CHAPTER 6

Effects of Electromagnetic Energy on the Endocrine System

Introduction

The endocrine system consists of a number of glands that secrete liquid into the bloodstream (rather than through a duct into one of the body cavities). The chemical products elaborated by these glands are called hormones, and they have profound effects upon their target cells and organs. The overall function of the endocrine system is that of homeostatic control, and the level of each hormone is regulated via a complex monitoring and feedback mechanism. As an example, the parathyroid glands regulate the level of blood calcium, thereby controlling the overall level of excitability of the nervous system. Under the control of the parathyroids, calcium can be rapidly moved in or out of the bones to maintain an animal's blood levels within appropriate limits.

Some glands such as the thyroid, parathyroid, and the islet cells of the pancreas, secrete primarily a single hormone which has a relatively specific function. As examples, the thyroid hormone regulates oxidative metabolism, and the islet-cell hormone assists in glucose metabolism. The adrenal gland is more complex; it is a "defensive" gland, and is activated in stressful circumstances in which the organism must decide whether to fight or flee. In both cases, the adrenal promotes the general body functions that facilitate such reactions. The adrenal has two dis tinct anatomical portions (the cortex and medulla) and rich connections to the nervous system. The cortex secretes the glucocorticoids (corti coids), hormones that are involved in coping with stressful situations arising out of circumstances that are not immediately life-threatening. In contrast, the adrenal medulla secretes the catecholamine class of hormones—the most active are epinephrine and norepinephrine—which promote practically instantaneous preparations for fight and flight.

The pituitary, a small tissue mass located at the base of the brain below the hypothalamus, is the most important and complex endocrine gland. It secretes at least eight hormones that orchestrate the response of the other glands and that produce effects on general body functions such as growth and water balance. Pituitary activity varies dynamically depend ing on blood-stream hormone levels.

The interaction between EMFs and this interrelated group of endocrine glands—which themselves are only partially understood—is very com plex. It could involve particular glands such as the calcium-parathyroid-bone axis. On the other hand, the brain itself might be sensitive to alterations in the electromagnetic environment. Such a sensitivity could result in activation of a number of hormonal systems by virtue of the direct connection between the brain and the pituitary. If an EMF constituted a threat to the integrity of the organism, the pituitary-adrenal stress re sponse system would be called into action. Indeed, the bulk of the endocrine system studies have involved the pituitary-adrenal system. These studies illustrate the difficulty in establishing the precise causal chain of events in the functioning of a hormone system, as would be required to determine the level at which the EMF acts in the first instance.

Friedman and Carey measured the corticoid production in monkeys exposed to a 200-gauss DC magnetic field for 4 hour/day (3). Daily urine collections were combined into 72-hour period specimens to provide sufficient volume for biochemical determination of corticoids (presumed to reflect the levels in the blood). The pre-experimental level and the levels found during the four subsequent specimen periods are shown in figure 6.I. As judged by the increase in corticoids, there was a stress response which lasted for about the first 6 days and then subsided despite the continued exposure.

Corticoid synthesis by the adrenal cortex is controlled by the pituitary. When it is appropriate, a hypothalamic releasing factor stimulates the pituitary to produce adrenocorticotropin (ACTH) which in turn stimu lates and controls adrenal corticoid production. Thus, Friedman's results were consistent with an effect at any level in the hormonal system. In a series of experiments, we exposed rats to 15,000 v/m at 60 Hz to de termine whether the field produced an effect on the serum corticoids concomitantly with an effect on the pituitary (4). We found that following 30 days' continuous exposure, the corticoid levels were generally lower and the final pituitary weight was higher in the exposed animals (Table 6.1). These results indicated that both pituitary and adrenal function were

