magnetic field increased positive affective responses displayed to visual stimuli compared with sham-exposure. Arousal, as measured by skin conductance, gave variable results. Table 38 summarizes the studies on effects of ELF field exposure on mood and alertness.

Table 37. Hypersensitivity

Test	Exposure	Response	Comments	Authors
Skin symptoms 30 patients	VDU: static electric field 0,2 and 30 kV m ⁻¹ ELF magnetic field: 50 and 800 nT dB/dt: 23 and 335 mT s ⁻¹	No response related to exposure.	Heat, reddening, itching, stinging, oedema in exposed and sham exposed situations.	Swanbeck & Bleeker, 1989
Perception and symptoms 17 patients	Fields from VDU, pre-tested as causing symptoms in open prov- ocation prior to double blind ses- sions. In shielded laboratory.	16 individuals failed to detect (guess) presence of the fields, symptoms were related to guesses, not to the fields.		Andersson et al., 1996
Perception and symptoms 15 patients and 26 controls	Fields from VDUs and other objects. Subjects tested in their normal home environment, using a variety of devices.	15 individuals failed to detect pres- ence of the fields, symptoms were not related to the fields.		Flodin, Seneby & Teegenfeldt, 2000
Provocation study of stress hormone lev- els, skin biopsies and facial skin sensa- tions 24 patients and 12 controls	VDUs: 5 Hz–2 kHz: 12 V m ⁻¹ 198 nT 2 kHz–400 kHz: 10 V m ⁻¹ 18 nT 30 min / week for 4 weeks	None of the test parameters differed between exposed and sham exposed conditions, but skin symp- toms appeared in the open provoca- tion tests.	Double-blind study.	Lonne- Rahm et al., 2000

Table 37. Continued

<p>EEG, visual evoked potentials, electrodermal activity, ECG and blood pressure. 20 patients and 20 control subjects</p>	<p>60 Hz intermittent 15 sec on/off cycle at 10 T magnetic field exposure and sham exposure applied randomly during a 40 min period</p>	<p>Magnetic field exposure had no effect on any of the parameters examined.</p>	<p>Patients reporting EHS differed from control subjects in baseline values.</p>	<p>Lyskov, Sandström & Hansson Mild, 2001b</p>
<p>General health survey of 133 office employees. Exploratory study of skin disease, office ergonomics and air quality in 3 office workers reporting EMF hypersensitivity compared to 5 controls</p>	<p>VDUs: 5 Hz–2 kHz ~ 10–15 V m⁻¹ 100–150 nT</p>	<p>10% (13) of general staff reported EMF hypersensitivity; no differences in skin symptoms between EMF hypersensitives and controls in exploratory study.</p>	<p>The authors were not able to attribute EMF hypersensitivity to any particular environmental factor.</p>	<p>Arnetz, 1997</p>
<p>Perception and symptoms in one female patient 10 double-blind tests</p>	<p>Fields from VDU</p>	<p>The discomfort the patient experienced had no correlation to whether or not the monitor actually was on.</p>	<p>The patient reconsidered her own perception of the illness, and in time the symptoms receded completely.</p>	<p>Keisu, 1996</p>
<p>Perception and symptoms in one patient</p>	<p>50 Hz 34 or 100 µT 1 or 10 s repeated</p>	<p>Positive response when humming of the coils audible, disappeared when “camouflaged” by masking noise.</p>	<p>.</p>	<p>Toomingas, 1996</p>
<p>Symptoms and physiological reactions 100 subjects</p>	<p>Low level magnetic fields (< 1 µT) at varying frequencies (0.1 Hz–5 MHz), in shielded laboratory.</p>	<p>16 out of 100 individuals reacted repeatedly to fields by several parameters (symptoms, pupil diameter changes etc.).</p>	<p>Not sure whether fully blind study.</p>	<p>Rea et al., 1991</p>

Table 37. Continued

EMF perception 49 subjects with EHS and 14 controls	50 Hz 100 V m ⁻¹ 6 µT randomly presented as 2 min block of exposure / sham expo- sure	Perception by 7 subjects, but no dif- ference in perception between sub- jects with or without self-reported EHS.	Mueller, Krueger & Schierz, 2002
Electrocardiogram, visual evoked poten- tials (VEP) and electroretinograms 10 subjects reporting EMF hypersensitiv- ity and 10 controls	Exposure to flickering light at between 25 and 75 flashes per second. No EMF exposure	Higher VEP amplitudes in EMF hypersensitive patients.	Sand-ström et al., 1997 Differences between mean age of patients and controls (37 vs 47 year).
Self-reported symptoms, blood pressure, No EMF exposure heart rate, (skin) electrodermal activity, EEGs and visual evoked potentials 10 subjects reporting hypersensitivity and 10 controls	No EMF exposure	Differences between patients and controls regarding self-reported symptoms, heart rate, electrical activity of the skin, and visual evoked potential amplitudes.	Lyskov, Sand-ström & Hansson & Mild, 2001a
Immuno-fluorescent staining of mast cells from skin biopsies 13 healthy subjects	VDU (TV or PC) exposure for 2 or 4 h	Increase in number of mast cells in papillary and reticular dermis in 5 subjects.	Johansson et al., 2001

