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Evolution and Results of Biological Research with Low-Intensity Nonionizing Radiation

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INTRODUCTION

Until the late 1940's, the primary interest in the biological effects of radio frequency (RF) radiation was in heating for medical applications (1). Thus, the dominant theme of the research was the use of high powers to heat tissue. With the development and increasing use of RF radiation as radar in the 1940's, however, questions were increasingly raised about the possibility that exposure to this energy would have adverse biological effects on military personnel and workers.

In the mid-1950's, the Department of Defense's (DoD) RF hazards assessment establishment contracted for research to determine if there were adverse biological effects of RF radiation: the Tri-Service Program. The primary thrust of the program was essentially determined by the implicit assumption upon which prior work was based. It was assumed that the only way the energy could affect an organism was through overloading its heat-dissipation mechanism. Thus, little effort was expended to determine the effect of low-intensity energy. This assumption also resulted in an acrimonious dispute between those who con tended that only thermal effects could occur and those who thought that nonthermal effects could also occur. But the fruitless argument was really the result of a semantic problem. The participants were talking past each other, for there never was a common definition of the words thermal and nonthermal. It was also assumed in the Tri-Service Program that nervous-system function and behavior could not be affected, so the possibility that modulation would be of consequence was essentially ignored (2). The Tri-Service Program was terminated in 1961, after gathering some data on overloading the temperature-regulating system.

Through the 1960's and early 1970's, there was some research on the biological effects of low-intensity RF energy. This was a distinct departure from the pattern of prior research. It was possible because the very limited funds available for the research were not controlled by those whose interests were in hazards or medical applications. This funding for research on low-intensity RF bioeffects continued through most of the 1970's.

Beginning in the early 1970's, a new program of research on high-intensity radiation effects, again primarily sponsored by the DoD's RF hazards establishment, was superimposed on and

overshadowed the low-intensity research. By the late 1970's, the low-intensity research was being squeezed out because of the concentration of control of the funding into the hands of those in the DoD RF hazard establishment. The details on the control of research funds and its effects can be found elsewhere (1,3,4).

In the early 1960's, I initiated some of the early research in this country on bioeffects of exposure to low-intensity RF radiation. I was the most active investigator in this area during the 1960's and on into the 1970's. Thus, I have been given the task to trace chronologically, through my own research and the research of others in the US, the development in this country of biological research with low-intensity RF energy. The objective is not to give a comprehensive in-depth review of all aspects of RF biological research during those two decades and into the 1980's. Rather, the objective is to indicate the development of the more significant patterns of research, and to indicate where the research would likely lead if pursued as science. Since I was almost alone in doing research on low-intensity RF radiation bioeffects in this country during the 1960's, the beginning of this narrative will be primarily about my research.

THE QUIET DECADE

In the late 1950's, neurophysiological theory on information transfer in the nervous system did not provide much understanding of neural function. It was about this time that I became curious about electric fields and the possibility of their interaction with the nervous system. In 1960, I was working at General Electric's Advanced Electronics Center at Cornell University doing biological research. One line of research I had initiated there was concerned with electrostatic fields and nervous-system function. I was also experimenting with air ionization and its biological effects. Late that year, while attending a small conference sponsored by the General Electric Company (GE), I happened to talk to a GE technician whose job was to measure RF radiation in the vicinity of radars. He mentioned that he "heard" radars. I found this to be interesting, since I, as well as everyone trained in the life sciences, had been taught that people hear acoustic energy and see, as light, electromagnetic energy. He was rather surprised when I asked if he would take me to a site and let me hear the radar. It seemed that I was the first person he had told about hearing radars who did not dismiss his statement out of hand.

A few weeks later, I went to the radar site and I heard the RF radiation. I performed a few simple tests to assure myself it was not an artifact. I then undertook a series of experiments which resulted in the publication of a brief article about the phenomenon in 1961 and a more detailed article in 1962 (5,6). I laid out the data from a variety of tests with humans. I suggested that there were probably multiple mechanisms for such an effect, but there was not sufficient data to specify mechanisms. Although the articles provoked interest in some members of the biological community and disbelief in others, there was little immediate activity by others to pursue the findings.

I searched the literature for in formation about the nature of RF field interaction with biological organisms and tissues. In essence, I found that there had been little effort in this country to consider sensory phenomena such as I was reporting, nor was there any significant research on neural effects of RF radiation. Virtually all of what little research existed had been done in the Soviet Union, but the translations were generally of poor quality and almost uninterpretable.

I expanded my literature search and published a comprehensive paper in 1965 (7). I assessed biological inter- actions with a wide portion of the electromagnetic spectrum, from the infrared down to low frequency. I critiqued the literature available, offered suggestions as to the portions of the spectrum with which the more significant research could be done, and pointed out the possibility of micron-wavelength emission from active nerves. This analytical review evoked a considerable amount of interest, for I received almost 5000 reprint requests.

After the initial exploratory work with the hearing phenomenon and concurrent with the preparation of the analytical review, I initiated further research with RF radiation. The series of experiments I carried out in the 1960's centered about four major themes: (1) experimental controls and techniques; (2) brain function and behavior; (3) sensory function; and (4) heart function.

Although the results of my work on experimental controls and techniques are too extensive to review in detail here, they are critical for accurate data collection. As a sampling, comparative studies of biological data recording techniques were done, including assessment of recording electrode systems in RF experiments. It was found that certain conventionally used systems yielded artifacts as data, due to induced currents stimulating the tissue as well as feeding into the recording preamplifier. It was found that filtering had limited usefulness and that lead placement was of consequence. New types of recording electrodes were developed which showed excellent characteristics in the RF field. In fact, the sponsor of one of these studies had the electrode patented (8,9).

Experiments were also carried out to develop techniques to remotely monitor the activity of nerves in an RF field. A method to record neural activity with no recording devices in the field was developed (10). Studies were made of restraint devices to hold animals, and of the RF field distorting effects of these devices. Polystyrene head holders were developed for use with cats. Teflon and nylon chairs and restraints were developed in studies with monkeys, and wooden enclosures and restraints were developed for use with cats (11,12).

Experiments were carried out using three-dimensional field plots to investigate the effect of the biological object itself on the field within an RF an echoic enclosure. Similar studies were made on the perturbing effect of field measurement devices on the field. Standardized methods of measurement and reporting of measurements were developed. Experimentation was also carried out to determine the effect of body position and its orientation on results. Studies were made of shielding materials and their usefulness in experimentation (11). I found in my other experiments that carrier frequency and modulation had to be controlled because they were

critical in the effect of low-power-density RF radiation on some functions of higher organisms (6,11,13-15).

As may be seen from this sampling, there are many variables that need to be controlled and special techniques that must be used in biological work with RF radiation. But the literature shows that many of these variables have not been controlled.