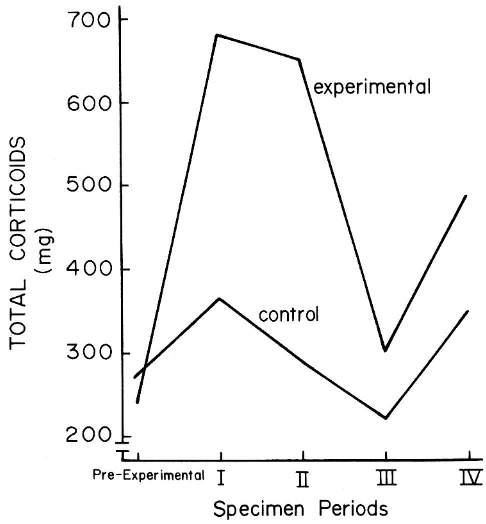

Fig. 6.1. Urine corticoid levels in monkeys during exposure to a DC magnetic field.

Table 6.1. BIOLOGICAL EFFECTS OF EXPOSURE TO A 60-HZ ELECTRIC FIELD

EXPERIMENT	NUMBER OF RATS	WATER CONSUMED (ml/rat)	PITUITARY WEIGHT (µg/g)	SERUM CORTICOIDS (µg/100 ml)
1	15 experimental	846 ± 68*	38.7 ± 3.2*	6.8 ± 0.8*
	18 control	940 ± 142	35.2 ± 3.8	8.7 ± 1.2
2	14 experimental	749 ± 80*	43.9 ± 4.1*	7.2 ± 1.5
	20 control	891 ± 93	40.6 ± 3.1	7.6 ± 2.1
3	19 experimental	819 ± 83*	32.9 ± 3.1	
	21 control	890 ± 83	35.2 ± 2.6	
4	16 experimental	901 ± 50*	38.0 ± 2.4	6.0 ± 0.7
	14 control	1054 ± 84	39.0 ± 2.6	6.4 ± 0.6
5	20 experimental	1003 ± 82*	31.4 ± 2.4*	9.1 ± 2.0*
	20 control	1099 ± 117	29.4 ± 2.9	16.3 ± 3.8
6	14 experimental	1143 ± 157	31.2 ± 1.8	9.5 ± 2.0
	16 control	1202 ± 107	30.6 ± 1.8	9.7 ± 4.0

NOTE: The average values were determined following 30 days of continuous exposure. There were no statistically significant changes in water consumption during the first 14 days of any experiment.

$p < 0.05$

altered following exposure, but, because of the feedback nature of the hormonal system, it was not possible to determine which tissue was affected initially. Recently Novitskiy (23) measured the endocrine system response at each level following brief exposure of rats to 10-1000 µW/cm^2 at 2.4 GHz. He found increased levels of serum corticoids, pituitary

ACTH, and ACTH releasing-factor in the hypothalamus.

Because the pituitary's activities are synchronized with the nervous system via intimate chemical and neuronal pathways in the hypothalamus, any EMF impact involving pituitary function would be expected to reach beyond ACTH and the classic stress-response system. There is some direct evidence that other pituitary secretions are affected by EMF's. For example, antidiuretic hormone (ADH) Is a pituitary secretion that participates in the regulation of the body's water balance. An increase in ADH fosters the reabsorption of water by the kidney's distal renal tubules thereby leading to a reduction in diuresis (flow of urine). Several studies have reported that EMFs increase serum ADH levels (5, 6) and reduce diuresis (6, 7). In many cases, however, the evidence of EMF impacts involving the pituitary is indirect and consists of effects on growth, metabolism, the cardiovascular and hematopoietic systems, and other body functions and systems that are under the influence and control of the endocrine system. In the remainder of this chapter we describe the EMF studies that involve the endocrine glands-principally the adrenal and thyroid. In succeeding chapters we present evidence of the effects of EMFs on other body functions and systems.

The Adrenal Cortex

The adrenal corticoid response to EMF stimulation is highly time-dependent (7). When groups of rats were exposed to 500, 1000, 2000 and 5000 v/m at 50 Hz, the average urine-corticoid level of the latter two groups changed similarly during the 4-month exposure period (7): approximately the same maximum value was achieved in both groups and they exhibited increased corticoid levels as compared to the controls. The 1000-v/m group, however, exhibited lower corticoid levels for the first 2 months of the exposure period followed by a rise above the control level during the last half of the exposure period; at 500 v/m the pattern of corticoid excretion was identical to that of the controls. The biological response was reversible in the sense that when the field was removed, the corticoid level returned to normal within 2 months.