Table 38. Mood and alertness

Test	Exposure	Response	Comments	Authors
Mood Adjective Checklist before and after exposure; Stanford Sleepiness Scale before during and after exposure 30 male subjects	60 Hz 9 kV m ⁻¹ and 20 μT 2 x 3 h / day for 4 days	No effect.	Double-blind, counterbalanced study.	Cook et al., 1992
Alertness Rating Scale, Mood Adjective Checklist before and after exposure 54 male subjects	60 Hz 6 kV m ⁻¹ and 10 μT 9 kV m ⁻¹ and 20 μT 12 kV m ⁻¹ and 30 μT 2 x 3 h / day for 4 days	No effect.	Double-blind, counterbalanced study.	Graham et al., 1994
State-Trait Anxiety Inventory, Profile of Mood States, Visual Analogue Scales of mood and vigilance before and after exposure 21 male subjects	50 Hz 100 μT 30 min, continuous or intermittent Head only exposures	No effect.	Double-blind studies.	Crasson et al., 1999
State-Trait Anxiety Inventory, Profile of Mood States, Visual Analogue Scales of mood 18 subjects	50 Hz 100 μT 30 min, continuous or intermittent Head only exposures.	No effect.	Replicate and extension of Crasson et al., 1999	Crasson & Legros, 2005
Mood checklist before and after exposure 76 male subjects	50 Hz current; 500 μA directly applied to head and shoulders 5.5 h / day for 2 days	Decreased arousal in one of two groups; no effect on mood.	Possible differences between groups. Double-blind procedures with cross-over design.	Stollery, 1986
Skin conductance and self-assessed arousal and affective content 20 male, 9 female subjects	20 Hz 50 μT 5 s with concurrent visual stimulus on image content.	No effect on skin conductance and arousal but positive effect of exposure on image content.	Subject blind as to exposure status.	Stevens, 2001

Table 39. Depression

Study base and subject identification	Definition and estimation of exposure	Study design and numbers	RR (95% CI)	Authors
Persons who lived near a 132 kV line and persons who lived 3 miles away Questionnaire asking about depression	Distance between home and overhead line	Cross-sectional 132 near line, 94 away from line, 1 with depression	Strong association of depression to proximity to overhead power line.	Dowson et al., 1988
Persons discharged with depression from hospital (England) and controls from electoral list	Measurements at front doors. Average for case and control groups compared	Case-control 359 persons discharged with depressive illness	Average measurement cases: 0.23 μ T; controls 0.21 μ T.	Perry, Pearl & Binns, 1989
Residents in 8 towns along a transmission line right-of-way (ROW) in the US, 1987. A sample was interviewed. Depressive symptoms obtained by CES-D ^a scale. Cut-off for depression was median of score.	Distance from power-line: near vs far Near: properties abutting ROW or towers visible	Cross-sectional 382 persons interviewed	2.8 (1.6–5.1)	Poole et al., 1993
Male veterans who served in the US army first time 1965-71. Two diagnostic inventories used: the Diagnostic Interview Schedule and the Minnesota Personality Inventory. Life time depression used for this report	Present job identified in interview together with duration Electrical worker	Cross-sectional 183 electrical workers (13 with life-time depression) 3861 non-electrical workers	1.0 (0.5–1.7)	Savitz & Ananth, 1994
Population of neighborhood near a transmission line in Orange County, CA, USA, 1992. A sample of homes near a power line and one block away from the power line. Depressive symptoms identified through questionnaire CES-D* scale	EMDEX measurements at the front door. Average for homes on easement: 0.486 μ T and one block away 0.068 μ T	Cross-sectional 152 women	0.9 (0.5–1.9)	McMahon, Ericson & Meyer, 1994
Finnish twins who had answered the Beck Depression Inventory (BDI) in 1990	Residential magnetic field estimated from power lines near the homes	Cross-sectional 12063 persons	BDI scores not related to exposure.	Verkasalo et al., 1997

^a CES-D scale: Centre for Epidemiologic Studies-Depression scale.

5.3 Epidemiological studies

With regard to neurobehavioural effects, epidemiological studies have focussed on depression and suicide. Studies of an association between EMF exposure and neurodegeneration are covered in Chapter 6.

5.3.1 Depression

Two early studies relating ELF EMF exposure to depression (Dowson et al., 1988; Perry, Pearl & Binns, 1989) are difficult to interpret because of methodological limitations to the procedures for selection of study subjects, because they did not use validated scales for identification of depressive symptoms (ICNIRP, 2003). Moreover, Perry, Pearl & Binns (1989) also reported unusually high average EMF levels that remain unexplained.

More recent studies used validated depression scales. One of these studies showed a clear association between proximity to power lines and depression (Poole et al., 1993), whereas three more recent studies (McMahan, Ericson & Meyer, 1994; Savitz & Ananth, 1994; Verkasalo et al., 1997) provided little evidence for such an association. The study by Poole et al. (1993) is well designed: it compares subjects on properties abutting a power line right-of-way to subjects further away, and the results appear internally consistent. The investigators report a relative risk of 2.8 (95% CI: 1.6–5.1). McMahan, Ericson & Meyer (1994) employed a similar design and measurements to confirm that the homes close to the line have considerably higher EMF levels than those further away. This study also appears valid but yields a relative risk of 0.9 (95% CI: 0.5–1.9). McMahan, Ericson & Meyer (1994) offer a number of possible explanations for the lack of consistency between these two studies but none of the explanations is convincing (ICNIRP, 2003).

Overall, ICNIRP (2003) conclude that the literature on depressive symptoms and EMF exposure is difficult to interpret because the findings are not consistent. This complexity cannot easily be resolved by suggesting that one type of result can be confined to a group of studies with methodological problems or some other limitation.

A summary of studies on the effects of ELF field exposure on depression is given in Table 39.

5.3.2 Suicide

An early case control study carried out in England (Perry et al., 1981; Reichmanis et al., 1979) found significantly higher EMFs in case homes than control homes. However, ICNIRP (2003) considers the study methodologically limited both for the way subjects were selected and for the statistical analysis employed. Subsequent studies have used a range of different approaches to assess exposure, varying from crude techniques based on distance between home and power lines, or on job titles, to more sophisticated approaches based on detailed information about cohorts of utility workers (Baris et al., 1996a; Baris et al., 1996b; Baris & Armstrong, 1990; Johansen & Olsen, 1998a; McDowall, 1986; van Wijngaarden et al., 2000). Only the latter study provides some support for the original findings,

although McKinlay et al. (2004) note that the findings were variable. The two more recent occupational study, based on job titles recorded on death certificates, report contradictory results (Järholm & Stenberg, 2002; van Wijngaarden, 2003). However, the exposure assessments in these studies were not as detailed as in the previous occupational studies listed.