Turning now to the second theme, data specific to brain function, I shall summarize the information obtained. Cats were illuminated with pulse-modulated RF radiation and evoked activity in the brain was observed (11). The threshold average power density necessary to evoke activity was approximately 20 $\mu W/cm^2$. The controls used indicated that the activity was neural evoked activity rather than an artifact of the situation. Using an Echosorb shield to cover the entire cat, or head, or body, it was found that the head must be exposed to the radiation in order to have an effect occur. Within the carrier frequency range used, there appeared to be a reduction of effect at the highest frequency. Variation in power density had a distinct effect on the evoked activity. Polarization of the energy, whether perpendicular or parallel to the spine, did not seem to matter. As pulse repetition frequency (PRF) was changed, the evoked activity did not change significantly until the PRF was greater than approximately 50 pulses per second (pps). In general, recording from the rostral brain stem did not yield evoked activity as diffuse and persistent as recording from the caudal portion of the reticular formation of the brain.

In view of what I was seeing in using RF radiation to influence neural tissue, and because of ideas I had about neurophysiological theory, I expanded the brain function experimentation to assess the possibility that nerves, when active, would emit coherent electromagnetic energy. It seemed that the channel capacity indicated by neurophysiological theory was insufficient to encompass the results of many neurophysiological and behavioral experiments, and that there might be communication between nerves via the emission of electromagnetic energy at micron wavelengths. To assess this possibility, I set up an experiment using some of the equipment I developed for remote sensing. I used live nerves from the legs of blue crabs because of their characteristics. I sought to determine whether there was emission of micron wavelength energy when the nerves were active. I found that the emission w as considerably greater than what would be expected from a black-body nerve model. I established that the emission was not an artifact, that the emission was from the surface of the nerve, and calculated the amount of emission and its spectral band (10). A number of subsequent papers by others used these findings in their development, at the molecular level, of new conceptualizations of neural function. These include Lee's concepts on the role of excitons and phonons on nerve permeability and propagation of impulses (16), Cope’s micron-wavelength concepts on phonon coupling and IR involvement in nerve (17), and Maurel and Galzigna’s (18) definition of the involvement of the dipole moment of acetylcholine in neural chemical transmission. There are other similar papers relevant to low-intensity RF radiation bioeffects (19-32).

The third theme was an extension of the RF hearing research and an exploration for other sensory effects. No visual effects were found at that time, but tactile stimulation in humans at

very-low frequency (VLF) carrier frequencies was found (13,14). An attempt was made to determine the locus of the RF hearing mechanism. I searched for cochlear microphonics in guinea pigs and cats exposed to RF radiation, but found none (13,14). The in-air RF hearing thresholds for humans were determined for two carrier frequencies. Since they were quite different, a mathematical model of layers of head tissue was constructed. As RF energy passes through each layer of tissue, the absorption of the energy differs as a function of carrier frequency. Thus, I sought to determine mathematically where in the head the RF energy from the two frequencies became equal. Such an equality point, the crossing of signal strengths, would suggest where to look for the sensing mechanism. In constructing the model, all tissue electrical values were selected in advance, standard values for tissue thickness were used, and first reflections were taken in to consideration. The calculations indicated that the RF energy crossing was in the fluid at the first bone/soft- tissue interface. This suggested a locus in the cochlea or at the surface of the cerebral cortex.

Experimentation was also carried out with cats, using the avoidance conditioning technique to determine if they could sense RF energy. Cats avoided the radiation and thresholds were established, In experiments with rhesus monkeys, avoidance behavior also appeared.

The last major theme of my 1960’s experimentation concerned heart function. The isolated frog heart, stripped of its neural and hormonal buffer systems, was exposed to RF radiation (15). It was found that the heart was responsive to RF radiation when the pulses were synchronized with certain phases of the heart cycle. When the RF pulse occurred about the time the QRS complex occurred, the beat rate increased. In half the cases, arrhythmias occurred, and occasionally the heart ceased beating after a period of arrhythmia. No such effect appeared when the heart was illuminated at earlier points in the cycle.

During the 1960’s, others also reported on experiments with low-intensity RF radiation. For example, Hearn (33) explored the effect of long continued low-intensity RF energy on visual acuity. He found significant differences in the flicker thresholds of irradiated as compared to nonirradiated subjects. Korbel and Thompson (34) exposed rats to what they believed to be low-intensity RF energy. They found that irradiated subjects were more active than nonirradiated subjects for a short period of time during the early part of the experiment, but they became less active than the nonirradiated subjects as the days of radiation exposure increased. In a follow-up study, Korbel and Fine (35) explored a possible relationship between RF frequency range and activity level, but they had equipment problems that left their results in doubt. Bourgeois (36) found that exposure to RF radiation resulted in a significant decrease in auditory thresholds in humans. The threshold change was found to be a function of the type of modulation used, since auditory thresholds were significantly lower upon exposure to 1000-Hz modulated RF radiation than upon exposure to 300-Hz modulated RF radiation.

The foregoing summarizes the primary lines of biological research with low-intensity RF radiation in this country during the 1960's. I had spent most of the decade laying a foundation in data for the study of RF radiation interaction with biological organisms and tissues. Although I

would get reprint requests in the thousands for some of my reports on experiments, it was a rather quiet and lonely effort that was, however, quite interesting.

THE LIVELY DECADE OF THE 1970's AND INTO THE 1980's

INTRODUCTION

The period of my quietly doing research came to an end in 1969 with the passage of Public Law 90-602, the Radiation Control for Health and Safety Act. The purpose of the law was to protect the public health and safety "…from the dangers of electronic product radiation." The Bureau of Radiological Health, Department of Health, Education and Welfare, became active in the area because of the law. The hazards people of the DoD, who had been involved in the Tri-Service Program, again became active in the area.

The Bureau convened a symposium in September of 1969 in Richmond, Virginia, that I helped organize. The topic of the symposium was "Biological Effects and Health Implications of Microwave Radiation." I presented a paper entitled "Effects of Microwaves and Radio Frequency Energy on the Central Nervous System" (37). In it, I detailed why there was so much misunderstanding and confusion in the area, and summarized some of my research. I spelled out lines of research I considered to be worth pursuing, techniques that could be used, and the controls that had to be used in order to get valid data. During the next few years, I found myself spending a large proportion of my time answering phone calls and letters from scientists. DoD had started funding research in the area. The world was not so lonely any more.

MECHANISMS

The decade of the 1970's opened for me with the preparation of a paper in which I presented some of my thinking on possible mediators or mechanisms for biological effects of very low-intensity RF radiation (2). It is my nature to look at the broad picture and to integrate. Most of my experimentation is done because I have reached a choice point in my theorizing. In order to decide which way my thinking should go, I do an experiment to provide data for the choice. This is why I do such a diversity of experiments.

In the preparation of that paper, I made explicit some of my thinking (2). Much of what I said then is still relevant, for much of the research that was done during the 1970's was irrelevant to the questions about the biological effects of low-intensity RF radiation. The DoD sponsors w ho determined what would be done appear to have been primarily interested in research that used high power levels or used techniques relevant to thermoregulation questions.