One of the important factors governing the time course of the corticoid level—and hence the dynamics of the pituitary-adrenal response—is the ratio of the exposure period to the nonexposure period. This was established by Udinstev who exposed groups of rats to 200 gauss, 50 Hz, intermittently for 6.5 hours/day, for 1, 3, 5, and 7 days, and, continuously for 1 and 7 days (9) (Table 6.2). The corticoid level in the continuously exposed rats was significantly greater than in the controls: following

Table 6.2. SERUM CORTICOID LEVELS IN RATS FOLLOWING EXPOSURE TO CONTINUOUS AND INTERMITTENT (6.5 hr/day) 50-HZ MAGNETIC FIELDS

TYPE OF FIELD	SERUM CORTICOID LEVEL (µg/100 ml)	
	Control	Experimental
Continuous		
1 day	22.6 ± 1.6	33.4 ± 3.0*
7 days	21.2 ± 2.9	32.8 ± 2.5*
Intermittent		
1 day	16.2 ± 3.5	26.3 ± 2.9*
3 days	19.7 ± 0.8	26.1 ± 2.1*
4 days	19.8 ± 2.1	14.3 ± 0.8*
5 days	19.7 ± 1.8	16.5 ± 2.2
7 days	19.6 ± 1.0	17.4 ± 1.6

$p < 0.05$

intermittent exposure, however, the corticoid response was considerably different. After 4 days—the total cumulative exposure was 26 hours—it was significantly lower in the exposed rats, and this trend continued after 5 and 7 days of intermittent exposure.

At 3 GHz, rats exposed to 5-10, µW/cm^2, 8 hours/day, had elevated levels of excreted corticoids after I-3 months of exposure (10). At 60 GHz, 15 minutes/day, rats exhibited depressed levels of serum corticoids after 2 months (11). In such high-frequency EMF studies it is usually impractical to continuously expose the animals, because the fields can interfere with norrnal feeding and watering practices, thereby introducing artifacts. Thus, judging from the Udinstev studies, the intermittent exposure aspect of high-frequency studies is an additional factor—along with the characteristics of the EMFs and the physiological state of the organism—that will affect the time course of the corticoid response.

Changes in the gross weight of the adrenal gland reflect changes in its activity. Demokidova showed that I hour/day EMF exposure of rats produced changes in adrenal weight that were both time and frequency dependent (12-14). After 2 weeks, exposure at 3 GHz, the adrenals of the exposed rats were significantly larger than those of the sham-irradiated group: after 5 months, however, there were no adrenal-weight differences. At 70 MHz, adrenal weights, in the exposed animals were elevated after 1 week's and 1 month's exposure, but following 3 months' exposure they were depressed. After 8 months' exposure at I5 MHz, adrenal weights were similarly depressed below the corresponding control weight.

There are two reports of EMF-induced histological changes in adrenal tissue (14, 15). The relative size of the innermost or reticular zone of the adrenal cortex was decreased following 3 months' exposure at 70 GHz (14). Exposure to 130 gauss, 50 Hz, (4 hours/day) for I month resulted in changes in the blood vessels in the reticular zone along with some hemorrhage and dystrophic cellular changes (15). Four months' exposure to 5000 v/m, 50 Hz, produced no histological changes and no change in gross adrenal weight (7).

The Thyroid

Thyroid activity is regulated by the thyroid-stimulating hormone (TSH) secreted by pituitary. Elevated TSH levels induce the thyroid to elaborate thyroxine, a hormone which functions in at least 20 enzyme systems; one of its major influences involves the acceleration of protein synthesis.