In a review of ICNIRP (2003) it was observed that, despite methodological limitations, particularly relating to the earlier studies, the detailed study by Van Wijngaarden et al. (2000) suggested that an excess risk for suicide might exist.

A summary of the ELF suicide studies is given in Table 40.

Tabel 40. Suicide

Study base and subject identification	Definition and estimation of exposure	Study design and numbers	RR (95% CI)	Authors
Suicide cases and controls in England	Estimates of residential exposure from power lines Measurements at the homes of subjects	Case-control 589 suicide cases	Higher estimated and measured fields at case homes.	Reichmanis et al., 1979 Perry et al., 1981
Male employees in Danish utility companies observed during 1974–93 Cases: deaths from suicide in mortality registry	Employment records and job exposure matrix estimated average exposure level Medium and high exposure	SMR ^a 21 236 males in cohort; exposed cases	1.4 (non-significant)	Johansen & Olsen, 1998a
Persons resident in the vicinity of transmission facilities, in specified areas in the UK, at the time of 1971 Census	Home within 50 meters from substation or 30 meters from overhead line	SMR ^a 8 cases	0.75 (non-significant)	McDowall, 1986
Deaths in England and Wales during 1970–72 and 1979–83	Job titles on death certificates Electrical workers in aggregate as well as specific jobs	PMR ^b 495 cases in electrical occupations	No increase for electrical workers.	Baris & Armstrong, 1990
Male utility workers, Quebec, Canada, 1970–88 Cases: deaths from suicide in mortality registry Controls: 1% random sample from the cohort	Job exposure matrix based on Positron measurements was created. E- and B-and pulsed fields from average and geometric means and from cumulative and current exposure	Case-control 49 cases 215 controls	No evidence for effects of magnetic fields. Some support for some electric field indices.	Baris et al., 1996a; 1996b

Table 40. Continued

Male electric utility workers	Jobs and indices of cumulative exposure based on measurement survey	Case-control 36 cases 5348 controls	Electrician: 2.18 (1.25–3.80) Line worker: 1.59 (1.18–2.14)	van Wijngaarden et al., 2000
Swedish male electricians in construction industry Swedish death register	Job exposure matrix	Cohort study - 33 719 electricians (0.31 μ T) - 72 653 glass and woodworkers (0.27–0.29 μ T) - general population	SMR Electricians: 0.58 (0.47–0.71) Glass and woodworkers: 0.81 (0.72–0.91)	Järholm & Stenberg, 2002
United States death certificate files for the years 1991 and 1992	Occupation code; usual occupation and industry on the death certificates	Case-control 11 707 cases 132 771 controls	1.3 (1.2–1.4)	van Wijngaarden, 2003

^a SMR: Standardized Mortality Ratio.

^b PMR: Proportional Mortality Ratio.

5.4 Animal studies

Various animal models have been used to investigate possible field-induced effects on brain function and behaviour. These include effects on neurotransmitter levels, electrical activity, field detection and the performance of learned tasks. Overall, a few field-dependent responses have been tentatively identified but even the most consistent effects appear small in magnitude and transient in nature.

5.4.1 Perception and field detection

It is known that animals can detect the presence of low frequency electric fields, possibly as a result of surface charge effects (Weigel & Lundstrom, 1987). Using appropriate behavioural techniques, a number of studies using rats (Sagan et al., 1987; Stell, Sheppard & Adey, 1993; Stern et al., 1983; Stern & Laties, 1985; reviewed in ICNIRP, 2003; NIEHS, 1998; NRC, 1997) indicate that the threshold for field detection is about 3–13 kV m^{-1} . Detection thresholds are similar in a variety of other species, with thresholds reported at 5–15 kV m^{-1} in baboons (Orr, Rogers & Smith, 1995a), and 30–35 kV m^{-1} in miniature swine (Kaune et al., 1978).

Detection thresholds for magnetic fields in animals are less clear and show greater variability than those for electric fields (ICNIRP, 2003). Using a conditioned suppression paradigm, Smith, Clarke & Justesen (1994)

reported that rats were able to detect ELF magnetic fields as low as 200 μT , although the validity of this result has been questioned by Stern & Justesen (1995).

A summary of studies on perception and detection of fields is given in Table 41.

Table 41. Perception and field detection				
Endpoint	Exposure	Response	Comment	Authors
ELF electric fields				
Rats: operant behaviour Electric field acting as cue or discriminative stimulus	60 Hz up to 55 kV m^{-1} brief daily exposures	Threshold of between 3 and 10 kV m^{-1} .		Stern et al., 1983 Stern & Laties, 1985
Rats: operant behaviour Electric field acting as cue	60 Hz up to 27 kV m^{-1} brief daily exposures	Threshold of 8 or 13 kV m^{-1} depending on the test protocol.		Sagan et al., 1987
Rats: effect of air current on operant behaviour Electric field acting as cue	60 Hz up to 25 kV m^{-1} brief daily exposures	Threshold of 7.5 kV m^{-1} unaffected by wind-induced hair movement.	Detection below threshold increased; results difficult to interpret.	Stell, Sheppard & Adey, 1993
Baboons: operant behaviour Electric field acting as cue	60 Hz 4–50 kV m^{-1} brief daily exposures	Average threshold of 12 kV m^{-1} ; range of 5–15 kV m^{-1} .		Orr, Rogers & Smith, 1995a
Handford miniature swine: drinking behaviour (n=4) Electric fields acts as conditioned stimulus	60 Hz up to 55 kV m^{-1} brief (20 s) repeated exposures	Threshold of 30–35 kV m^{-1} .		Kaune et al., 1978
ELF magnetic fields				
Rats: conditioned suppression of operant behaviour	7, 16, 30, 60 and 65 Hz 200 μT – 1.9 mT 1 h / day, 5 days / week, 5 weeks	All magnetic fields effective as cue for conditioned response suppression.	Temporal rather than magnetic field conditioning?	Smith, Clarke & Justesen, 1994; Stern, 1995