In that paper, I identified the mistaken assumptions that formed the basis of Schwan's notions about nervous-system function. Those notions had inhibited research on low-intensity and nervous-system effects since the 1940's. He had set up a mathematical model of the axon membrane, and assumed that it was a reasonable representation of the nervous system (38). His

calculations with the model indicated that at field strengths that are "not thermally significant," the induced potentials across the nerve membrane are many orders of magnitude smaller than the nerve resting potential. He stated that such induced fields applied to the resting potential of the axon cannot excite the nerves, and essentially, on the basis of this, he concluded that the nervous system could not be influenced by low-intensity RF radiation.

I pointed out that there were at least two faults in his reasoning. One was that his implied model of the nervous system was unrealistic. Nerves function, and the resting potential is only one extreme of a continuum of potentials on the axon. He ignored most of the nerve cell, including the most important part, when he considered only the axon in his model. Further, nerves interact, and the points of interaction on the cell bodies are the most sensitive to disturbance, not the axon. Thus, his model, based upon the resting potential of the axon, did not correspond to reality, at least not to the reality of the nervous systems of man, monkey, cat, or frog.

Another fault was his assumption that we have a good understanding of nervous system function. Our understanding then, and even now, of how information is coded, transferred, and stored in the nervous system is negligible. We have, at best, only multiple hypotheses. None of these have much support, nor are generally accepted as truth. Thus, a conclusion such as Schwan's, based upon calculations using assumptions about information coding, transfer, and storage in the nervous system is hardly acceptable.

I also showed that by simply changing one of his model assumptions to a more realistic one, and then doing his calculations leads to the conclusion that the nervous system would have to be affected by RF radiation.

I went on in the paper to discuss some of the possible mechanisms for electromagnetic-field effects considering only the electrophysiology of the nervous system. I noted that Valentinuzzi (39) used a mathematical approach to explore the possibility that magnetic fields affect the nervous system. He used equations to evaluate the effects of magnetomotive force on ions, magnetic induction of electrical fields, and magnetic changes of inductance. The equations indicated that the effect of a static magnetic field upon an axon would be almost undetectable. But he recognized that living organisms are composed of more than a single axon. Thus, he extended his equations to consider the nervous system functioning as a whole. The results of this extension led him to suggest that an appropriate magnetic field may influence the activity of the nervous system. And these kinds of effects are now being observed (27).

I also discussed the analyses and hypothesis of MacGregor (40). I noted that he started with a reasonably realistic model of a functioning nervous system. Using it, he mathematically explored the idea that the electrical component of RF radiation might induce transmembrane potentials in nerve cells and thereby disturb neural function and behavior. He considered steady and modulated RF fields and estimated through a series of equations the transmembrane currents and potentials that could be expected. He concluded that the intracranial electric fields associated with low-intensity RF radiation "may induce transmembrane potentials of tenths of millivolts (or

more) and that , therefore, such externally applied fields may disturb normal nervous function through this mechanism." His analyses indicated that the induced transmembrane potential would exhibit a maximum at frequencies in the UHF band. Further, he found that large cell components in regions of high cell density should be most influenced by extracellularly applied fields. Recent (41-43) and older (11) experiments indicate the usefulness of this line of thought.

I also pointed out some of the more recent conceptualizations of nervous-system functioning, and suggested how they could guide research to determine the biological interactions of low-intensity RF radiation. I noted that Szent-Gyorgyi (44) showed that molecules with low reactivity and with a major role as metabolites or hormones can give off an electron and form a free radical. This suggested to him that charge transfer might be one of the most common and fundamental biological reactions. On the basis of his experimental results, he proposed a quantum mechanical view of biology that had relevance to the mechanisms of RF radiation effects (45).

I wrote that a variant of Szent-Gyorgyi's view, a view specific to the nervous system, had been detailed by Wei (46-48). He suggested that the neuron has the structure and potential profile of a PNP transistor and may function like it. In part, Wei used as evidence for the accuracy of his model the discovery by Segal (49) of negative fixed surface charge on membranes, the birefringence phenomenon observed by Cohen et al. (50), and the report of micron wavelength emission from nerve by Fraser and Frey (10). Wei also suggested that what are considered to be transmitter chemicals in the central nervous system (e.g., acetylcholine) are electrical dipoles which when oriented and arranged in a large array could produce an electric field strong enough to drive positive ions over the junction barrier of the postsynaptic membrane. I noted that this hypothesis could provide an explanation for cleft size at synapses, synaptic delay, subthreshold integrations, facilitation with repetition, and the effects of calcium and magnesium. There was another line of thinking related to Wei's hypotheses that I described. Becker (51) had carried out an extensive series of experiments exploring what he considered to be a neural semiconduction control system in various living organisms. On the basis of the data he had gathered, he suggested as a conceptual framework the movement of mobile charge carriers within a solid-state neural system.

I also detailed how Cope (52), using nuclear magnetic resonance spectroscopy, reported that the water in brain tissue is bound in a highly ordered structure that can best be described as crystalline. Also mentioned was the Fritz and Swift (53) study of the high-resolution proton magnetic resonance spectrum of the sciatic nerve of the frog while active and resting.

I also pointed out that new concepts on the nature of neural function relevant to RF radiation effects have also come from Batteau (54) as a result of his study of the mechanisms of hearing. He suggested that sensation in the organism was due to the shifting of the probability of transition of electrons from the excited state to the ground state in organic molecules. He obtained data that he interpreted to indicate a transition energy gap of about 0.35 eV, corresponding to a 3 micron wavelength signal.

I went on to detail a number of other concepts and data that could have been used as a guide for research with RF radiation. I brought out the possibility of what could be called microthermal effects involving localized temperature gradients. I pointed out that some of my calculations indicated that this was a real possibility. Recent research indicates that such effects exist and are significant (55,56).

My conclusions in that paper were that if we break out of the thermoregulatory mind set, use realistic assumptions in our conceptualizations, and recognize that our knowledge of how the nervous system codes, transfers, and stores information is almost nil, a number of possible mechanisms through which RF radiation could affect higher organisms were apparent (2). The question, I said, is not whether there is a possible mechanism, but rather which of numerous possible mechanisms to use as a guide for experimentation. I also noted the seemingly forgotten possibility that more than one mechanism can be involved in RF radiation effects.

EXPERIMENTAL STUDIES

The above paper on possible biological mediators or mechanisms was published in January, 1971 (2). By that time, I had laid a foundation of data on low-intensity RF radiation bioeffects as I had intended to do. My thinking on possible biological mediators had jelled, and, as can be seen in the foregoing, I could spell out a number of these possible mediators as guides for research. Interest was rising in the area and funds were becoming available for other scientists to begin experiments which could provide data that would support a quest for biological mediators. Thus, in 1971 I moved on to such a quest. I anticipated finding multiple mechanisms and the quest was formulated with that expectation in mind. This led to my pursuing multiple interacting lines of biological research with RF radiation.