High-frequency EMFs seem to have a general stimulatory effect on the thyroid. At 70 MHz, 150 v/m, 3 months' exposure resulted in an increase in the height of the follicular epithelium in rats—there was no change in thyroid weight (14). At 3 GHz, 153 ,$\mu W/cm^2$, an increase in thyroid weight was found after 2 weeks' exposure, but after 5 months' exposure the thyroid weights were normal (12). Following 4 months' exposure to 5000 W/cm^2, cellular incorporation of radioactive iodine and serum protein-bound iodine were increased by 50 and II7%, respectively (16). Electron micrographs revealed enhanced cellular activity that was manifested by an increased number of cytosomes and an enlarged Golgi apparatus and endoplasmic reticulum (16).

At 50 Hz thyroid activity was depressed as judged by radioactive iodine uptake (7, 17). Continuous exposure at 1-5 kv/m depressed thyroid activity after 4 months (7): when the field was removed thyroid activity returned to normal within 6 weeks. Four months intermittent exposure (2 hr/day) at the same field level did not affect thyroid activity, but depressed activity was observed at 7-15 kv/m (17). Ossenkopp et al. found that both male and female rats exposed in utero to 0.5 Hz, 0.5-30 gauss, had increased thyroid weights at 105-130 days of age (21). Based on this and several other physiological and behavioral studies, Persinger has implicated the thyroid as a significant factor in the rat's response to a magnetic field (22).

The Adrenal Medulla and the Pancreatic Islets

The catecholamines, which are produced by the adrenal medulla, have a significant influence on body metabolism. Epinephrine, for example, sets in motion a large number of physiological mechanisms required to sustain vigorous activity; one of its consequences is the stimulation of ACTH secretion by the pituitary. The activity of the adrenal medulla is primarily under the control of the sympathetic nervous system.

Udinstev and his colleagues (18) exposed rats to 200 gauss, 50 Hz, for 24 hours, and then sacrificed groups of animals up to 14 days later and examined the catecholamine levels in the brainstem, hypothalamus, liver, spleen, and heart. The results, presented in table 6.3 demonstrated a phasic series of changes of concentration of the catecholamines in each of the tissues; normalcy was not re-established until 7-14 days after exposure.

Table 6.3. CATECHOLAMINE LEVELS IN RAT TISSUES FOLLOWING TWENTY-FOUR HOURS' EXPOSURE TO A 50-HZ MAGNETIC FIELD

TISSUE	CATECHOLAMINE LEVELS μg/g)					
	Control	0 days	1 day	2 days	7 days	14 days
Brainstem						
epinephrine	0.059	0.0397*	0.04*	0.062	0.065	0.047
norepinephrine	0.611	0.590	0.493	0.345*	0.476*	0.560
dopamine	0.140	0.048*	0.206	0.103	0.093	0.134
dopa	0.50	0.042	0.043	0.05	0.05	0.05
Hypothalamus						
epinephrine	0.018	0.021	0.022	0.012*	0.020	0.019
norepinephrine	0.862	0.510*	0.932	0.586*	1.408*	0.764
dopamine	2.530	3.56*	2.770	0.920*	2.920	3.080
dopa	0.310	0.202*	0.317	0.312	0.310	0.314
Liver						
epinephrine	0.008	0.014*	0.010	0.003*	0.008	0.008
norepinephrine	0.122	0.190*	0.183	0.174	0.142	0.153
dopamine	0.159	0.158	0.130*	0.154	0.151	0.158
dopa	0.018	0.018	0.030*	0.016	0.018	0.017
Spleen						
epinephrine	0.007	0.001*	0.006	0.006	0.007	0.007
norepinephrine	0.143	0.201*	0.201*	0.097*	0.118	0.166
dopamine	0.062	0.070	0.042*	0.029*	0.058	0.062
dopa	0.038	0.05*	0.045*	0.037	0.033	0.038
Heart						
epinephrine	0.063	0.0936	0.012	0.064	0.059	0.063
norepinephrine	1.314	1.175	1.628	1.768	1.630	1.273
dopamine	0.164	0.158	0.177	0.074	0.152	0.178
dopa	0.056	0.057	0.061	0.078	0.061	0.061

Note: The values were measured at the indicated time (days) after exposure.