5.4.2 Arousal and aversion

Initial exposure to power-frequency electric fields in excess of detection thresholds may cause transient arousal and stress responses in rodents and non-human primates (Coelho, Easley & Rogers, 1991; Easley, Coelho & Rogers, 1991; Rosenberg et al., 1983; Rosenberg, Duffy & Sacher, 1981; reviewed in IARC, 2002; ICNIRP, 2003). These responses appear to habituate quickly following prolonged exposure. There is also some evidence that animals may avoid exposure to intense electric fields (e.g. Hjersén et al., 1980; 1982), and that such fields can elicit aversive behaviours following exposure to high field strengths in rats (Creim et al., 1984) and in non-human primates (Rogers, Orr & Smith, 1995; Stern & Laties, 1989). The results of the latter study indicated that electric fields at levels of up to 65 kV m^{-1} are not highly aversive to non-human primates.

Exposure of baboons to combined 60 Hz electric and magnetic fields at 6 kV m^{-1} and $50 \text{ }\mu\text{T}$ or at 30 kV m^{-1} and $100 \text{ }\mu\text{T}$ did not produce significant changes in social behaviour (Coelho, Rogers & Easley, 1995) previously seen to be affected by exposure to electric fields alone (Coelho, Easley & Rogers, 1991; Easley, Coelho & Rogers, 1991). While it is possible that the magnetic field may have modulated the electric field-induced responses, it was considered that some of the animals in the later experiment may have become desensitised by prior subthreshold electric field exposure.

Acute exposure to power frequency magnetic fields at up to 3 mT does not appear to induce aversive behaviour (Lovely et al., 1992). Such results suggest that the arousal responses observed using electric fields are not caused by field-induced internal electric fields, and may be attributed to body-surface interactions. One study reported that long-term, intermittent exposure to 50 Hz at 18 mT reduced behavioural responses (“irritability”) induced by tactile and somatosensory stimuli in rats (Trzeciak et al., 1993). Another study reported that exposure to specific combinations of static and low frequency fields affected exploratory behaviour in rats (Zhadin, Deryugina & Pisachenko, 1999). Exposure to conditions corresponding to the putative cyclotron resonance for calcium ions reduced this behaviour, and exposure to conditions for magnesium ions increased it.

Studies on arousal and aversion in experimental animals are summarized in Table 42.

Table 42. Arousal and aversion

Endpoint	Exposure	Response	Comment	Authors
Arousal and activity				
ELF electric fields				
Mice: arousal assessed by activity, oxygen consumption, carbon dioxide production during exposure	60 Hz 10, 25, 35, 50, 75 and 100 kV m ⁻¹ Four 1 h exposures at 1 h intervals	Increased arousal during the first exposure to fields of 50 kV m ⁻¹ and above; little effect during subsequent exposures.		Rosenberg et al., 1983; Rosenberg, Duffy & Sacher, 1981
Mice: exploratory activity in open arena after exposure	15, 30 and 50 Hz 50, 100, 400 V m ⁻¹ 30 min / day for 5 days	No effect.		Blackwell & Reed, 1985
Baboons: social behaviour in 8 adult males	60 Hz 30 kV m ⁻¹ 12 h / day, 7 days / week for 6 weeks	Initially, exposed animals showed passive affinity (e.g. huddling), tension and stereotypy (e.g. scratching).	Indicative of stress.	Coelho, Easley & Rogers, 1991
Baboons: social behaviour in 8 adult males	60 Hz 60 kV m ⁻¹ 12 h / day, 7 days / week for 6 weeks	Increased initial levels of passive affinity, tension and stereotypy.	Repeat of previous study using higher electric field strength.	Easley, Coelho & Rogers, 1991
ELF magnetic fields				
Rats: rearing, ambulatory and grooming behaviour in an open arena after exposure.	50 Hz 80 µT 4 h at beginning of light (quiet) period or dark (active) period	Increased rearing after exposure in quiet but not active period. No effects on ambulation or grooming.	Effect replicated in 2nd experiment. No sham exposed controls.	Rudolph et al., 1985

Table 42. Continued

Rats: irritability, exploratory (open field) activity and locomotion	50 Hz 18 mT 2 h / day for 20 days	Decrease in irritability, no effects on exploratory activity or locomotion.	Trzeciak et al., 1993
Rats: open field behaviour	DC fields of 50 or 500 μ T corresponding AC fields set for cyclotron resonance conditions for several ionic species	Reduced locomotor and exploratory behaviour during calcium ion resonance conditions; opposite effect for magnesium.	Zhadin, Deryugina & Pischchenko, 1999
ELF Electric and Magnetic Fields			
Baboons: social behaviour in 8 adult males	60 Hz 6 kV m ⁻¹ and 50 μ T 30 kV m ⁻¹ and 100 μ T 12 h / day, 7 days / week for 6 weeks	No effects on passive affinity, tension and stereotypy.	Coelho, Rogers & Easley, 1995
Avoidance and aversion			
ELF electric fields			
Rats: avoidance behaviour in a shuttlesbox (which has exposed and unexposed ends)	60 Hz 25–105 kV m ⁻¹ 45 min / week for 4 weeks or once for 23.5 h	Significant preference for shielded region above 90 kV m ⁻¹ (short exposure) or 75 kV m ⁻¹ (long exposure).	Hjeresen et al., 1980
Rats: taste aversion to electric field plus flavoured water	60 Hz 50, 101 or 196 kV m ⁻¹ (unperturbed fields) 20 min	No effect.	Creim et al., 1984
Rats: avoidance behaviour in a shuttlesbox	60 Hz 30 kV m ⁻¹ 20 h	Significant preference for shielded region.	Hjeresen et al., 1982
		Positive control with chemical inducer.	
		Follow on to chronic study.	