It appeared to me that the nervous system and its function would be one of the systems most sensitive to RF radiation. Thus, my quest for biological mediators in the 1970's was heavily weighted to experiments involving nervous system function.

One line I pursued was to look at a known electrosensing system in action to develop an understanding of how that system worked. Thus, I undertook experimentation on weakly electric fish. Another line was to identify the locus of the mechanism of the RF hearing phenomenon. Although I had found that one could induce skull vibration with very high power pulses, the data with very low-intensity energy suggested that the hearing effect was occurring in the cochlea. A third line stemmed from my expectation that brain chemistry would be involved in RF radiation effects. After considering data from the pharmacological literature, I developed the hypothesis that the dopamine systems of the brain could be influenced by exposure to this radiation. This led me to do a line of neuropharmacological experiments which, subsequently, led to a broadening of the hypothesis to include the opiate systems of the brain. The fourth line of experiments involved selectively permeable membrane function. I hypothesized that RF radiation exposure would disturb biological membranes, and this was explored in a series of studies involving the blood-brain barrier of the brain and the blood-vitreous barrier of the eye. This also led, in part, to

my experiments with RF radiation and the placental barrier and also to experiments exploring developmental effects.

During this decade, I also carried out experiments that do not fall into the broad categories above. Some I did to clarify an aspect of my theorizing as it evolved, or I did an experiment to explore an idea. An example of the former are the additional experiments I did with the heart. An example of the latter is an experiment I did to explore the possibility of affecting the treatment of leukemia by modifying the blood-brain barrier with RF .radiation to influence the passage of methotrexate. Chang and her associates have pursued this possibility in a somewhat different way (57,58). They have found an interaction between RF radiation exposure and methotrexate effect.

Of the four primary lines of research that I pursued, the first was to determine how a natural electrosensing system worked. There exists a number of weakly electric fish that generate a field and gather information about their environment apparently by analysis of perturbations in their field. My analysis of the literature and the experimental work I did with electric fields, sensors, and objects in various sized bodies of water led to the development of a mathematical model of the fishes' electrosensing system. This allowed me to interpret much of the data that had been previously published on the sensory system of the fish. I suggested a working hypothesis for an electrosensor mechanism. I showed the linkage among the various neural coding schemes that had been suggested for the fish and showed their essential identity (59).

RF HEARING

The earlier RF hearing research led to an extensive series of experiments by others, as well as several more by me. Most of the former were supported by DoD agencies concerned with hazards of RF radiation. The investigators controlling the work, such as Guy and Lin, were not biologists. Consequently, the work was hazards oriented. There was also inappropriate mathematical modeling and some biological experiments that had an unrecognized confounding variable. In papers published in 1979 and 1980 (60,61), I identified the confounding factor and noted the fault in the assumptions underlying their conclusions from the modeling. Besides the research leading to the paper on the confounding variable noted above, I carried out psychophysical experiments exploring modulation effects (62). I also explored the use of the periodicity pitch phenomenon (63,64). The results of these indicated that the locus of the effect is in the cochlea.

During this time and subsequently, RF hearing research was also done in the Soviet Union (65), and in other laboratories in the United States (66-73). Most notable was the experimentation of Wilson and Joines (56), which showed that at low power densities the locus of the mechanism of the hearing effect is in the cochlea. Thus, the efforts by multiple laboratories, using a variety of techniques, showed that the mechanism of the hearing of low-intensity RF radiation occurs in the cochlea. This finding opened up the possibility of new

techniques for studies of ordinary hearing, and offered a new approach to understanding how hearing takes place.

The results of the experiments on the RF hearing mechanisms also clearly indicate that questions can be raised about whether RF radiation affects the labyrinthine system and implies a possible effect on the balance mechanism. I carried out an experiment to assess this possibility. I exposed animals on a rotating rod and determined how quickly they fell off. I found that they fell off more quickly when exposed to the radiation (74,75). But there is a confounding factor which will be noted later.

One other line of study that derived in part from the RF hearing work has significant medical implications. The pattern of clinical reports from the Soviet Union, as well as some observations by me and others in this country, suggest that a small percentage of people may incur what is called closed head injury as a result of exposure to RF radiation. This type of injury has sometimes been referred to as "post-concussive syndrome." Closed head injury may not show up in neurologic examinations such as CAT scans or EEGs because they are not appropriate tests of the functions affected. But such head injury is shown by clear-cut behavioral changes which include reduced attention span, impaired complex information processing, memory disturbance, and personality changes such as increased emotional lability, irritability, anxiety, and depression.

The neural damage and subsequent behavioral dysfunction in such head injuries is considered to be due to a shear-strain type of injury. It has been hypothesized that acceleration results in axonal tearing and neural degeneration in the brain stem as well as stretching and tearing of fibers within the cortex. This interpretation is supported by head injury research which found microscopic lesions within white matter and in particular brain stem structures. Behavioral measures seem to be the most sensitive indicators (76-78).

After publication of my 1968 paper giving further details on the. RF hearing phenomenon, White (personal communication) wrote to me suggesting that the hearing effect was due to conversion of the RF energy into pressure waves via a thermoacoustic conversion mechanism, possibly in the cochlea. White, a physicist, had done the original work on defining the thermoacoustic conversion phenomenon of electromagnetic energy in material a few years earlier (79). It was immediately apparent to me that, if such conversion was taking place in the brain, damage could be caused that could account for the numerous reports of behavioral changes after long-term RF exposure such as reduced attention span, memory disturbance, irritability.

The reports of Olsen and Lin indicated the existence of the requisite pressure waves in the brain (80,81). Spiegel et al. (82) demonstrated mechanical motion in the brain as a consequence of field exposure. These data provide a reason to believe that pressure pulses occur in the brain.

It is ironic that it is such a shear-strain effect in the brain that the engineers concerned with hazards were implicitly assuming when they were trying to explain away the RF hearing effect

as not being an indication of hazard (83,84). They never realized that shear-strain due to thermoacoustic expansion in brain tissue would itself damage the brain (61). I would expect that this effect would be noticeable particularly in those who have had long-term exposure to modulated RF radiation.

SENSORY AND CARDIAC EFFECTS

I also did incidental experiments to extend several earlier lines of research, in particular the sensory effects and cardiac effects lines. The possibility of other sensory effects of the energy was explored using several techniques. One was a shuttle box avoidance experiment using a box I developed for use in RF fields (85,86). One side of the shuttle box was shielded from exposure to the RF radiation. Each animal was placed in the box separately and the box was exposed to the radiation. It was found that the animals could detect and would avoid the pulse-modulated RF energy. The avoidance behavior occurred in response to exposure to power densities less than 1 mW/cm^2. It was found that varying the pulse modulation did not significantly influence this behavior. Unmodulated energy appeared to have little effect; the animals either did not perceive or did not care about exposure to unmodulated energy.