$p < 0.05$

Chronic intermittent EMF exposure also produced changes in adrenal-medulla physiology. Three-hour daily exposures of rats at 90 gauss, 50 HZ, resulted in increased catecholamines in the adrenals after 6 months (19). The adrenal-medulla cross-sectional area of rats exposed to 70 MHz, 150 v/m increased by 60% after 3 months exposure for 1 hour/ day (14).

The pancreas contains aggregations of cells called islets, which produce insulin, a hormone that promotes the synthesis of carbohydrates, proteins, and nucleic acids. The pancreas is innervated by sympathetic and para-sympathetic fibers whose terminals are in contact with the cell membranes of the islet cells. In a study involving the endocrine function of the pancreas, rats were exposed to 200 gauss, 50 Hz, continuously (24 hr) or intermittently (6.5 hr/day for 7 days) (20). In both instances, an insulin insufficiency was produced. Blood glucose was not affected by the continuous exposure but it was increased by 37% following the intermittent exposure.

Summary

Adrenal corticoid production can be influenced by EMFs, and the dynamics of the effect depend on many factors: field strength, frequency, duration of exposure, whether the exposure is continuous or intermittent, the ratio of the exposure to the nonexposure period in intermittent exposures, and the organism's predisposition. Since the adrenal-cortical response to EMFs is the same as that caused by known stressor agents (2), it follows that EMFs can also be biological stressors. Other endocrine organs that can be triggered by EMFs include the thyroid, pancreatic islets, and the adrenal medulla.

There are many important but unanswered questions. Where within the organism does the EMF-tissue interaction occur? What is the level of the interaction-organ, cellular, or molecular? What is the temporal sequence of events and the factors which influence it? Are the thyroid, adrenal, and pancreas particularly sensitive to certain types of EMFs, or are the changes in these organs reflective of an EMF interaction with more central structures-or both? Suppose, for example, that the thyroid is sensitive to a particular EMF: an EMF-induced change in thyroxine production would alter pituitary production of TSH, but measurements of thyroxine and TSH would not, in themselves, tell us either the location, level, or sequence of the interaction. Indeed, given the pervasive changes that can be induced by EMFs in the nervous system and the endocrine system—and in view of the intimate interconnection and synchronization of the two—there is a serious question concerning whether it is methodologically possible to demonstrate a specific causal sequence in many instances. The diversity of the reported effects suggests that EMF-induced changes in the endocrine system are mediated by the CNS. However, until now, most investigations have focused on the need to demonstrate an EMF impact on the endocrine system, and thereby to lay the foundation for more in-depth studies. Only Udinstev has even approached what might be called a systematic study of a particular EMF (200 gauss, 50 Hz). When other EMFs are studied systematically, perhaps it will be possible to delineate the sites and the level of the interaction (see chapter 9).

Most of the endocrine system effects seemed to be compensatory rather than pathological (see table 6.2 for example). But even though the homeostatic mechanism generally brought the corticoid level back to normal, it does not follow that the animal became physiologically equivalent to what it would have been at that point in time if it had not been exposed to the EMF. Animals that have been exposed to one stressor are known to have a diminished capacity to deal with a second simultaneous or contemporary stressor. Thus, animals that have accommodated to an EMF would, in general, be more susceptible to a second stress, compared to animals that experienced only the second stress.

There is, of course, a difference between the existence of an EMF-induced biological effect, and its detection in a given experiment. In our study, for example, the lack of a consistent statistically significant difference between the exposed and the sham-irradiated rats in each experiment suggested that uncontrolled variables were present in the study. Possibilities include zoonoses, and genetic predispositions. This can cause individual animals, in an apparently homogeneous population, to react in completely opposite ways to the same EMF. In such cases there is no average response of the group to the EMF, despite the occurrence of individual responses. The most sensitive experimental paradigms for EMF research, therefore, do not rely on the comparison of group averages for the assessment of an effect.

Despite the difficulties with experimental design and interpretation, the evidence clearly indicates that exposure to EMFs can result in an activation the neuro-endocrine axis that is expressed in a general way as the stress syndrome.

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