Table 42. Continued

Baboons: behavioural aversion through operant responses (lever press) to terminate exposure	60 Hz up to 65 kV m ⁻¹ during testing	Field perceived but did not act as negative (aversive) re-inforcer.	Rogers, Orr & Smith, 1995
Baboons: behavioural aversion through operant responses (lever press) to terminate exposure	60 Hz 90 or 100 kV m ⁻¹ brief exposures	Exposure did not induce lever pressing (field termination) behaviour.	Stern & Laties, 1989
ELF magnetic fields			
Rats: avoidance behaviour in a shuttlebox	60 Hz 3.03 mT 1 h	No effect.	Lovely et al., 1992

5.4.3 Brain electrical activity

A number of animal studies have investigated if acute exposure to low frequency electric and magnetic fields can affect brain electrical activity demonstrated in the EEG or as evoked potentials following presentation of a sensory stimulus (e.g. Blackwell, 1986; Dowman et al., 1989, reviewed by NIEHS, 1998; Sienkiewicz, Saunders & Kowalczyk, 1991). The results of these studies are somewhat mixed and difficult to interpret, but none suggests any obvious hazard (ICNIRP, 2003). Some of these studies may have been confounded by experimental design: for example, it has long been recognised that recording electrical potentials through electrodes attached to the skull is liable to produce artefacts in the presence of EMFs. Two more recent studies reported significant EEG changes in rabbits during magnetic field exposure (Bell et al., 1992) and in rats following magnetic field exposure (Lyskov et al., 1993c). However, the possibility of an artefact or of false positive results complicates interpretation of both studies (NIEHS, 1998). A summary of studies on brain electrical activity in experimental animals exposed to ELF fields is given in Table 43.

Table 43. Brain electrical activity

Endpoint	Exposure	Response	Comment	Authors
ELF electric fields				
Rats: CNS neuronal activity in anaesthetised animals during exposure	15, 30 and 50 Hz 100 V m ⁻¹ (peak-peak)	No overall effect on firing rate; some synchrony at 15 and 30 Hz.	Anaesthesia-depressed responsiveness.	Blackwell, 1986
ELF magnetic fields				
Rabbits: EEG recordings during exposure	5 Hz, 100 μT DC + 25 Hz, 64 μT 25 Hz, 1 μT	Increased EEG signal in response to 5 Hz.	Possibility of induction artefact.	Bell et al., 1992
Rats: EEG recordings from Sprague-Dawley rats before and after exposure	45 Hz 126 μT, intermittent 1.26 mT, 24 h exposure twice, 24 h apart	Dose-dependent increase in significant changes to EEG pattern following exposure.	Induced currents possibly increased due to permanent electrodes.	Lyskov et al., 1993c
Electric & magnetic fields				
Macaque monkeys: auditory, visual and somatosensory evoked potentials recorded during "field off" period.	60 Hz 3 kV m ⁻¹ and 10 μT 10 kV m ⁻¹ and 30 μT 30 kV m ⁻¹ and 90 μT 3 weeks	Most measures unaffected. Decreased amplitude of late components of somatosensory evoked potentials.		Dowman et al., 1989

5.4.4 Neurotransmitter function

A number of studies have investigated the potential of ELF fields to affect the levels of different neurotransmitters within various regions of the brain. Neurotransmitters are chemical substances released from nerve cells which enable the transmission of information to adjacent nerve cells equipped with appropriate receptors and may also have more widespread effects when released into the circulation. Different neurotransmitter systems are associated with different functions: the main groups are the cholinergic neurotransmitters such as acetylcholine, the biogenic amines comprising the catecholamines, including dopamine, norepinephrine (noradrenaline), epinephrine (adrenaline), and serotonin, the amino acid neurotransmitters such as glutamate and aspartate, and the peptide neurotransmitters such as the opioids. Most groups have important roles in brain function, the latter two almost exclusively so. Altered transmitter levels can be associated with functional changes but interpretation is usually difficult (NIEHS 1999).

These data have been most recently reviewed by ICNIRP (2003). Early studies (e.g. Vasquez et al., 1988; Zecca et al., 1991) reported effects of both acute and chronic exposure to intense electric fields on catecholamine and amino acid neurotransmitter levels in some parts of the brain, but values often stayed within the normal range. More recently, Margonato et al. (1995) reported that chronic exposure to 50 Hz magnetic fields at 5 μT had no effect on levels of norepinephrine, dopamine and its major metabolites, or 5-hydroxytryptamine or its major metabolite in the striatum, hypothalamus, hippocampus or cerebellum. However, in a companion study, Zecca et al. (1998) reported effects on norepinephrine levels in the pineal gland but not elsewhere in the brain following chronic exposure to combined electric and magnetic fields at either 1 kV m^{-1} and 5 μT or 5 kV m^{-1} and 100 μT . In addition, intensity-dependent changes were reported in the opioid receptor system in the frontal cortex, parietal cortex and hippocampus, but not in other brain areas investigated.