The numerous other behavioral experiments I did as measures of neural function are cited in various places in this chapter. In the late 1970's and early 1980's, behavioral experiments by others were reported. These latter are well described in a recent analytical review by Medici (87), and by her chapter in this volume. She also offers useful guidance for behavioral research with RF radiation. Particularly notable among the experiments she described are those of Thomas and his associates. In their most recent paper (88), they reported that the central nervous system is affected by a combination of a magnetostatic field and a 60-Hz magnetic field, as evidenced by changes in operant behavior.

The heart research was extended with an experiment involving intact frogs (89). Because of the low pulse repetition rate used, the average power used was 3 $\mu W/cm^2$. The heart rate was modified in the group exposed to pulses synchronized with the R wave of the ECG. The group with exposure synchronized with the T wave and the sham exposed group were significantly different from the R wave group. Others have carried the heart research much further.

Lords et al. (90) exposed isolated turtle hearts to RF fields using CW exposure. They found they could induce a bradycardia. They suggested the effect might be due to the stimulation of the parasympathetic and sympathetic nerve remnants in the turtle heart. In a follow-up experiment using an isolated turtle heart with the same exposure arrangement, Tinney et al. (91) found that over a narrow power range there was apparent stimulation of sympathetic and parasympathetic nerve remnants which could increase or decrease the heart rate, respectively. Galvin et al. (92) reported that RF radiation induced alterations in the cardiac cell membrane. Schwartz et al. (93) have shown RF fields with certain modulations will significantly increase calcium efflux from the heart. Other experiments along this line have also been reported (94-100).

BRAIN CHEMISTRY

My third line of research in this decade involved brain chemistry. In the early 1970's, I hypothesized that the dopamine systems of the brain could be influenced by exposure to RF energy (101). If this was the case, then certain behavioral measures of neural function should reflect such an effect. I initially set up two experiments to test this hypothesis. One used the intermittent tail pressure technique with rats, which provided a measure considered to be one of irritability and aggression. The other was a rotating rod experiment which would indicate if there was influence on motor coordination through the nigrostriatal tract or via a labyrinth effect.

In the aggression experiment, animals were placed in a box in pairs and intermittent pressure was applied to their tails. This induced them to emit aggressive actions, behaviors that are clear cut and which can be readily quantified, A clear-cut "docility" effect was seen when the animals were exposed to incident average power densities of 50 $\mu W/cm^2$ during the procedure. The RF radiation exposed group took significantly longer to begin aggressive behavior, the number of episodes and duration of the behavior was significantly less, and it ended significantly sooner than in the control group. This result was consistent with what would be expected with an RF radiation influence on the dopamine systems of the brain (101).

If there is such an effect on the dopamine system, it would also be expected that fine motor coordination would be influenced by exposure to the energy. This was tested, as was a possible labyrinthine effect as noted before, by placing animals on a horizontal rotating rod, The rod speed was slowly increased until the animal fell off. The animal was exposed to pulse-modulated RF radiation. Exposure power levels of less than 1 mW/cm^2, average power density, were effective in disrupting their balance capability (74,75).

In view of the outcome of the foregoing research suggested by the dopamine hypothesis, additional experiments were undertaken. The influence of an electromagnetic field on emotionality was explored using the conditioned emotional response (CER) technique (102,103).

The CER has been used in drug testing as an animal analog of anxiety. The specific prediction was that a CER learned and tested outside the field would be affected in an animal living in a low-frequency field. The animals lived in a low-intensity 60-Hz field and were trained and tested outside of the field. It was found that living in such a field significantly increased emotionality as defined by the test. It was also found, as we had observed in several other experiments, that some animals were particularly sensitive to exposure to such fields. This finding is not particularly remarkable since individual hypersensitivity reports are common in the pharmacological literature. But such idiosyncrasies in sensitivity had not been recognized in the RF radiation literature of the United States. (It had been recognized in the Soviet Union.) The recognition of it is important though, since, as I suggested, it has to be considered in the data analysis of an RF radiation experiment. It can lead to an erroneous conclusion of no effect when in fact an effect is real, what is called in statistics a type II error .

The dopamine hypothesis also suggested that internal timing capability would be disturbed by exposure to RF radiation. To test this, a Sidman avoidance experiment was carried out using exposure to 60-Hz fields. With the Sidman technique, an animal must make sensitive use of timing behavior to minimize work, but, in doing so, work enough to avoid an aversive stimulus. It was found that there were significant effects on timing behavior with animals living in a low-intensity low-frequency field. The exposed animals incurred significantly more aversive stimulation than those sham exposed. After this was established, the exposure conditions for the exposed and sham exposed groups were reversed. There was no change in the pattern of Sidman behavior for the first 24 hours, but after 48 hours the behaviors of the two groups reversed (102).

Direct changes in dopamine were reported about that time by Stith and Erwin (104). They found that tyrosine hydroxylase in the hypothalamus and brain stem is significantly decreased by exposure to low-intensity RF radiation. Dopamine is synthesized from tyrosine and tyrosine hydroxylase acts on tyrosine in a rate-limiting enzyme step.

The dopamine hypothesis also suggested another experiment that would involve an animal analog of a human clinical state. An isolated rat subjected to a steady light tail pressure emits certain behaviors such as chewing, licking, and gnawing that are situationally peculiar. These types of behaviors are referred to as stereotypic behaviors and are considered to be analogs of clinical states in humans involving dopamine system defects. Experimentation was undertaken to determine if RF radiation exposure would influence stereotypic behaviors. It was found that it did (105,106). Average power densities on the order of 8 $\mu W/cm^2$ were sufficient to modify stereotypic behavior. In addition, interactions between pressures, certain odors, and pulse repetition rates influenced the nature of the effect. Certain odors, for example, heightened the RF effect. Further, the responses to RF radiation in the exposed animals were bimodally distributed. We had noted similar effects on distribution in other experiments (107). This again called attention to the importance of individual differences in sensitivities when low-intensity RF radiation is used. The bimodal distribution finding has important implications. RF radiation effects may well have appeared but been overlooked in some experiments, for commonly used statistical tests are not appropriate when data is distributed bimodally. Use of them in such circumstances would mislead the experimenter into believing there was no effect when, in fact, there was an effect of the radiation (a type II error). Thus, several lines of evidence indicated that dopamine and/or dopamine receptors were involved as a mediator in RF energy exposure effects.

By the time the above experiment was being done, the advances in knowledge in pharmacology reported in the literature provided a basis to expand the dopamine hypothesis to involve the opiate systems of the brain. The literature by the late 1970's indicated that there is a complex interaction between the dopamine and opiate systems. It also suggested that the dopamine system may be the final step through which opiate system function is expressed. Thus, I extended the theorizing about RF radiation and the dopamine systems to include certain interactions with the opiate systems (107,108).

It was relatively straightforward for me to predict that RF radiation exposure would disturb these interactions and to set up a simple experiment to test the hypothesis. I set up and carried out a direct test of the predictions using a classic test of opiate system function—tail flick. In this test, the animals' tails are exposed to an aversive stimulus. The measure is the time it takes for them to flick their tails away from the aversive stimulus (106,109,110).

I hypothesized that apomorphine, a dopamine agonist, which at low doses was reported to inhibit presynaptic DA release by stimulating presynaptic receptors, would increase tail-flick latency, an effect similar to a high dose of morphine. Further, it had been found that stimulation of postsynaptic DA receptors with high doses of apomorphine antagonized morphine effects, thereby decreasing latency. I used high and low dose apomorphine groups with and without RF radiation exposure to assess the interactions that could be predicted. The group getting only a low dose of apomorphine had a significantly increased flick latency. The group getting only a high dose of apomorphine had a significantly decreased latency. The comparable groups that were, in addition, exposed to RF radiation showed that such exposure blocked the effects of apomorphine on tail flick latency. It was also found that exposure to RF radiation alone decreases latency. This suggested the possibility of increased presynaptic firing or direct stimulation of postsynaptic receptors. The results supported the dopamine-opiate system hypothesis.

I did additional experiments with apomorphine, as well as with librium, nalaxone, haloperidol, and morphine, with results consistent with the hypothesis. For example, in the morphine experiments with RF radiation, tail flick latency was again used as a measure (110,111). It was found that a high dose of morphine had a significant effect on flick latency but a low dose did not. But when the low dose of morphine was given with exposure to RF radiation, tail-flick latency increased significantly. Thus, RF radiation exposure potentiated morphine analgesia, an effect similar to classic dopamine (DA) inhibitors such as haloperidol. This effect occurred with average incident power densities of 200 $\mu W/cm^2$.

The dopamine-opiate system hypothesis suggested that one way these effects could occur was through an alteration of DA receptor sites by changing protein conformation at the neuronal membrane. Binding of DA would be inhibited and calcium metabolism would be altered. Frey and Wesler's data suggest the former is occurring and the latter is indicated by the results of Blackman et al. (112) and Bawin and Adey (113).

Other investigators pursued the line of study involving brain chemistry. Lai et al. (114) explored the effects of apomorphine, d-amphetamine, and morphine in animals exposed to RF radiation. They found irradiation enhanced apomorphine effects and attenuated amphetamine effects. Morphine effects were also enhanced. Schrot et al. (115) extended previous work with drugs using chlordiazepoxide, chlorpromazine, and diazepam. The y found that the latter two drugs decreased response rate with animals on an operant conditioning schedule, while chlordiazepoxide increased response rate. They found some complex interactions between drugs and field, and suggested that the field parameters may be an important variable in the nature of

the effect obtained with various psychoactive drugs. In a study by Ashani et al. (116), the combined effects of low-intensity RF radiation and anticholinesterase drugs were investigated. They found complex interactions and suggested that use of such drugs would provide significant information on the effects of RF radiation. Nakas et al. (117) and Jamakosmanovic et al. (118) considered the effect of repeated daily exposure to RF radiation on levels of acetylcholinesterase in the brain. They found that chronic exposure to the radiation induced significant depression of the acetylcholinesterase activity in the brain. They also found other effects which led them to suggest that the central nervous system is very sensitive to low-intensity RF radiation. In two other studies, Lai et al. (119,120) report RF radiation potentiated an effect of apomorphine and attenuated an effect of ethanol and also amphetamine. They also found that pulsed, but not continuous, radiation decreased hippocampal choline uptake, a measure of cholinergic nerve activity. This effect was blocked by the opiate antagonist naloxone as would be expected by the dopamine-opiate hypothesis. Miller et al. (121), using 60-Hz magnetic fields, found that exposure to the fields attenuated the behavioral response of mice to morphine.

One interesting implication of the dopamine-opiate hypothesis is that RF radiation could affect the hypothalamic set point for body temperature regulation. As I have pointed out before (107), the mechanism that sets the body's temperature is located in the hypothalamus. Dopamine is believed to play an important role in the adjustment of this mechanism (122). One can, of course, dump enough energy in to a mammal to raise its temperature directly. But it seems likely that at low-intensity exposures an effect of the RF radiation on the hypothalamic set point via the dopamine system could result in a temperature shift. This is an ironic twist in view of the hazards establishment's efforts to press all findings of radiation effects into the "due to thermal effects" mold. It may be the other way around, with some of the "thermal effects" a result of an effect in the brain.

BLOOD BARRIERS

The remaining line of investigation that I pursued in my quest for an understanding of the mediators or mechanisms of RF radiation effects involved the blood barriers of the body, i.e., blood-brain barrier, blood-vitreous-humor barrier, and placental barrier.

The initial experimentation in this line of research was with the blood-brain barrier, which separates the brain and cerebral spinal fluid of the central nervous system from the blood. The locus of the barrier is considered to be at the interface between them, i.e., in the choroid plexus, the blood vessels of the brain and subarachnoid space, and the arachnoid membrane. The barrier consists of cells connected with tight junctions in an essentially continuous layer that regulates intercellular diffusion. Solutes that are lipid soluble readily penetrate the barrier. But lipid insoluble substances or proteins encounter a set of regulatory interfaces between the blood and the nervous system that control their transport.

Several fluorescent dyes bind to serum protein when injected into the bloodstream. These have been used to study the nature of these regulatory interfaces and have been found to be quite

useful. I used one of these, sodium fluorescein, to explore the effects of exposure of the animal to RF radiation. The procedure was to irradiate the animals with RF energy, inject them intravenously with the dye, and then several minutes later, exsanguinate, perfuse, section, and measure the fluorescence of the brain sections under ultraviolet light. It was found that there was penetration of the barrier as indicated by this classic technique in response to exposure to RF radiation. Fluorescence was seen in the diencephalon level of the brain as well as, to some extent, in the mes- and metencephalon. The differences in brain fluorescence between the sham-exposed and the exposed animals was statistically significant.

Oscar and Hawkins (123) extended the work by exposing rats to RF radiation to assess the uptake of several radioactive neutral polar substances in the brain. Barrier permeability increases were observed for mannitol and inulin but not for high molecular weight dextran. The apparent permeability change, which was reversible, was greatest in the medulla, followed, in decreasing order, by the cerebellum and hypothalamus. It was also found that RF radiation of the same average power, but with different pulse characteristics, produced different uptake levels.

Albert (124) exposed Chinese hamsters to RF radiation and injected them with various electron dense tracers. Specimens were then prepared for light and electron microscopic examination. The exposed and sham-exposed groups differed in that exposed animals showed tracer penetration of the barrier in the cerebral and cerebellar cortices, medulla, thalamus, and hypothalamus.

Merritt et al. (125) reported doing a replication of the first two studies and stated, “No transfer of parenterally administered fluorescein across the BBB of rats after 30 minutes of 1.2 GHz radiation at power densities from 2–75 mW/cm^2 was noted. But a statistical analysis of the data presented in their paper by several scientists showed that, in fact, their data supported the opposite conclusion and provided a confirmation of the findings of Frey et al. (126). They may also confirm Oscar and Hawkins, but sufficient data were not provided in their published paper to allow an appropriate statistical analysis.