Other studies have also investigated field-dependent changes in opioid-related physiology in molluscs and in mammals. In a series of related experiments, Kavaliers, Prato and colleagues (e.g. Kavaliers & Ossenkopp, 1986a; Kavaliers & Ossenkopp, 1986b; Kavaliers, Ossenkopp & Hirst, 1984; Ossenkopp & Kavaliers, 1987) have indicated that various types of ELF magnetic fields may affect the endogenous opioid systems and modulate the response of both groups of animals to the analgesic effects of injected opiates such as morphine (reviewed by Kavaliers et al., 1994; Kavaliers & Ossenkopp, 1991). These responses are complex, and magnetic fields appear to have a differential effect on the functions of different opioid receptor subtypes. There is evidence that the mechanism for these effects may involve changes in calcium ion channel function in mice (Kavaliers et al., 1998) and in protein kinase C activity, nitric oxide (NO) release and NO synthase activity in the land snail *Cepaea nemoralis* (1998; Kavaliers, Ossenkopp & Tysdale, 1991). Further studies with land snails suggest that the field induced analgesic effects depend on the relative direction of the applied fields (Prato

et al., 1995) as well as the presence of light (1997; Prato, Kavaliers & Carson, 1996; 2000).

In another series of experiments, it was reported that the acute exposure of rats to a 60 Hz magnetic field at 0.75 mT decreased activity in the cholinergic pathways in the frontal cortex and hippocampus (Lai et al., 1993). These effects were blocked by naltrexone, but not by naloxone methiodide, which was taken as evidence that magnetic fields affected endogenous opioids only within the central nervous system. Further studies showed the changes in cholinergic activity appeared to be mediated by activation of endogenous opioids (Lai, Carino & Ushijima, 1998). There also appears to be some interaction between exposure duration and field intensity, such that longer exposures (3 hours) at lower intensity fields (0.05 mT) could induce changes in cholinergic activity similar to those induced by shorter exposure at higher intensity (Lai & Carino, 1999).

Overall, limited changes in neurotransmitter levels in different parts of the rodent brain have been reported. Although of less direct relevance to human health, similar results have been reported in the molluscan nervous system. The biological significance of the changes seen in mammals is difficult to assess without corroborative changes in brain function and behaviour. However, several studies suggest possible EMF effects on the opioid and cholinergic systems which can be modulated by appropriate antagonists and should be studied further. Studies on the effects of ELF fields on neurotransmitters and analgesia are summarized in Table 44.

5.4.5 Cognitive function

Early studies with macaque monkeys reported that exposure to ELF electric fields at well below detection thresholds may affect operant performance (IARC, 2002; ICNIRP, 2003). However, well-conducted studies using baboons found that exposure to 60 Hz electric fields at 30 and 60 kV m⁻¹ had no sustained effect on the performance of two operant schedules (1995b; Rogers et al., 1995a) although initial exposure may contribute towards producing a temporary interruption in responding.

Similarly, studies using 60 Hz electric and magnetic fields (Orr, Rogers & Smith, 1995b) indicated that combined exposure to 6 kV m⁻¹ and 50 µT or to 30 kV m⁻¹ and 100 µT had no effect on operant performance on a delayed match-to-sample task in baboons. This result is generally consistent with earlier results from other research groups using non-human primates (reviewed by ICNIRP, 2003; NIEHS, 1998; Sienkiewicz, Saunders & Kowalczyk, 1991). However, one study using rats (Salzinger et al., 1990) suggested exposure to 60 Hz fields of 30 kV m⁻¹ and 100 µT may exert subtle effects on performance that depend on the time of testing within the light-dark cycle.

Table 44. Neurotransmitters and analgesia

Endpoint	Exposure	Response	Comment	Authors
Neurotransmitters				
ELF electric field				
Rats: biogenic amine levels in striatum, hypothalamus and hippocampus	60 Hz 39 kV m ⁻¹ 20 h / day, 4 weeks	No effects in hippocampus; some changes in striatum and hypothalamus.		Vasquez et al., 1988
Rats: amino acid levels in striatum	50 Hz 25 and 100 kV m ⁻¹ 8–22 h / day, 5–7 days/ week for 320, 640, 1240, or 1408 h	General increase after 320 h exposure; decreased levels after longer periods.	Observed values within normal range. Three replicate experiments.	Zecca et al., 1991
ELF magnetic field				
Rats: central cholinergic systems in brain	60 Hz 0.5, 0.75, 1 mT 45 min	Reduced high-affinity choline uptake in frontal cortex and hippocampus.	Effect blocked by central but not peripheral opioid antagonists.	Lai et al., 1993
Rats: biogenic amine levels in regions of the brain	4 50 Hz 5 μT 22 h / day, 32 weeks	No effect.	Two replicate experiments.	Margonato et al., 1995
ELF Electric and Magnetic Fields				
Rats: neurotransmitter and receptor levels in brain and pineal	50 Hz 5 μT and 1 kV m ⁻¹ 100 μT and 5 kV m ⁻¹ 8 h / day, 5 days / week, 8 months	Increase in norepinephrine levels in the pineal gland; changes in the distribution of μ-opioid receptors in the brain.		Zecca et al., 1998

Table 44. Continued

Opioids and analgesia

ELF magnetic fields

Land snails: morphine-induced analgesia	60 Hz 100 mT 2 h	Exposure-induced reduction in analgesia.	Effect enhanced by PKC activators.	Kavaliers & Ossenkopp, 1991
Land snails: morphine-induced analgesia	10–240 Hz 0–547 μ T with parallel static magnetic field	Non-linear dose-response; frequency response relationships seen in analgesia reduction.	Results suggested direct effect of magnetic field.	Prato et al., 1995
Land snails: morphine-induced analgesia	60 Hz 141 μ T 15 min	Exposure-induced reduction in analgesia.	Effects enhanced by NO releasing agent, and reduced by NO synthase inhibitor.	Kavaliers et al., 1998
Land snails: morphine-induced analgesia	ELF magnetic fields consistent with the PRM for Ca^{2+} or K^{+} ions	Effects on morphine-induced analgesia consistent with PRM mechanism.	Effects dependent on the presence of light.	Prato, Kavaliers & Thomas, 2000
Mice: morphine-induced analgesia	0.5 Hz 150 μ T – 9 mT in mid-light-phase and mid dark phase 5–10 days	Reduction in the increased night-time latency to respond to hot-plate.	Exposure system comprised motor-driven, rotating horseshoe permanent magnets.	Kavaliers, Ossenkopp & Hirst, 1984
Mice: stress (restraint) induced analgesia and hyperactivity	0.5 Hz 150 μ T – 9 mT 30 min in mid-light-phase and mid dark phase	Reduction in the increased night-time latency and day-time activity.	As above; similar effect with opioid antagonist naloxone.	Kavaliers & Ossenkopp, 1986b
Mice: opioid-induced analgesia	0.5 Hz 150 μ T – 9 mT 60 min in mid-light-phase	Inhibition of daytime opioid analgesia.	As above; affects actions of mu, delta and kappa but not sigma agonists.	Kavaliers & Ossenkopp, 1986a