Preston et al. (127) reported on the permeability of the barrier to mannitol under RF radiation. They reported that they did not confirm Oscar et al.’s work. But they made a type II statistical error in their data analysis. Using binomial tests to correct for this, Frey (126) found that their data revealed significant RF radiation effects that were consistent with Oscar et al.’s results.

Thus, Merritt et al. and Preston et al. did, in fact, find a RF radiation effect in the brain. What appeared at first to be conflicting and controversial data actually are quite consistent and indicate that something involving the blood-brain barrier occurs in the brain subjected to low-intensity RF radiation. Other blood-brain barrier experiments of varying quality have been reported (128-135). In an interesting one, Quock et al. (136) found that RF radiation exposure facilitated a quaternary ammonium derivative antagonism of pilocarpine and oxotremorine. They suggest this may be due to an enhanced passage through the barrier. In another interesting study, Lange et al. (137) found that RF radiation facilitated depletion of brain ca techolamines by drugs

otherwise restricted to peripheral effects. But the DoD terminated funding for such research, so the nature and extent of such effects have not been determined (1).

But before the funding was terminated, I extended the work to other blood barriers. The eye was the first, since it is derived from the neuroectoderm, as is the brain. It has blood barriers much like the blood-brain barrier, i.e., the blood–aqueous barrier and the blood–vitreous barrier. The blood–vitreous barrier is important inasmuch as it regulates the composition of the vitreous humor and is involved in controlling the ionic and metabolic environment of the retina.

In a blood–vitreous barrier experiment, the animals were exposed to average incident power densities of 75 $\mu W/cm^2$ for 25 minutes then injected with sodium fluorescein. There were several variants of this basic procedure used. A small but significant increase in vitreous humor fluorescence occurred with the animals exposed to RF energy (138,139).

The analysis of Neelakantaswamy and Ramakrishnan (140,141) could be extended from the lens to provide an explanation for this finding. Their work indicated that RF radiation could induce bending moments and stresses in the tissue that could upset physiochemical processes in the eye. This might also provide an explanation for the finding that RF radiation apparently causes cataracts in humans (142).

The writer's work on barriers was extended to placental barriers with exposure of rats *in utero* to 60-Hz fields. But it was not possible to complete this line of work and the question of permeability changes in the placental barrier was unresolved until recently. Vodicnik et al. (143) exposed pregnant mice to RF radiation in a single dose. They found a significant change in fetal drug uptake as well as placental uptake. The effect for mannitol and glucose occurred only if the RF exposure occurred prior to the administration of the drug. Other experiments involving prenatal exposure to RF radiation have now shown effects on various measures in the newborn (144-146).

EFFECTS ON THE BRAIN

There are a variety of other experiments that indicate an influence of low-intensity RF radiation on the brain. Sanders and his associates have studied the effects of RF radiation on the energy metabolism of the brain. They found that exposure to the energy modified the ATP levels in the brain. They also found that CP-kinase, a divalent metallo-enzyme, was susceptible to interaction, and concluded that there was a resonant energy inhibition of CP-kinase (147,148). They have also explored the effect of a field on nicotinamide adenine dinucleotide (NADH), adenosine triphosphate (ATP), and creatine phosphate (CP) in the brain. They found changes in NADH levels and ATP and CP concentrations. They believed the results suggested that RF radiation inhibited electron transport chain function in brain mitochondria and caused a decreased energy level in the brain (149). Wilson et al. (150), in a series of studies, have shown changes in the energy metabolism of the brain using [^{14}C]-2-deoxy-D-glucose.

McKee et al. (151) found morphological changes in the central nervous system, particularly in the hippocampal, hypothalamic, and cortical regions of the brain. Albert et al. (152) also reported morphological change in the brain as a consequence of exposure to RF radiation.

In other work bearing on the central nervous system, Sheridan et al. (153) reported lipid chain disorder induced by low-intensity RF radiation. Stevens (154) concluded that the rate at which brain protein makes the transition from one conformational state to another depends on the particular relationship between the membrane potential and the equivalent dipole moment change of the protein.

Barnes and Hu (24) offered a useful model for RF radiation effects on biological membranes. They indicated that shifts in ion concentrations across the membrane and the orientation of the long-chain molecules are possible. Others, such as Schwartz (155), Lee (26), and Frohlich (156) offered mechanisms that might be implicated in RF effects in the brain. Liboff (27) and McLeod and Liboff (157) offered a particularly noteworthy conceptualization involving cyclotron resonance as an explanation of calcium efflux effects of RF radiation. A prediction from it involving lithium ions was recently supported by the results of a behavioral experiment by Thomas et al. (88).

Wachtel (158) and Wachtel et al. (159) reported experiments which indicate minimum RF threshold energy pulse widths for evoking fast neuronal effects as well as RF induced hypokinesis. Bearing on this is the report of Brown and Larsen (160). They used change in resting birefringence of crab nerves, which coincides with propagation of the action potential, as a measure of nerve response to RF radiation. They found that pulsed radiation influenced birefringence.

In another study, McRee, working with Wachtel, reported RF radiation effects on nerve vitality. They indicated that long-term regulatory processes were involved (161,162). Wachtel and his associates also offered a mathematical model for the selection of RF pulse parameters. They have done other modeling and suggest an influence on electrogenic pumps in nerves (41-43).

Another line of investigation with the central nervous system which has been fruitful has been concerned with calcium efflux. This line stems from the behavioral experiments with nonionizing radiation that Medici began in 1966 while she was at UCLA (163). She examined the effect of low-frequency fields using inter-response time schedules of reinforcement with monkeys. Her studies showed that the animals' behavior was significantly modified by the fields. She also showed that the animals were particularly sensitive to frequencies that were in the EEG range of the animals, that is 7 Hz, as contrasted with 45 Hz and 75 Hz. A change in the spectrum of the EEG was found when the animals were exposed to RF radiation.

Because of these results, Kaczmarek, a neurochemist at UCLA, was asked to consider other ways to measure brain response to the fields. He initiated experiments in which calcium efflux

was measured following exposure to RF fields (164). A series of experiments followed from this that have provided useful information about the effects of RF radiation on the brain.

At first, Bawin and her associates (113,165) carried forward the work with calcium efflux. They found that isolated brain tissue responds to exposure to an RF field of a narrow frequency band and a narrow amplitude window. Skeletal muscles did not respond to the radiation in a similar fashion. Lin and Adey (166) extended the work to synaptosomes and concluded that their data indicated that whole cells or organized tissue are not required for the effect to occur.