Table 44. Continued

Mice: morphine-induced analgesia	60 Hz 50, 100 or 150 μ T 1 h	Dose-dependant reduction in analgesia.	Ossenkopp & Kavaliers, 1987
Mice: steroid-induced analgesia	60 Hz 141 μ T 30 min	Exposure-induced reduction in analgesia.	Kavaliers, Wriebe & Ossenkopp, 1998
Rat: central cholinergic systems in brain	60 Hz 2 mT 1 h	Reduced high-affinity choline uptake in frontal cortex and hippocampus.	Lai, Carino & Ushijima, 1998
Rat: central cholinergic systems in brain	60 Hz 0.5, 1.0, 1.5 or 2.0 mT, 1 h 1.0 mT, 30, 45, 60 or 90 min	High-affinity choline uptake in frontal cortex and hippocampus reduced.	Lai & Carino, 1999

Several recent studies using the Morris water maze or radial arm maze have investigated the effects of magnetic fields on spatial memory and place learning. These studies provide evidence that exposure of rats, mice or voles to power frequency fields at $\sim 100 \mu\text{T}$ and above may modulate task performance (Kavaliers & Ossenkopp, 1993; Kavaliers et al., 1996; Lai, 1996; Lai, Carino & Ushijima, 1998; Sienkiewicz et al., 1998; Sienkiewicz, Haylock & Saunders, 1998). Exposure to complex pulsed magnetic fields may also affect performance (McKay & Persinger, 2000; Thomas & Persinger, 1997). In addition, much evidence has accrued over the last decade that effects may also occur using specific combinations of static and time-varying fields (see Sienkiewicz, Haylock & Saunders, 1998). The mechanism for these effects has been partly explored and the changes in behaviour have been attributed to decreases in cholinergic functions caused by field-induced changes in endogenous opioid activity (Lai, 1996; Lai, Carino & Ushijima, 1998; Thomas & Persinger, 1997).

The conditions to produce any of these phenomena are not well defined, and both deficits and enhancements in performance have been observed and one study did not report any field-dependent effects (Sienkiewicz, Haylock & Saunders, 1996). It is feasible that these differences in outcome may depend on experimental or other variables including the timing and duration of exposure relative to learning (McKay & Persinger, 2000; Sienkiewicz et al., 2001). While these results suggest that the neural representations or processes underlying the performance of spatial memory tasks may be vulnerable to the effects of magnetic fields, some part of the observed outcome may be attributable to changes in arousal (IARC, 2002; ICNIRP, 2003) or in motivation (Thomas & Persinger, 1997). Nevertheless, the transient nature and small magnitudes of the responses do not suggest an obvious deleterious effect.

Two studies using rodents have investigated the effects of magnetic fields on recognition memory. Using the field conditions putatively identified as having an acute effect of spatial memory, Sienkiewicz et al. (2001) found no effects on the performance of an object recognition task by mice. Animals were exposed for 45 minutes to a 50 Hz field at 7.5, 75 or 750 μT . However, Mostafa, Mostafa & Ennaceur et al. (2002) reported that discrimination between familiar and novel objects was impaired in rats following chronic exposure at 200 μT for 2 weeks.

Stern et al. (1996) failed to replicate the results of earlier studies (Liboff, McLeod & Smith, 1989; Thomas, Schrot & Liboff, 1986) suggesting exposure to combined static and power frequency magnetic fields, arranged to simulate the cyclotron resonance conditions for lithium ions, significantly impaired operant performance. The earlier positive results were attributed to possible confounding.

A summary of studies on cognitive function in animals is given in Table 45.

Table 45. Cognitive function

Endpoint	Exposure	Response	Comment	Authors
Spatial memory				
ELF magnetic fields				
Meadow voles and deer mice: water maze performance	60 Hz 100 μ T 5 min during task acquisition	Enhanced performance opiate-induced reduction abolished by magnetic field exposure in deer mice.	Suggests magnetic field reduces opiate activity.	Kavaliere & Ossenkopp, 1993 Kavaliere et al., 1996
Rats: radial arm maze performance	60 Hz 750 μ T 45 min prior to behavioural testing	Performance reduced. Effect abolished by cholinergic antagonist.	Suggests magnetic field reduces cholinergic activity.	Lai, 1996
Mice: radial arm maze performance	50 Hz 5, 50 or 500 μ T or 5 mT during behavioural testing (up to 15 min)	No effect.		Sienkiewicz, Haylock & Saunders, 1996
Rats: radial arm maze with operant task at the end of each arm	Pulsed (burst firing pattern for 1 sec every 3 sec) 1–4 μ T 5 or 30 min immediately or 30 min after 8 training sessions	Some differences were seen between the exposed and sham exposed animals.	Small number of animals; complex post hoc interpretation of data.	Thomas & Persinger, 1997
Rats: water maze performance	60 Hz 1 mT 1 h prior to behavioural testing	No effect on performance but retention impaired.	Reduced swim speed.	Lai, Carino & Ushijima, 1998
Mice: radial arm maze performance	50 Hz 7.5, 75, or 750 μ T or 7.5 mT prior to behavioural testing	No overall effect but transiently reduced acquisition rate.	No effect on movement or motivation.	Sienkiewicz et al., 1998; 1998
Rats: complex radial maze performance	A complex low intensity magnetic field of between 200–500 nT for 1 h of a 2 h period between training and testing	Exposure immediately after training impaired spatial memory and those immediately before testing impaired motivation.		McKay & Persinger, 2000

Table 45. Continued

Mice: spontaneous object recognition task	50 Hz 7.5, 75, or 750 μT between initial testing and re-testing	No significant field-dependent effects.		McKay & Persinger, 2000 Sienkiewicz et al., 2001
Rats: spontaneous object recognition task	50 Hz 200 μT 1 or 2 weeks	Significant decrease in discrimination between familiar and novel objects.	Significant corticosterone elevation in exposed animals.	Mostafa, Mostafa & Ennaceur, 2002
Operant behaviour				
ELF electric fields				
Baboons: multiple FR (fast) and DRL (slow) schedules	60 Hz 30 or 60 kV m^{-1} 6 weeks during behavioural testing	Exposure on day 1 induced temporary work stoppage.		Rogers et al., 1995a
Static and ELF magnetic fields				
Rats: multiple FR (fast) and DRL (slow) schedules	Static field of 26 μT plus 60 Hz field of up to 200 μT 30 min prior to operant testing	DRL response impaired; temporal discrimination reduced.	Cyclotron resonance conditions for lithium.	Thomas, Schrot & Liboff, 1986 Liboff, McLeod & Smith, 1989
Rats: multiple FR (fast) and DRL (slow) schedules	Static field of 26 or 27 μT plus 60 Hz field of 50 or 70 μT 30 min prior to behavioural testing	No effect.	Attempted replication of Thomas et al. 1986,	Stern et al., 1996
ELF electric and magnetic fields				
Rats: multiple random interval (RI) schedule in adult males exposed perinatally followed by extinction and reconditioning	60 Hz 100 μT , 30 kV m^{-1} 20 h / day, 22 days in utero and 8 days post-natally	Reduced performance in exposed rats.	Two replicate studies.	Salzinger et al., 1990
Baboons: delayed match-to-sample procedure (light-flash stimulus)	60 Hz 6 kV m^{-1} , 50 μT 30 kV m^{-1} , 100 μT 6 weeks during behavioural testing	No effect.		Orr, Rogers & Smith, 1995b

5.5 Conclusions

Exposure of volunteers to power frequency electric fields causes well-defined biological responses, ranging from perception to annoyance, through surface electric-charge effects. These responses depend on field strength, ambient environmental conditions, and individual sensitivity. The thresholds for direct perception by 10% of volunteers varied between 2 and 20 kV m⁻¹, while 5% found 15–20 kV m⁻¹ annoying. The spark discharge from a person to ground is found to be painful by 7% of volunteers in a field of 5 kV m⁻¹. Thresholds for the discharge from an object through a grounded person depend on the size of the object and therefore require specific assessment.

High field strength, rapidly pulsed magnetic fields can stimulate peripheral or central nerve tissue; such effects can arise during MRI exposure and are used in transcranial magnetic stimulation. Threshold induced electric field strengths for direct nerve stimulation could be as low as a few volts per metre. The threshold is likely to be constant over a frequency range between a few hertz and a few kilohertz. People suffering from or predisposed to epilepsy are likely to be more susceptible to induced ELF electric fields in the CNS. Furthermore, sensitivity to electrical stimulation of the CNS seems likely to be associated with a family history of seizure and the use of tricyclic antidepressants, neuroleptic agents and other drugs that lower the seizure threshold.

The function of the retina, which is part of the CNS, can be affected by exposure to much weaker ELF magnetic fields than those that cause direct nerve stimulation. A flickering light sensation, called magnetic phosphenes or magnetophosphenes, results from the interaction of the induced electric field with electrically excitable cells in the retina. Threshold electric field strengths in the extracellular fluid of the retina have been estimated to lie between about 10–100 mV m⁻¹ at 20 Hz. There is, however, considerable uncertainty attached to these values.

The evidence for other neurobehavioural effects in volunteer studies, such as the effects on brain electrical activity, cognition, sleep, hypersensitivity and mood, is less clear. Generally, such studies have been carried out at exposure levels below those required to induce effects described above, and have produced evidence only of subtle and transitory effects at best. The conditions necessary to elicit such responses are not well defined at present. There is some evidence suggesting the existence of field-dependent effects on reaction time and reduced accuracy in the performance of some cognitive tasks, which is supported by the results of studies on the gross electrical activity of the brain. Studies investigating EMF-induced changes in sleep quality have reported inconsistent results. It is possible that these differences may be attributable in part to differences in the design of the studies.

Some people claim to be hypersensitive to EMF. However, the evidence from double blind provocation studies suggests that the reported symptoms are unrelated to EMF exposure.

There is only inconsistent and inconclusive evidence that exposure to ELF electric and magnetic fields causes depressive symptoms or suicide. Thus, the evidence is considered inadequate.

In animals, the possibility that exposure to ELF fields may affect neurobehavioral functions has been explored from a number of perspectives using a range of exposure conditions. Few robust effects have been established. There is convincing evidence that power-frequency electric fields can be detected by animals, most likely as a result of surface charge effects, and may induce transient arousal or mild stress. In rats, the detection range is between 3 and 13 kV m⁻¹. Rodents have been shown to be aversive to field strengths greater than 50 kV m⁻¹. Other possible field-dependent changes are less well-defined and generally laboratory studies have only produced evidence of subtle and transitory effects. There is some evidence that exposure to magnetic fields may modulate the functions of the opioid and cholinergic systems, and this is supported by the results of studies investigating the effects on analgesia and on the acquisition and performance of spatial memory tasks.