In a series of studies Blackman and his associates verified and extended the findings of Bawin and her associates (112,167-176). They also found frequency windows and power density windows in which calcium efflux was enhanced by exposure to modulated RF radiation. They also found that they could shift carrier frequencies and get effects. In another experiment they found that the enhanced calcium efflux phenomenon was more dependent on the electric field intensity in the brain than on the power density of the incident radiation. They hypothesized that brain tissue is electrically nonlinear at specific field densities, and that this nonlinearity demodulates the carrier and releases a particular modulated signal within the tissue. They suggested that the signal is selectively coupled to the calcium ions by some mechanism, perhaps a dipolar type (Maxwell–Wagner) relaxation which enhances the efflux of calcium ions. Tenforde (177) has suggested that the field interaction involving calcium may involve a resonance or cooperative energy transfer mechanism.

IMMUNE SYSTEM

There has been scattered work concerning RF radiation and the immune system. Some of it has used radiation that I would not expect to influence the immune system; other work has used more appropriate, though not optimal, frequencies and has revealed effects that are of consequence. Schlagel and Wiktor-Jedrzejczak (178) and Wiktor-Jedrzejczak et al. (179) studied complement receptor positive cells and exposure to RF radiation. They found an increase in complementary positive spleen cells in mice. They concluded that the response was not due to alterations of lymphocyte recirculation patterns, but rather was mediated by a soluble, humoral factor produced by cells within the spleen which induced an increase in complement receptor positive B cells. In a later study, Schlagel et al. (180) concluded that complement receptor positive cell response was not regulated by the T-cell population. They suggested that the data indicate that the RF radiation induced change in the population of cells with specific cell surface receptors. Further, they suggested that susceptibility to these changes was under genetic control; that endotoxin, corticosteroids, and regulatory T cells do not play a significant role in the mechanism regulating the increases that they found. Liddle et al. (181) explored the effect of RF radiation on the circulating antibody response of mice. They immunized the mice and then exposed them to the pulse-modulated RF radiation. The $\log_2$ hemagglutination titers among the RF-exposed mice were significantly higher than among those sham irradiated. They concluded that the increase in circulatory antibody response provided some protection to the mice. Schlagel

and Yaffe (182) and Schlagel and Ahmed (183) report that the transitory increase in complement receptor bearing lymphocytes induced by a single exposure to RF radiation is under genetic control. In the report of their study with several strains of mice, they concluded that the essential regulatory gene was to the right of the PgM-1 locus and to the left of the rd locus on chromosome 5. Rama Rao et al. (184) reported that exposure of hamsters to RF energy resulted in viricidal activation of peritoneal macrophages and extended survival of hamsters injected with a lethal dose of vesicular stomatitis virus. They also reported highly significant increases in plaque production, measured using the hemolytic plaque assay, when animals were injected with sheep red blood cells.

In sum, the immune system data suggests a responsiveness to RF radiation. But the investigators have used radiation of marginal frequency and modulation for inducing such effects. The optimal RF parameters for exploring such effects have not been used.

DNA

There are some suggestions that DNA may be influenced by RF radiation. Swicord and Davis (185), using an optical heterodyne technique, found that the DNA of *E. coli* in aqueous solution absorbed RF radiation. Edwards et al. (186) carried out similar studies using dielectrometric methods. They report significantly increased absorption of RF radiation by a DNA solution relative to the solvent. They also stated that the data suggested a chain length dependence of the absorption. Liboff and Homer (187) studied the uptake of ^{3}H-thymidine in cell culture as a function of sinusoidal magnetic field intensity. Their data led them to infer that DNA synthesis in the exposed cells was significantly greater than in unexposed cells. The effect occurred with a wide range of modulation frequencies and was maximum during the mid-S phase of the cell cycle.

Kohli and VanZandt (188) calculated what the absorption of RF radiation would be by a DNA molecule. They presented curves of expected absorption vs frequency for various damping parameters and reflection conditions. In a somewhat similar approach, Van Zandt et al. (189) calculated absorption of DNA double helix in aqueous solution and compared the theoretical results with experimental data. They report that the calculated absorption values agreed strikingly with experimental values for the relative absorption of water and DNA solution. Edwards et al. (186) concluded that their studies, noted above, partially supported the theoretical work of Kohli, Prohofsky, and Van Zandt.

CONCLUSIONS

What has been done in most of the biological research with RF radiation in the United States has been determined by the thermoregulatory mind set of those involved in the research. That research has not been considered to any extent in this review since it contributes little to our knowledge and understanding of the biological effects of low-intensity electromagnetic fields.

As I stated in 1971 (2), the question is not whether there is a mediator or mechanism for biological effects of low intensity RF radiation. Rather, the question is how many are there and how are they related. There are some answers to these questions, but a discussion of them is beyond the scope of this chapter.

It is clear that there are a diversity of biological effects of RF radiation, effects such as those on neuropeptides. Understanding the nature of these various effects can lead to significant advances in biology. Neuropeptides, for example, have been shown to have behavioral and neuroendocrine effects. Data indicating that they exert effects on immune system function is accumulating. These ligands and their receptors are abundantly distributed in areas of the brain that mediate emotion and higher cognitive functions. Thus, as Ruff et al. (190), writing about other matters, put it, "…it seems plausible that the same neurohumoral mediators of various mood states in brain may also communicate to monocytes and other cells involved in healing and homeostatic processes. Short signal peptides (neuropeptides) and their surface receptors define a group of cells whose function may be to integrate information from the central nervous, immune, and endocrine systems through a psychoimmunoendocrine network, thereby altering the behavior of the whole organism." Angeletti and Hickey (191) also see such linkages. And it is in this direction that the low-intensity RF radiation bioeffects data is taking us.

As another example, consider memory and RF radiation. Recent findings in pharmacology have led to the hypothesis (192) that one mechanism of memory involves "Brief bursts of high frequency activity (that) cause a transient elevation of calcium in spines that activates a membrane-associated calpain. This enzyme then breaks up a localized portion of the fodrin network, producing structural and chemical changes in the region of the postsynaptic membrane. As a result, previously occluded glutamate receptors are exposed, thereby increasing the size of the postsynaptic response to the released transmitter. More prolonged or repetitive bursts of activity can be expected to produce a larger calcium disturbance and more widespread activation of the calcium-dependent proteinase, events that we propose will produce alterations in the ultrastructure of the dendritic spine." The implications of RF radiation exposure with such a memory mechanism are significant.

Appropriate research with low-intensity RF radiation, and I include magnetic fields, will likely lead to substantial advances in knowledge of biological processes. But that research will not be done in the United States in the foreseeable future. The more interesting and more significant research with electromagnetic fields will be and is now being done in other countries. An analytical review of that work, though, is beyond the scope of this chapter.

As I noted earlier, the significant research, that which does not use high intensities and is not thermoregulatory oriented, began to be tapered off about 1980. Though such research received only a very small fraction of the huge amount that has been spent (several hundred millions of dollars) on RF bioeffects research since 1970, it has been largely squeezed out for reasons unrelated to science. These reasons can be found in a recent book by a historian of science who has made a study of this field of research (1).

But this will only hinder and delay science, for the significant research with electromagnetic fields will continue to move forward in other countries. And this will contribute to the broad revolution in biology that is now taking place.

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